CURRENT STUDIES IN HEALTH AND LIFE SCIENCES 2022

EDITOR
Prof. Dr. Mehmet ÖZASLAN

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PREFACE

Current Studies in Health and Life Sciences 2022 is published annually from the selected chapters invited by the editors. This edition includes 2 sections and 12 chapters from the field of Health and Life Sciences including Nanomedicine, Nutrition, Molecular Genetics & Tumor Biology.

All submissions are reviewed by at least two international reviewers. The purpose of the book is to provide the readers with the opportunity of a scholarly refereed publication in the field of health sciences and life sciences. **Current Studies in Health and Life Sciences 2022** is published by ISRES Publishing.

This book is intended for the fundamental aspects of the medical sciences such as Epidemiology, Anatomy, Physiology, Pharmacy, Dentistry, Nutrition, Clinical Medicine, and even Alternative Medicine subjects or new idea for life sciences.

I wish the book will present curiosity about the LIFE and RESEARCHS in Life sciences. I wish the book will be useful for new scientists, science readers and anyone who intended to learn about the mystery of the science.

December 2022

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TABLE OF CONTENTS

SECTION 1: MEDICAL SCIENCES

SECTION 2: LIFE SCIENCES

SECTION 1
MEDICAL SCIENCES

ROLE OF NANOTECHNOLOGY IN CANCER

Muhammad SAFDAR

Mehmet ÖZASLAN

Yasmeen JUNEJO

1. Background of Nanotechnology

Nanotechnology is a technology that deals with dimensions and tolerances of less than 100 nanometres, especially the manipulation of individual atoms and molecules. The word Nano came from the Latin word “dwarf” which means small. Basically, nanoparticles are used in drug delivery with the size of 100-200nm (Poon, Kingston, Ouyang, Ngo, & Chan, 2020). It is also important to know that the nanoparticle behaves as a chemical as well as the physical agent that effects on the target tissue or organs of the body (Zolnik & Sadrieh, 2009).

2. Nanoparticles

Nanoparticles are belonged to nanoscience that deals with the chemistry, biology, medicine, engineering, and chemistry etc. So, it is the swift advancing discipline and continuously attracting interest from the researchers across the world. Furthermore, they are being used in various industries such as environmental remediation, textile, catalysis, cosmetics, and pharmaceuticals (Emerich & Thanos, 2003).

3. Synthesis Approaches of Nanoparticles

Nanofabrication employs both top-down and bottom-up methodologies **(Figure 1).** The bottom-up strategy is preferable to the top-down strategy because it has a higher likelihood of developing nanostructures with fewer flaws, a more homogeneous chemical composition, and better short- and long-range ordering. According to a bottom-up synthesis process, crystal planes are formed by stacking atoms on top of one another, and these crystal planes are then stacked on top of one another to form the nanostructures on the substrate. Thus, the building blocks are added to the substrate to create the nanostructures in a bottom-up fashion, which can be thought of as a synthesis method (Ariga, Hill, & Ji, 2007). According to a top-down synthesis process, crystal planes that are already existent on the substrate are removed in order to create the nanostructures. Thus, a top-down technique can be thought of as a method where the components of the nanostructure are taken out of the substrate (Biswas et al., 2012).

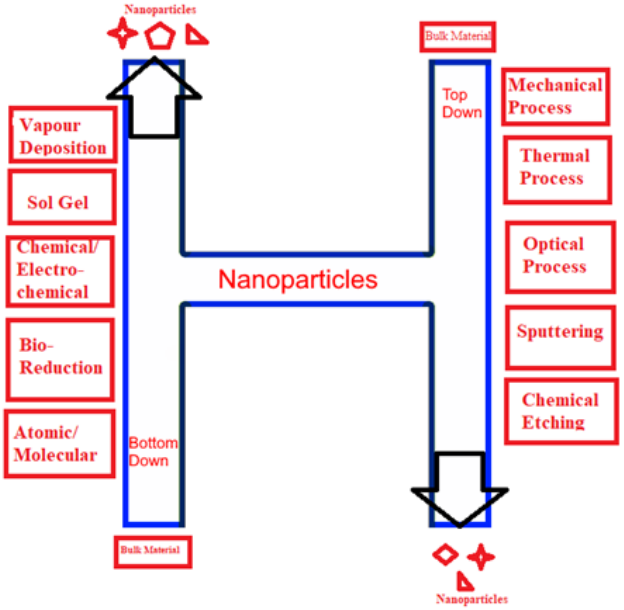

Figure 1. Top-down and bottom-up methods for nanofabrication (Bayda, Adeel, Tuccinardi, Cordani, & Rizzolio, 2019)

4. Types of Nanoparticles

There are many types of nanoparticles (Sircar, Rayavarapu, Bist, Yadav, & Singh, 2021) that have role to treat different cancers via various mechanisms. The classification of nanoparticles has been discussed in the **Figure 2** (Sircar et al., 2021).

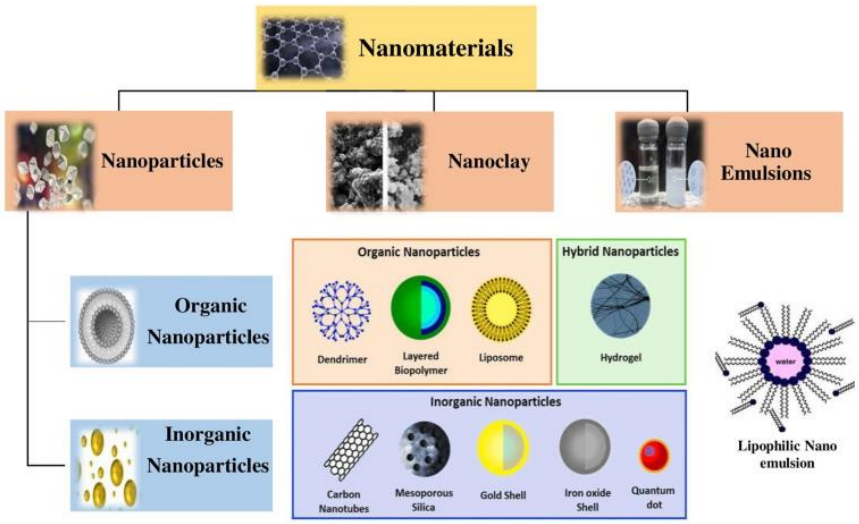

Figure 2. Classification of various nanoparticles (Mageswari, Srinivasan, Subramanian, Ramesh, & Gothandam, 2016; Sircar et al., 2021)

4.1. Carbon Nanotubes

Carbon nanotubes are the third allotropic crystalline form of the carbon sheet. These crystals have electrical properties. The diameter typically varies in the range 0.4-40 nm, but the length can be from 0.14 nm to 55.5 cm. They enhance the solubility and increase the penetration to

the nucleus as the carrier for the gene and peptide delivery. They have been widely used in the cancer diagnosis and therapeutics due to its physiochemical properties (Ji et al., 2010).

4.2. Nanocrystals Quantum Dots

Nanocrystals Quantum dots, a semiconducting material have been synthesized by II-VI and III-V column. They occupy the small space that is closely related to atoms due to their small size (2-9.5 nm). They have also been used in the (Tang, Huang, He, Ma, & Wang, 2020).

4.3. Solid Lipid Nanoparticles

Solid lipid nanoparticles vary in size, made up of spherical solid and lipid particles; dispersed in the aqueous solution. These nanoparticles have been used in a wide range of diagnostic and therapeutic implications. Tumor targeting has been achieved with the combination of solid nanoparticles with other drugs such as methotrexate, camptothecin, and tamoxifen (Hashem, Nasr, Khairy, & technology, 2014).

4.4. Polymeric Nanoparticles

These nanoparticles are made up of solid particles, which can be present as synthetic or semi-synthetic polymers. They are 10-1000 nm in size. They have been used in the food industry as well as in the treatment of cancer (Begines et al., 2020).

4.5. Functional Nanocarriers

Functional nanocarriers are made up of protein, enzymes, and peptides. These nanocarriers are the backbone of medical fields as it has a significant role in drug delivery system. These nanocarriers could be delivered the drug to the specific point thus enhancing its specificity and efficiency (Mejía, Sánchez, Vásquez, & Orozco, 2021). Therapeutic agents or drugs are loaded into the matrix (linked to the core surface) of functional nanocarriers either during or after synthesis of such nanocarriers which increases the efficiency of drug delivery to the targeted organs (Zhang, Jin, & Stenzel, 2021).

4.6. Magnetic Nanoparticles

Magnetic nanoparticles have a small size, large surface area and strong magnetic response towards therapeutic agents (Li, Li, Wang, & Liao, 2021). These nanoparticles have been used in the oncology field as the drug carrier by binding with other antibodies, chemotherapeutic medicines and drugs (Khizar et al., 2021). These nanoparticles have also been used in the photothermal therapy (PTT) (Wang & Hou, 2021) and photodynamic therapy (PDT) (M.-H. Lee et al., 2021).

4.7. Silver Nanoparticles

Silver nanoparticles are widely used in the paints, clothing and medical devices due to their specific antimicrobial activities (Safdar et al., 2019). These nanoparticles have also been used in DNA sequencing and surface-enhanced Raman scattering (Vo-Dinh, Yan, Wabuyele, Brillouin, & Scattering, 2005).

4.8. Gold Nanoparticles

Gold has 79 atomic number and its symbol is Au. The synthesized gold nanoparticles (AuNPs)

are present from vibrant red to pale blue in color due to different size and resonance of light. They are divided into various types on the basis of their size and shape. They range in size from 0.02 nm to 100 nm that have a high surface to volume ratio. These nanoparticles have been designed to treat many harmful diseases such as cancer. The conventional therapies such as chemotherapy not only destroy the cancer cells but also affects the other cells or tissues of the body such as liver, kidney, and spleen (Arshad et al., 2019). Conversely, these nanoparticles may only kill the cancer cells and do not have any significant adverse effect on other tissues of the body (Safdar, Ozaslan, Junejo, Channa, & Sciences, 2021).

For instance, the newly developed AuNPs injected into the patient and after injection, these nanoparticles selectively infiltrated cancerous cells as they are very small in size so that they could easily enter inside the cell where the cancer transcripts are present. When the patient with AuNPs was treated with the short laser pulses, nanoparticles heated up and evaporated the water inside the cancer cell which created very small water bubbles inside the cancer cells. These small bubbles expanded rapidly and burst and ripped cancer cell apart. Because the gold did not react with the oxygen and it moved via the bloodstream and the blood enter into the kidney where it filtered and, in the heart, where it carried out oxygen and sent it to the major organs such as liver and muscles (Arshad et al., 2019).

These AuNPs have widely been used in the medicine and industries, but the safety of the NPs exposure remains unclear. They are used in the laboratory for the purpose of the tracer in the process of DNA fingerprinting for the detection of the DNA sequence in the sample. In a study, it was evaluated that the liver, brain, heart and kidney and other tissues. They were examined for the effects and unclear mechanism of AuNPs using mice models (Arshad et al., 2019). Their results showed that the NPs distributed via blood and accumulated in the major organs such as heart, kidney, and other tissues. Additionally, it depicted that the excess dose of the NPs was damaged the functions of kidney and liver. After further analysis, they showed the irregular function of mitochondria that led to necrosis and apoptosis of the hepatocytes due to production of the reactive oxygen species and the disorder of the expression of the genes (p53, caspases 2, 3, 8, 9,) in the various organs of mice such as liver and kidney (Arshad et al., 2019). The scientists believe that the size of the AuNPs play important role in the toxicity of the NPs. The large size of the nanoparticles accumulates in the membrane and do not cross the membrane and so they showed hepatotoxicity. Actually, they have particular physicochemical properties including the surface Plasmon resonance and could form the bond with the thiol groups allowing surface modification and use in the many other applications especially biomedical applications (Arshad et al., 2019; Safdar et al., 2021; M. SAFDAR & M. J. Z. B. S. ÖZASLAN).

In a study, the AuNPs demonstrated a successful treatment of various deadly disease (Arshad et al., 2019; Safdar et al., 2021; M. SAFDAR & M. J. Z. B. S. ÖZASLAN) and showed the ability to combine with the other proteins and peptides. Actually, these nanoparticles attached with the specific ligands that interact with other compounds to treat such diseases (McNeil, 2005).

In addition, the AuNPs play a vital role to stop the false DNA replication and these particles intercalate in the groove of DNA and induced cell death in the cancer cell. They also produce the change in the membrane of the cell and cause the cell death or the apoptosis. It is classified

into two pathways; extrinsic and intrinsic and, both are caspase-dependent. In this process, three signaling cascades are reported and these signaling pathways activate the caspases. They trigger the extrinsic and intrinsic pathways so the oxidative stress paradox of the nanoparticle induces cell death. Due to high potency of the AuNPs, they induce lysosomal membrane destabilization and destroy the cancer cells. Another way of killing cancer cells is autophagy. In this process they produce oxidative stress that is caused by the accumulation of the damaged proteins and mitochondrial stress (Safdar et al., 2021).

5. Functional AuNPs

Surface properties of the AuNPs play a vital to identify their bonding with the biological system and these bonding indicate the toxicity of the AuNPs (Carnovale, Bryant, Shukla, & Bansal, 2019). Some scientists investigated that the toxic effect of the AuNPs associated with the anionic and cationic side chain in the kidney of monkey. They evaluated the properties of cationic and anionic nanoparticles and found that they are equally toxic (Mironava, Hadjiargyrou, Simon, Jurukovski, & Rafailovich, 2010). Another parameter is the surface hydrophobicity. It is examined by Chompoosor and their colleagues. They investigated the toxicity of the gold nanoparticle with the hydrophobicity of the surface ligands that induced higher cytotoxicity in the cells (Srijampa et al., 2020).

6. Biomedical Applications of the AuNPs

Due to the biological modification and optical properties, AuNPs are being used for the biomedical applications. The SPR effect is sensitive to the dielectric environment so any change in the environment (aggregation and refracting index of the medium) leads the shift of SPR band and such property is used for the huge range of the biomedical applications (K.-S. Lee & El-Sayed, 2006).

7. Cancer

It is a group of diseases that are characterized by the invasive abnormal growth of the cell. The origin of the cancer word was described by the Greek physician Hippocrates and he described a tumor as a karkinos and karkinona. Galen described that a tumor was similar to the legs of a crab and that was the reason the name of the disease karkinos (cancer) which meant crab in Greek (Iavazzo, Trompoukis, Siempos, & Falagas, 2009).

In 2008 about 12.7 million cancer cases were diagnosed with the deaths of 7.6 million globally. In the UK 325,000 people were found with cancer in 2010. Many women feel that stress and anxiety caused them to be diagnosed with breast cancer. Because there has been no clear proof of a link between stress and a higher risk of breast cancer, researchers in the United Kingdom conducted a large prospective study on the issue and they are trying to find the exact link of the cause.

8. Cancer and Nanotechnology

Cancer and nanotechnology are one of the newest fields on which researchers are keeping work on the treatment of cancer that involve primarily its detection, diagnosis, and treatment of cancer. This technology is intersected with the chemistry, biology medicine and the engineering (Roco, 2003). In cancer, nanotechnology-based fluorescence is used to detect the tumor cells.

The quantum dots named semiconductors are also developed that regulate the limitations of organic dyes and also improve optical qualities which were important for the applications of biological methods and decrease the limitations of the organic dyes.

9. Nanomedicine

Recently, some nanomedicine products are available in the market which is used to optimize the nano-sized devices that have been used to deliver drugs. This industry is flourishing from the past few decades. These nano size devices having a high demand in the clinical trials (Safdar et al., 2021). These nano-resonance imaging and tracking of the cell are exploited by the magnetic nanoparticles (Khizar et al., 2021). It showed metastasis in the tumor cells. Therefore, the fluorescence probes in the biomolecular and cellular imaging are the significant use of the nanomaterials for the imaging applications regarding the labeling of cells.

10. Role of Mitochondria and Nanomedicine

The role of the mitochondria is a vital role in the cell life. It controls cellular parameters such as the modulation of the redox status, maintenance of the calcium homeostasis and energy production. The effects of nanoparticles may improve the dysfunctional of mitochondria that cause many chronic diseases such as multifactorial cancer. It may be a great opportunity in the field of biomedicine in the next few years.

11. Mitochondria Role and Cell Death

The pro-apoptotic factors such as cytochrome c and caspases are located in the mitochondrial intermembrane space. In the apoptotic stimuli, pores are formed in the outer membrane of the mitochondrial membrane and it gets permeabilization in the outer membrane of the mitochondria. This event is known as the “point of no return” cell death. It releases particular proteins from the cytosol. These proteins such as cytochrome c and second mitochondria-derived activators of the caspase inhibitor of the apoptotic–binding protein starts the cell death through the activation of the caspases.

Caspases play a vital role in the apoptotic responses to cell death. There are 11 human caspases that are identified till now and only 7 caspases are responsible for the apoptotic process. There are four caspases (2, 8, 9, 10) that are initiators caspases while others (caspase 3, 8, 7) are effectors.

In the normal cells (non-tumor), caspases are zymogens or catalytically inactive. For the activation of the caspases, the proteolytic activity is important. In the apoptosis, stimuli activates the auto-activated initiator caspases which further activates the effector caspases through the breakage or the cleavage at the aspartate residues between the large (p20) and small (p10) subunits and these two subunits are attached by forming the caspase monomers (Riedl & Shi, 2004).

For the activation of caspase, multi-component complex is required. A particular protein such as cytochrome c releases into the cytosol and forms this complex called apoptosome with the dATP, APAF1, and initiator caspase 9 that activates caspase 9 (Riedl & Shi, 2004). After the activation of the initiator caspases, the effector caspases proteolytically cleaved and following factors has developed such as blabbing of the membrane, phosphatidylserine, and condensation

of chromatin happens (Riedl & Shi, 2004).

12. Anti-Apoptotic Family

Anti-apoptotic family include Bcl-2, Bcl-w, Bcl-x that are responsible for the inhibition of the multi-component complex (MOMP) and release the cytochrome c for apoptosis and cell death (Suk, 2005).

13. Pro-Apoptotic Family

Pro-apoptotic family include Bax and Bax that are responsible for the initiating of the mitochondrial apoptotic pathway. These proteins are found in the cytosol (Suk, 2005).

Apoptotic molecules such as Smac/DIABLO, apoptosis-inducing factors (AIF) and endonuclease G (EndoG) are released from the intermembrane of the mitochondria and cause the cell death through the various ways. The release of the cytochrome c activates the caspase cascade and as result apoptosis occurs. Htra2/Omi and Smac/DIABLO stop the inhibitors of the apoptosis and EndoG and AIF enters into the nucleus and damages the nuclear DNA (Suk, 2005).

14. Advantages of Nanoparticles

Nanoparticles have various advantages such as followings

(a) They can only bind to the specific ligand and target specific cells.
(b) To improve the stability and therapeutic index.
(c) To minimize the toxic effects.
(d) They can be administered by the nasal, oral and ocular routes.
(e) They have active and passive drug targeting pathways.
(f) Their pathways can be done by the manipulating after changing their particle size and the surface characteristics.

15. Disadvantages of the Nanoparticles

Despite of many advantages, these nanoparticles have few drawbacks such as followings.

(a) Limited drug loading
(b) Small size
(c) Large surface area led to the aggregation of the particle

In addition, drawing conclusions from tests on healthy animal models may be unsuitable as some of the effects of nanoparticles may only be a risk for susceptible organisms and predisposed individuals, but not to healthy people. For instance, age, respiratory tract problems and other pollutants can modify the pulmonary inflammation and oxidative stress induced by nanoparticles.

16. Green and Non-Toxic Nanoparticles

Green synthesis of nanoparticles involves the use of non-toxic chemicals for the bio-reduction of metal ions into their elemental form in the size range 1-100 nm. They are required to avoid the production of unwanted or harmful by-products through the build-up of reliable, sustainable, and eco-friendly synthesis procedures. The use of ideal solvent systems and natural resources

(such as organic systems) is essential to achieve this goal (Arshad et al., 2019; Hashem et al., 2014; Safdar et al., 2021; M. SAFDAR & M. J. Z. B. S. ÖZASLAN; Safdar et al., 2019). The pathways and mechanisms of AuNPs has explained in **Figure 3** to inhibit breast cancer cells via green gold nanoparticles.

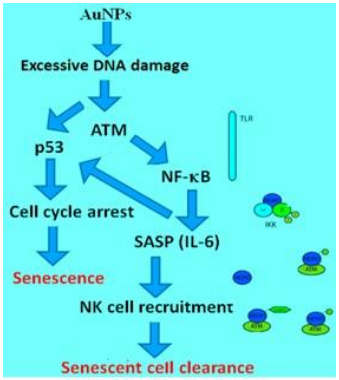

Figure 3. Pathways and mechanisms to inhibit breast cancer cells via AuNPs (M. Safdar & M. ÖZASLAN).

17. Limitations of Nanotechnology

Nanotechnology has a lot of potential to make new products and processes in the various fields, but there are a lot of problems. The main challenge is to make edible delivery systems in food and medicine that are cheap to make and that are safe for people to their health. It is very important to keep people safe by making green nanoparticles from packaging materials, it means they don't get into products. The nanomaterials that are added either directly or indirectly are sometimes left alone because they moved from other places. There is still a lot we don't know about how to analyse materials at the nanoscale, and the materials behave in completely different ways. The more we know about nanoscale functions and toxicities of nanomaterials, the more useful and safer they will be in the real world and in safety rules. The effects of nanoparticles, the risk they pose, and the toxicity issues and environmental concerns that come with them must be looked at. Nanoparticles have been reported to be able to get through the body's natural defences and into cells and organs. Synthesis of nanoparticles using different chemical methods can also have negative effects and produce harmful, non-ecofriendly byproducts that cause a lot of pollution in the environment. Because nano-based marketable products are becoming more popular and people want to eat them, they need to be processed, packaged, and eaten by humans in a way that takes into account safety, regulatory policy, biosafety, and public concerns. In addition, nanoparticle interactions with living things need to be studied in vitro and in vivo before they can be used in commercial products and for the production of antibacterial nanoparticles that are safe for the environment.

18. Future Prospective, and Recommendations of Nanotechnology

Nanotechnology helps with the detection of toxins, pathogens, and pesticides, as well as tracking–tracing–monitoring that can help keep body safe. Nanotechnology is not hampered by things like the lack of skilled workers, the high cost of analysis, or the need to buy high-tech equipment. However, some nanosystems are still in the early stages of development or are being

worked on to become powerful nanocomponents. Research can be done in the following areas for a wide range of applications. Safety and challenges can be taken into account at the same time.

Smart packaging is a new idea that can make antigen-specific biomarkers, and putting together nanoparticles to make nanocomposite polymer films that can slow the processes of breakdown of products, but extensive research is needed to fulfill this area.

Nanocomposites are biodegradable molecule, therefore, in the near future, they could be used to make food packaging material. In the meanwhile, Nanosilica could be used for commercial purposes in medical kits as it has better barrier properties.

Antigen-specific biomarkers can be used to detect pathogens, such as bacteria, viruses, and mycotoxins, quickly and accurately.

Use of nano-sensors in film packaging to detect gases that are released when our medicine or products are spoiled. This would benefit for producers, retailers, as well as consumers.

Nanomaterial based sensors can be used to cut the mechanisms of pathogens to overcome the drug resistance in various diseases.

Carbon nanotubes are also being used to make the sensors into packaging materials that are being used to detect microorganisms, toxic substances, and food spoilage but, extensive research is still needed.

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BEHAVIOR GENETICS FROM AN UPDATED PERSPECTIVE

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1. Introduction

The study of how genetic variation influences psychological phenotypes (traits), such as personality, mental disease, and social views, is known as behavior genetics. Turkheimer (2000) recognized three strong empirical regularities that by that time had arisen from the literature on behavior genetics in a major piece that was published in this magazine. These patterns became known as the "Three Laws of Behavior Genetics" by him. As follows:

1- Every aspect of human conduct is inherited. [That is, to some extent, genetic diversity has an impact on them.]
2- The impact of growing up in the same family is less significant than the impact of genes.
3- The impacts of genes or families cannot explain a sizable percentage of the diversity in complex human behavioral traits (Turkheimer, et. Al. 2014).

The study of the connection between genetic variation and psychological qualities is known as behavior genetics. Based on empirical regularities noticed in studies of twins and other kinships, Turkheimer (2000) suggested "Three Laws of Behavior Genetics." We suggest a fourth law of behavior genetics based on molecular research that directly evaluated DNA variation: Each genetic variant that contributes to a typical human behavioral feature accounts for a very small portion of the behavioral variability. This law explains a number of recurring patterns in the outcomes of gene discovery studies, including the inability of candidate gene studies to robustly replicate, the requirement for genome-wide association studies (and the reason why such studies have a much stronger replication record), and the critical significance of extremely large sample sizes (Chabris, et.al. 2015).

2. Behavioral genetics examples

Generalized anxiety disorder (GAD) has a hereditary component that makes up about 30% of the root cause and a 70% lived experience component. Researchers have also discovered that some people with genetic GAD features may never experience anxiety because of the caliber of their daily interactions with their surroundings. When identical twins are born separated, one twin may experience the symptoms of GAD while the other does not. This difference may be caused by differing environmental exposures.

The population of African Americans appears to have greater rates of mental problems, according to empirical data. Researchers hypothesize that this is caused by either genetic predispositions or exposure to environmental stressors such as systematic racism, violence, and poverty. sibling adoptions placed in the families of Due to their environmental exposure, people of different social and economic situations may develop diverse behavioral tendencies.

According to research, only one-sixth of educational attainment is genetically transmitted to offspring. One's socio-environmental experiences have the biggest impact on their academic aptitude (Pierce, 2022).

3. Types of Behavioral Genetic Studies

Exposure to the environment or genetic makeup have an impact on behaviors, personalities, and psychopathologies. Researchers have examined and quantified the relative importance of the environment and genetic makeup on behavior using data sets related to family, twins, and adoption. Whether or not environmental factors matter less than genetic features in influencing future behavior has been the subject of research (Pierce, 2022).

Behavioral genetics is what I'm interested in. It looks for genetic implications on behavioral differences between people, including why some people develop schizophrenia and certain kids struggle with literacy. Therefore, I'm curious about the reasons behind these discrepancies. For a century, psychology believed that the only factor that matters is the environment, particularly the environment that your parents created during the first few years of existence. That dates back to Freud. But using behavioral genetics, we've discovered that nearly half of individual variations are caused by changes in DNA. Genetics is important, but this effect is far larger than all the other psychological effects together. It has a significant impact on nearly all aspects of psychology, including mental health and sickness, cognitive. We refer to DNA as nature, and the environment as nurture. Therefore, the nature vs. nurture debate is the one in psychology that has persisted the longest. People once believed that everything about who we are comes from our upbringing. We've demonstrated the significance of nature and genetics. About a century ago, twin studies and adoption studies—the first behavioral genetic techniques—were created. The earliest ones were carried out in Europe in the early 1900s, mostly in England but also in other nations. The twin technique compares two different kinds of twins. Twin births make up 1% of all births worldwide. Identical twins make up one-third of those. Because they are made up of a single fertilized egg (monozygotic), They share the same DNA, making them seem like clones of one another. Two zygotes make up the second type of twins, which account for two-thirds of all twin births. They are identical to any other brother and sister, except they were born in the same womb at the same time. Comparing these two groups is what the twin approach entails. You would have to assume that identical twins share more similarities than non-identical twins if a trait like musical skill is influenced by heredity. It reminds me of an experiment in biology (Plomin, 2017).

It is simple to agree that human ailments with a solely hereditary origin include phenylketonuria, cystic fibrosis, and Huntington's disease. And you probably have little trouble accepting that your genetic makeup affects your likelihood of developing diseases like colon cancer, diabetes, or heart disease. However, when we take into account complex behaviors, the subject of heredity becomes more challenging.

Does having a positive outlook on life depend on your genes? What if you are a pessimist - is it a trait you inherited? Could your early rise or late bedtime, obsessive neatness, inability to empathize with others, or other characteristics be influenced by your genetic make-up? What percentage of our temperament is inherited?

How much of our intelligence—our capacity for language acquisition, reading comprehension, and spelling—is influenced by our DNA code? What about psychological conditions like

depression, bipolar disorder, and schizophrenia? Are those brought on by our environment or by our innate makeup?

The response is "both" Our conduct is influenced by both nature and nurture, our genetic make-up, as well as our environment and experiences. However, we believe that the genetic component may be more significant than most of us think (Fields and Johnston, 2021).

Take Susan Middlebrook from Colchester, Vermont, as an illustration. She typically sleeps for seven to eight hours every night, but Middlebrook goes to bed at 10:30 p.m. after the late-night news and wakes up at around 6:30 a.m. Very early in the evening, say 6:30 p.m., go to bed. And between 1:30 and 3 in the morning, right when you're fast asleep, Middlebrook is eager to start going. You may feel very alone as a result, she told National Geographic News in 2005. "Who wants to go out and have fun at three in the morning? Nobody I know, and I have no plans to check out the neighborhood pub. Instead, Middlebrook gets her daily tasks underway. Middlebrook has familial advanced sleep phase syndrome (FASPS), which causes her sleep patterns to deviate significantly from the norm. Sleep researchers give people a series of questions about their sleep habits in order to identify the norm and the abnormal exceptions: When do you feel your best in the day? Your ability to wake up in the morning is how simple? If you had total control over your schedule, what hour would you go to bed? What hour of the evening do you start to feel sleepy? Are you more of a "evening" or "morning" person? (The questionnaire was created by Swedish scientist Olov Stberg and British scientist James Horne.) Most of us fall somewhere in the middle of a broad bell-shaped curve of scores, but FASPS patients lie at the far "morningness" end of the scale, scoring higher than more than 99 percent of other respondents. The answers to these and other questions produce a score that lies on a scale running from extreme "eveningness" to extreme "morningness." (Fields and Johnston, 2021).

Because Middlebrook's condition is caused by a malfunction in her circadian rhythm, which is derived from the Latin words circa-, "cycle," and dies, "day," circadian literally means "the cycle of one entire day." This circadian clock regulates not just when we sleep and wake up but also several physiological, metabolic, and behavioral functions like blood pressure, mood, alertness, and hormone levels. Exposure to sunshine resets our biological clocks each day, putting us in tune with our surroundings. However, Middlebrook's internal clock has a faster cycle and is generally four hours ahead of everyone else's, allowing her to go to bed at the same time as her neighbors do (Fields and Johnston, 2021).

In the Middlebrook household, Middlebrook's sleep-wake cycle is about as uncommon as oatmeal for breakfast. Two of her three sisters, one of her parents, and her own child all maintain the same peculiar hours. Middlebrook's sleep-wake cycle may seem unusual to you because it deviates greatly from the statistical average. The word "familial" in the name of the disease may have hinted to the fact that this syndrome is definitely caused by a variation contained in the personal DNA code of these family members rather than by any external factor. Even though only three out of every thousand people have FASPS, understanding its genetic underpinnings was very worthwhile. Findings about this condition could help explain other, more prevalent sleeping disorders like narcolepsy and insomnia, or they could lead to treatments for seasonal affective disorder (SAD), in which sufferers' moods are significantly impacted by the absence

of sunlight in the winter, and they may offer health support and advice to millions of shift workers. Understanding human circadian cycles may even make it possible to time medical treatments for greater effect or offer solutions for lowering nocturnal traffic accidents (Fields and Johnston, 2021).

A individual can have 0, 1, or 2 copies of the minor allele at a certain SNP since every DNA sequence is inherited twice, one from each parent. The individual's genotype at that SNP can be described by the quantity of minor alleles. The average effect of gene replacement is the line that best represents the entire genotype-phenotype connection (Lee, et. Al. 2014).

However, the slope of the best-fitting straight line is equal to a weighted average of the phenotypic changes resulting from potential gene replacements. The genuine genotype-phenotype relationship will almost likely not be precisely linear. The nonlinear effects of genotype, as well as interactions between genes and their environments, can theoretically also be estimated. To choose a subset of SNPs that should be further explored, it will typically be a good initial step to estimate the average impact in practice due to the startling combinatorial explosion of potential ideas (Rietveld, 2014).

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METHODS FOR MANUFACTURING OF GOLD NANOPARTICLES AND THEIR APPLUCATIONS

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1. Synthesis of Gold Nanoparticles

Gold nanoparticles (AuNPs) were synthesized in 1951 had seen the development of a synthetic procedure for producing AuNPs, using the boiling water treatment of hydrogen tetrachloroaurate (HAuCl4) with citric acid, where the citrate serves as a reducing and stabilizing agent (Turkevich, Stevenson, & Hillier, 1951). The size, shape, and surface functionality of these nanoparticles was controlled using a variety of solution-based techniques that have been developed in recent years (Bayda, Adeel, Tuccinardi, Cordani, & Rizzolio, 2019; Safdar & Özaslan, 2022).

2. Methods of Gold Nanoparticle Synthesis

Many methods of gold nanoparticles are available these days such as, physical, chemical and biological methods which are according to the interactions of numerous natural as well as synthetic compound methods and these are included with many chemical branches (Patra et al., 2018).

3. Biological Synthesis

Several ways are available for biological and chemical synthesis of nanoparticles, which are corresponding to new synthesis of gold nanoparticles via *Jatropha curcas* leaf extract. Some authors represented synthesis of AuNPs utilizing jackfruit tree L. seed extract (Khadka et al., 2018). The scientists showed a way for AuNPs preparation with green and non-toxic way with the help of leaf extract which can be used as stabling agents.

In another report, AuNPs were green when they were prepared with the help of leaf extract of *Azadirachta indica* and *Triphala* as it was used as a flavoring mixture (Kora & Rastogi, 2013). They synthesized smaller size NPs as they contained the antioxidant factors. Some researchers used *staphylococci aureus* for the treatment of AuNPs and has been monitored via UV Visible for the formation of new materials (Kumar et al., 2018). In another report *Aspergillus flavus* has been used to synthesis of AuNPs for the treatment of plants diseases and the size of NPs was about 8 nm (Li, Zhao, & Astruc, 2014) of the NPs was established with the help diffraction spectrum and FT-IR spectrographic analysis displayed supply of super molecule for synthesis of AuNPs (Logeswari, Silambarasan, & Abraham, 2015). The exploitation of plant life to synthesize AuNPs provides eco-friendly environment for the production of health and use of technique for pilot scale (Maráková et al., 2017).

4. Chemical Synthesis

The AuNPs can be fabricated by different methods. Every technique includes each blessing and drawbacks with common issues concerning shapes, size distribution and particle sizes. Despite

the higher than mentioned ones, several chemical ways are delineated for production of AuNPs (Michailidis et al., 2017). Compared to others, chemical ways supply relatively easier to synthesize Au-NPs in resolution. Primarily, the reduction of many compounds or salts has Au+ ions forms gold atoms Au (0), leading to cluster formation (Minhas et al., 2018). These clusters ultimately form mixture of nanoparticles. With such metal salts employing a reductant adore borohydride, a really little particles, it absolutely was troublesome to manage the assembly of larger particles. In distinction, a change state has terribly weak reduction, however the dimensions distribution is slightly larger that comparatively show the good quantitative relation (Niedermeyer, 2018).

5. Photochemical Synthesis

The photo-induced artificial methods are classified into two various approaches. These should be divided into topdown and bottom up, that square measure the photo-physical (top down) and photo-chemical (bottom up) ones. The photo-physical might prepare the NPs via the subdivision of bulk metals and therefore the chemistry synthesis the NPs were generates from the ionic precursors (metal salts). The square nanoparticles measure were made by the reduction of metal salts directly by different physical and chemical methods as photos (Safdar, Junejo, & Balouch, 2015). We knows some direct photo-reduction methods for the salt of $HAuCl_4$ in presence of Na turn was through varied lightweight sources of different metals such as cyan, UV, blue, white, inexperienced and orange at temperature (Vijayakumar, Priya, Nancy, Noorlidah, & Ahmed, 2013). These variations were involving the dimensions and form of particles having totally different optical properties (Vijayan, Joseph, & Mathew, 2018).

6. Applications of Gold Nanoparticles

Further distinctive properties of gold nanoparticles comprise their utilization in light and surface plasmon resonance (SPR). To Illustrate, SPR happens upon irradiating gold nanoparticles with actinic radiation, that was then causes the oscillation of free electrons within the physical phenomenon band of nanoparticles. The position and breadth of SPR peak depends upon the particle form and size (Yallappa et al., 2017). These properties allow gold nanoparticles to be employed in sensing applications like optical device desorption/ionization mass qualitative analysis of peptides, quantitative analysis detector for essential amino acid, determination of fibrinogens in human plasma, detection of deoxyribonucleic acid sequences, colorimetric sensors for measure ammonia concentration, period searching of membrane transport in living microorganism cells, biolabeling, optical imaging of cancer, biosensors for detection of herbicides, increased IR absorption spectrographic analysis, and aldohexose detector for medical nosology (Zada et al., 2018). SERS analysis techniques will be used to observe trace analysis of anthrax, nuclear waste, pesticides, genetic nosology, prostate-specific matter aldohexose, identification of microorganism, detection of nitro-explosives, and immunochemical assay labeling (Zheng, Sip, Leong, & Huo, 2018).

7. Antibacterial Applications

Many researchers speculated about the potential medical benefits of ,AuNPs such as antibiotic based gold nanoparticles or composite of these nanoparticles, but unfortunately, the alleged outcomes were just not compared with one another (Yavari, Malakahmad, Sapari, & Yavari,

2018). It had been revealed that a medication's effect is really not specific to one level but rather includes several mechanisms of action. Due to this multi-level mode of action, gold-based nanomaterials exhibit exceptional activity not only against sensitive microorganism strains as well as against extremely resistant microorganism strains. It has been demonstrated that gold-based nanomaterials will disrupt microorganism metabolic processes, act with desoxyribonucleic acid, increase the protoplasm membrane porosity, etc. (Yallappa et al., 2017).

On the opposite hand it had been determined resistance to ionic gold. Despite the actual fact, that resistance to ionic gold originating from the power of microorganism to scale back Au+ to less noxious oxidation number or from active outflow of Au+ from the cell was rumored, no knowledge proving resistance to aluminous conductor nanoparticles were printed. Naturally, the medicinal drug impact of gold and gold based mostly nanoparticles depends on particle morphology and surface characteristics (Yallappa et al., 2017). Hence, it's necessary to seek out nanoparticles by the means that of size, form and surface modification applicable to be used within the biological applications. Gold NPs may be ready many various ways in which however wet chemical reduction ways unambiguously predominate (Wypij, Świecimska, et al., 2018). AuNPs may be ready by the reduction of either, soluble and insoluble gold compounds. Typical artificial methodology relies on the reduction of caustic by Na borohydride that is one in all the strongest reducing agents and thus little conductor NPs square measure created. However, a good range of milder reducing agents may be used for the assembly of gold NPs with numerous sizes, size distributions, shapes and morphologies (Wypij, Czarnecka, et al., 2018).

8. Gold Nanoparticles and DNA Repair

A cell predicts and fixes damage to the DNA that encodes its genes using different techniques for DNA repair. During the DNA repair mechanism, the gene P53 is linked to base correction of double-stranded breaks and nucleotide excision repair (Alhmoud, Woolley, Al Moustafa, & Malki, 2020). Following DNA damage, o ribonucleotide reductase which is important to repair, p53 induction can also transcribe p53R2 and leads to increase in 3-methyladenine an enzyme required for BER (Vlachostergios, Patrikidou, Daliani, Papandreou, & medicine, 2009). Permanent DNA damage accumulates in the cell which can lead to tumor formation and also damaged the neighbor cell in such type of DNA damage the normal repair processes fail to accrue and the mechanism of cellar apoptosis occurred (D, B, & Abrahamse, 2019).

The mechanism of DNA repair is mainly started after a set of cellular divisions in response to DNA deletion and cells either age or self-destructs through apoptosis due to damage that could not be repaired. This process is known as “Hay flick limit” (Effros & Walford, 1984). INK4a/ARF is the positive regulator of p53 stability, has shown to have increased p53 transcriptional action (Balakrishnan et al., 2017). The telomere restriction in the genetic code is halted by overexpression of the protein and downregulated when p53 is activated at a high expression level.

9. Chemotherapy by Using Gold Nanoparticles

The use of nanomaterials for chemotherapeutic agents was gained the fascination of scientists. Metal nanoparticles have shown excellent outcomes in the chemotherapy of cancer (Shreyash, Sonker, Bajpai, & Tiwary, 2021; Surapaneni, Bashir, & Tikoo, 2018). These particles were discovered to inflict significantly less toxicity on normal cells in addition to exhibiting cell growth inhibition toward many types of cancer cells (Safdar et al., 2019; Shreyash et al., 2021; Suk, 2005). Apoptosis induction is a primary target for cancer medications (El-Kassas & El-Sheekh, 2014; Emerich & Thanos, 2003), and such effects are readily represented by caspase research (de Oliveira Goncalves, Vieira, Levy, Bydlowski, & Courrol, 2020).

Additionally, the tumour suppressor p53 (Safdar, Ozaslan, Junejo, Channa, & Sciences, 2021) plays a crucial part in regulating cellular death signalling through the effects of gold nanoparticles. On the other side, breast cancer cells have high levels of NF-B, which is known to operate against p53 (Safdar et al., 2021). Therefore, inhibiting NF-B may be a target for chemotherapy. Additionally, the p53 and NF-kB pathways demonstrated the precise mechanism by which various medications and materials affect a variety of cellular processes, including apoptosis, development, and cancer (Hwang et al., 2012). Following the targeted gene alterations that rendered the p53 gene inactive and contributed to constitutive NF-kB activation in many malignancies (Hwang et al., 2012). There is a need for particular nano-drugs that can function in tandem with medications that can selectively activate p53 or inhibit NF-kB, despite the fact that some of these drugs are already on the market. Therefore, the NF-kB pathway and p53 activation are key targets for the creation of novel cancer medications (Hwang et al., 2012). Therefore, it is important to do new findings for synthesize and analyses of Au(0)NPs based on antibiotics to target p53 and NF-kB concurrently by MTT, relative gene and protein expressions on SKBR3 breast cancer cells. This may open new endeavours for new researchers.

10. Future Prospective, and Recommendations of Nanotechnology

The world is undergoing a technological revolution. All facets of our existence, including communications, health, and transportation, have undergone changes. It is important to say that "what was science fiction yesterday is science today". We are now developing our skills in every branch of science, including physics, chemistry, biology, and engineering. That specifically connected to space technology, constructing smart cities and new manufacturing hubs, as well as inventing quantum and artificial intelligence technology. Though the extremely small physical components of change known as nanotechnologies, which are fueling the revolution, the tremendous pace of technological development is abundantly visible. Although there are various applications for nanotechnology, but few of them are establishing the foundation for our future: Nanomedicine, Materials Science, and Device.

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INITIAL FINDINGS AND EVALUATION OF ALZHEIMER'S DISEASE

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1. Introduction

Alzheimer's disease (AD) is the most ordinarily observed type of dementia and mercilessly mortifies the neurons. A woman named as Augusta Deter was diagnosed as AD for the first time by psychiatry and neuropathology specialist Dr. Alois Alzheimer on 25th of November, 1901. It seems a long time since beginning but neither the pathophysiology of the disease has been clearly understood nor a therapeutic approach has been improved to even halt the progression, let alone a complete cure. The patient's husband said that Augusta had progressive forgetfulness, difficulty in expressing herself, daydreaming, jealousy, and difficulty in carrying out activities of daily living and all those signs actually had started and progressed in the last a few years of duration.

As very well–known today, there are two main pathological hallmarks of the disease, as being extracellular β amyloid (Aβ) deposits and intracellular neurofibrillary tangles (NFTs). In this part, however, we discuss the very early sign and symptoms, instead of discussing pathological consequences of the diseases. Despite the fact that the disease is widely accepted as being associated with old age, it also could develop in early decades. The disease might abruptly come into view before the age of 65 which is known as Early Onset of Alzheimer's Disease and it also might ordinarily arise after the age of 65 which is known as Late Onset of Alzheimer's Disease and constitutes of more 90% of cases. Nowadays, the most common question arising about the disease is "What are the very early signs and symptoms preceding AD?".

2. Mild–Cognitive Impairment

When we ponder upon 'very early signs and symptoms' of AD, we should first go into some detail of the mild cognitive impairment (MCI). MCI is defined as a cognition status of an individual, which is impaired further than expected with a healthily aging, but impairment does not interfere with the daily activities yet (Petersen et al., 1997). Easily understood from this definition, there is also a healthily cognitive decline by aging.

There are accepted to be six domains of cognition which are learning and memory, language, social functioning, visuospatial function, executive functioning and complex attention. MCI (Fig. 1) is usually points out a cognition status in which an individual has difficulty in learning novel knowledge and recalling stored information. It is further divided into two types, as being amnestic and non–amnestic. Amnestic MCI is defined mainly as difficulty in recalling stored information, whereas in non–amnestic type, individual experiences a decline in one or more of those cognitive domains with a relatively preserved memory functioning. Amnestic type is known to be more common. Actually, the term "amnestic" precisely distinguishes the variety of MCI which includes an impairment in memory domain from the other which does not (Fig. 2).

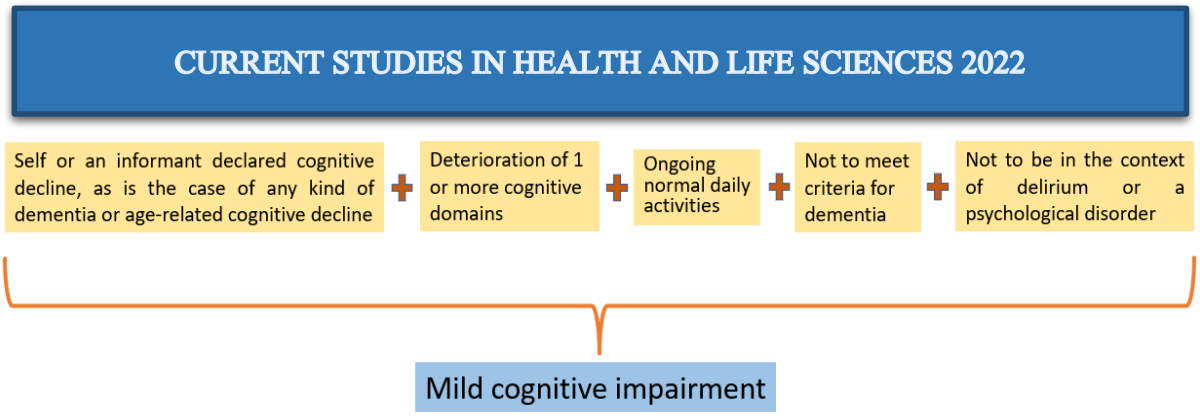

Figure 1. Mild cognitive impairment is actually diagnosed when you could not diagnose the case as dementia. Also, the case should not be in the context of delirium or a psychological disorder.

The risk factors for MCI display a high integrity and similarity with those of dementia. Vassilaki M. and colleagues declared that individuals with at least two of exceptionally four co–morbidities, hypertension (HT), hyperlipidemia (HL), coronary artery disease (CAD) and osteoarthritis carry the greatest risk of developing MCI (Vassilaki et al., 2015). Thus, inflammatory status of the individual seems to be one of the major determinants.

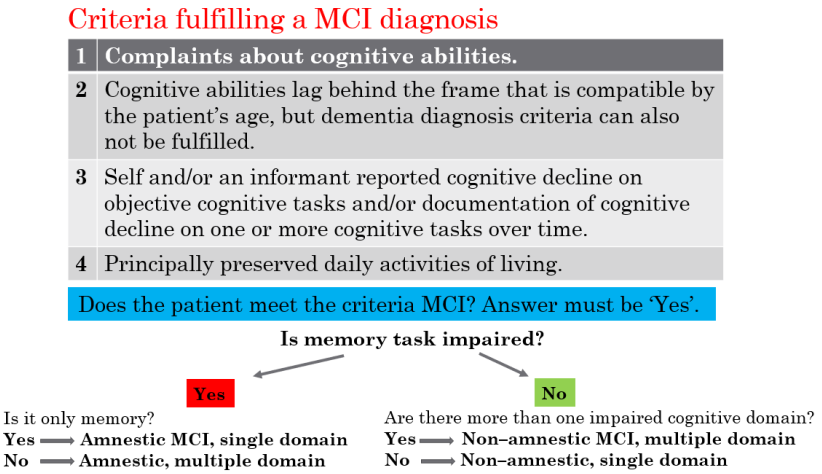

Figure 2. Subtypes of mild cognitive impairment (MCI) and distinguishing amnestic type from non–amnestic (Winblad et al., 2004).

The most plausible cause that's why MCI should be diagnosed is there are myriads of treatable reasons which can result in MCI and even be diagnosed as dementia clearly (Fig. 3).

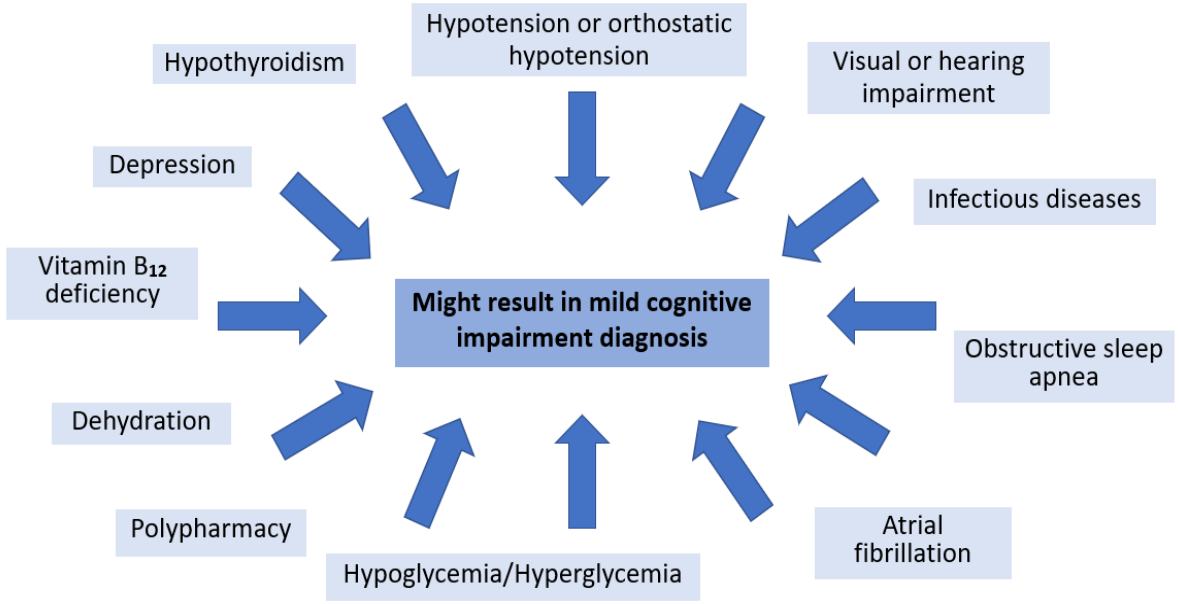

Figure 3. Main treatable reasons of mild cognitive impairment (Sanford, 2017).

Most of the treatable reasons might be easily neglected by the physicians. This may be because of mainly focusing on complaints about cognitive functions and partly due to existence of less than needed geriatric specialists and allied health staff. Despite the fact that a comprehensive geriatric assessment (Garrard et al., 2020) requires a devoted and steadfast educational discipline, which is the 'geriatrics', the circumstance is more complicated. Because cognitive complaints might arise in early decades, and this requires also well–equipped specialists from many others disciplines capable of managing cognitive complaints. So, leastways, differential diagnosis of cognitive complaints must be substantially placed in basic medical education. To start from scratch, depression is undoubtedly associated with cognitive decline and one of the most probably preventable reasons of the MCI. According to the one of the studies in which 6180 elderly aged 70 or more were observed in a collaborative observational type, patients with depression have an odds ratio of 2.7 compared to non–depressed ones for cognitive impairment (Scuteri et al., 2011). In another study, polypharmacy is associated with a significant decline in mini–mental state examination test (MMSE) (Oyarzun–Gonzalez et al., 2015). By conventional approach, a physician picks a therapeutic agent for his patient, according to the attributes of the patient, such as the age, gender, whether is there any chronical disease, existence of a pregnancy, malignancy etc. It seems that concept of selection of therapeutic agents is reshaped in the foreseeable future by taking into consideration novel approaches which predispose to select the best for cognition of the patient. It is well–known since recently that brain has its renin–angiotensin–aldosterone system (RAAS). Basically, pathways which are activated by angiotensin receptor type I (ATR–I) and angiotensin receptor type II (ATR–II) are found on poles exactly apart in brain. For instance, ATR–I chiefly heats up NADPH–oxidase system and generates pro–inflammatory and oxidative effects. In one of the studies, it is found that infarct bulk is scaled down in ATR–I knock–out mice after middle cerebral artery occlusion. On the other hand, an ATR–IV antagonist is found to weaken spatial memory abilities in rats (Royea

and Hamel, 2020; Wilson et al., 2009). So, angiotensin receptor blockers (ARBs) might attenuate co–existing cognitive impairment to a certain degree in patients with hypertension or stroke. These findings and hypothetical results show that, just as we are trying to choose the best blood pressure medication for a pregnant woman or a chronic kidney failure patient, approaches that will determine treatment options by considering cognitive functions will increase more and more in the near future.

The inter–relation between medical intervention and cognition is only one aspect to benefit maximum for cognitive status of individual. And as it is shown in Fig. 3, there are also many reasons other than medical therapeutics result in individual to display MCI or dementia like symptoms.

MCI, with its four major subtypes (Fig. 2), is believed to make the way for very early signs of dementing disorders which are AD, vascular dementia, Parkinson's disease dementia, Lewy body dementia and frontotemporal dementia. So, cognitive aging does not settle down in continuum of MCI and varieties of dementia (Tab. 1).

Table 1. Key features of normal cognitive decline with aging, mild cognitive impairment (MCI) and any type of dementia (Henderson, 2014).

Type of cognitive decline	Do the symptoms interfere with the person's independence?	Are the symptoms caused by a pathology in the brain?
Cognitive decline with normal aging	No	No
MCI	No	Yes
Dementia	Yes	Yes

Despite the fact that MCI is considered to be produced by certain types of brain pathology, it might display each of three possible aftermaths, progress to dementia, follow a stable course or symptoms might regress. Then, if it would progress to dementia, the patient is expected to display pre–dementia symptoms. Those of the patients with MCI who will complete the steps of pathological course of AD are believed to show symptoms mostly related to episodic memory (difficulty in learning and retaining new information) at the very early stages. Albert and colleagues (Albert et al., 2011) proposed a new concept to differentiate MCI prone to transform into AD from other types of MCI, 'MCI due to AD'. This new concept primarily depends on detecting very early signs of episodic memory impairment. This determination is so difficult that the earliest signs of episodic memory impairment should also not have a negative impact on the flow of one's occupational and social life. We should get the evidences of episodic memory impairment, but still it should be clearly established that the individual has been able to take care of himself and carry on daily activities. So only in this way, we can exclude a

diagnosis of dementia for the patient's condition. Although memory is the principal cognitive domain to be impaired involved in MCI patients who destinably progress into AD, other cognitive domains, such as executive functioning, language, visuospatial skills and attentional control should also be examined.

3. Challenges in Early Diagnosis of AD

All around the world, two third of all dementia cases are consisted of AD patients. Forecasts also show plausibly that the frequency of AD will increase gradually worldwide in the coming years. This seems a foregone conclusion principally due to taking into account increased life expectancy, population and incidence of cardiovascular disease. Arguments that will enable us to intervene in this whole process can be put forward easily relatively. For instance, what can be done to reduce the prevalence of cardiovascular diseases, which is an important risk factor for both AD and vascular dementia, could be ruminated on. High cholesterol level in middle age increases the risk of AD (Kivipelto et al., 2002; Whitmet et al., 2005). Whereas body mass index (BMI) populously negatively correlates with dementia after age of 65, obesity in middle ages clearly increases the risk of dementia seen in later ages (Fitzpatrick et al., 2009). Physical activity makes the individual less prone to develop dementia or AD (Larson et al., 2006). Findings about blood pressure level are controversial. While higher than normal blood pressure levels in the middle ages have been accused of increasing the risk of dementia, some other researches propose that low blood pressure level in old ages as a risk factor of developing dementia (Qiu et al., 2005; Ruitenberg et al., 2005). All these remarkable findings, actually a small part of those considered to be associated with AD, can be defined as modifiable risk factors for AD. Ensuring the control of modifiable risk factors will undoubtedly contribute to the reduction of the prevalence of dementia and AD. Hence, certain studies indicate a slightly decreased or still stable incidence of dementia in high–income countries (Roehr et al., 2018). This may be because of a more qualified control of modifiable factors in high–income and high–educated regions of the world. Early diagnosis of AD also provides a chance for control of those risk factors, because very early symptoms or diagnosis of MCI and AD make the clinician and the patient even more alarmed about controlling the risk factors to be able to halt the progression of the disease. So, MCI or early symptoms of AD should be made more recognizable or well–known.

According to the one of the previous studies, first symptom of MCI patients is a decline in memory, with 80%, in compliance with the anamnesis acquired from the informants. Depression like symptoms is the first sign in 9% of those patients. Following these two, decline in language abilities, weakening of high–order social or functional daily activities, disorientation and personality and behavioral changes are also seen as first symptoms, respectively and with a decreasing percentage. In that study, informants reported that a second symptom had currently been besides first symptom at the time of first/baseline evaluation of the patient. In those of patients whom MCI turns into AD, second symptoms appended to decline in memory as first symptom are mostly weakening of high–order social or functional daily activities and disorientation (Devier et al., 2010). It is very famously known that a neuropathologic examination is the gold standard to diagnose AD. Since this is unlikely, one of

the best ways to early diagnose the disease seems to provide a depiction of early signs and symptoms and place them in a proper continuum.

The preclinical phase is defined as a period in which the person is asymptomatic but neuropathological changes might have been present for a long time (Fig. 4). So, the most

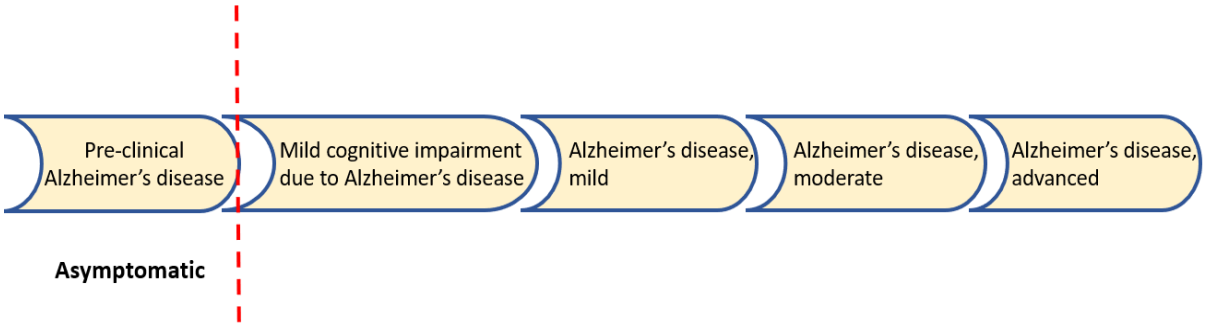

Figure 4. Alzheimer's disease continuum based on the 2011 National Institute on Aging and Alzheimer's Association (NIA-AA) guideline.

challenging issue seems pre–clinical phase. Because any sign or symptom cannot be readily observed, but devastating process of the disease has already started in this phase.

In the very early stages, the most critical determinant in revealing the signs and symptoms related to cognitive decline is the person himself or the person's closest family members, friends or caregivers. Whereas all these people may sometimes positively contribute to the diagnostic process, they also may behave in such a way that fail the early diagnosis. For instance, the patient himself may avoid to reveal or tell symptoms of certain kind of decline in his cognitive abilities due to fear of stigmatization (Dubois et al., 2016). And, relatives may misinterpret the signs, considering them as a natural consequence of advanced age (Galvin et al., 2012). Physicians' initial assessment has also a great importance for detection of signs and symptoms associated with MCI/AD. A comprehensive medical history; including recent and chronic illnesses; any medications that could cause memory loss or might adversely affect cognition; traumas; usage of illicit drugs or drug abuse; history of epilepsy or seizures should be questioned. In addition to an extensive neurological examination including history of any falls recently and notice of any gait disturbances, cognitive abilities of the patient should be examined in all aspects, including episodic memory, executive function, attention, language, and visuospatial skills. Under the heading of risk factors, whether there is a dementia patient in the family and the person's history of cardiovascular disease, obesity and smoking should be questioned in detail. Cognitive and behavioral changes should be questioned. In general, it should be questioned what a day means to the person, whether he has been forgetful recently or lost his belongings, whether he has recently felt depressed, hopeless, and whether he has been able to manage his financial affairs. As can be seen, in this evaluation process, which actually starts with the anamnesis, it is aimed at first to eliminate the causes that can be diagnosed and treated. Satndard laboratory tests and screening tests are also added if needed. Various algorithms have been developed for an initial assessment (Cordell et al., 2013; Porsteinsson et al., 2021).

In the first evaluation and afterwards, we can say that the things to be done to reach the diagnosis of Alzheimer's and to give the necessary up–to–date treatment are more or less clear. However, if we are going to talk about the difficulties of early diagnosis and treatment, we should also mention what studies on MCI have taught us. When the MCI period before AD is diagnosed correctly, it undoubtedly provides an important opportunity for the implementation of approaches that will prevent or delay the emergence of AD. Therefore, it may even be reasonable for any clinician to place more emphasis on diagnosing MCI or performing community screening for MCI than on diagnosing AD or conducting population screening for AD. Nevertheless, diagnostic criteria for MCI used in clinical trials seem to have insufficient preciseness (Visser et al., 2005; Jelic et al., 2006). A series of randomized controlled trials examined effects of non–steroidal anti–inflammatory drugs and acetylcholine esterase inhibitors on MCI patients, to detect whether those drugs prolong the period between the moment when the MCI is diagnosed and when MCI turns into a clear or probable AD. These studies gave us information about the effects of drugs on the transformation period of MCI to AD. However, it is extremely surprising to see that even small differences in criteria for identifying patients with MCI changed the results drastically (Visser et al., 2005; Jelic et al., 2006; Petersen et al., 2005; Thal et al., 2005). In one of those studies (Thal et al., 2005), less patient receiving placebo turns into AD than in group receiving rofecoxib. Cognitive function scales (MMSE test, auditory verbal learning test, cognitive scale of AD assessment scale, selective reminding test, clinical dementia rating, etc) are frequently used for the diagnosis of both AD and MCI. However, considering that the inclusion criteria have such an impact on the results of those trials and the importance of MCI progressing to AD, it is indisputable that the inclusion criteria should be very delineative. For instance, being positive with apolipoprotein ε4 allele is a definite risk factor for AD. Does apolipoprotein ε4 allele positivity deserve to be a heading in MCI inclusion criteria? Is it worth the cost? Positron emission tomography (PET) with fluorodeoxyglucose (FDG) has been approved for use in early diagnosis of AD (Silverman et al., 2002). Should it come into routine use for early detection of MCI and AD or be one of inclusion criteria? Cerebrospinal biomarkers like Tau (τ) and Aβ and in vivo imaging of Pittsburgh compound B (C–PiB), a carbon–11 labelled thioflavin–T derivative (C–PiB) might also extend the accuracy of early diagnosis (Jelic et al., 2006; Yamin et al., 2017). Novel randomized clinical trials are needed to be conducted to develop inclusion criteria of MCI and AD.

4. Very Early Manifestations of Alzheimer’s Disease

It is absolutely agreed upon by scientists that brain damage is starting even a few decades before deterioration of memory and cognition explicitly appears in AD. So, before signs and symptoms arise, there should be a silent period with ongoing damage in brain. Memory loss, forgetfulness, difficulties in completing daily tasks, indigent judgement and wrongful decisions, decrease in ability of taking action instinctively, loss of sense of initiative, repeating questions heard very recently, trouble in management of financial issues, being on the loose, getting lost, losing things, misplacing the objects and mood and personality changes are the notable symptoms of the AD. But, when and how these symptoms begin is questionable. For instance, do difficulties in remembering memories, names, people etc. always indicate the disease?

Undoubtedly, some memory changes are encountered by old age (National Institute on Aging, An Official Website of the United States Government). Especially, slimming of episodic memory is a foregone conclusion with age progression (Shing et al., 2010). All people understand that as they age, there are changes in their cognitive abilities. The most common question they ask themselves or the doctor they are examined is "Are these changes in my cognitive abilities normal or a sign of dementia?". One of the first of the changes that are considered normal with advancing age is a decrease in cognitive speed. For example, it may take longer time to remember a word or a person's name. Decline in complex attention also occur naturally with advancing age. For example, you may need to turn down the volume of your radio while setting up the medications you use daily. Working memory also weakens with advancing age. For example, it becomes difficult to remember the address you asked while listening to instructions on how to get there. When getting ready to go to a wedding, things like shaving first, taking a shower, getting dressed, and being able to do it all on time or when a friend starts acting cold towards you, things like noticing the situation, thinking over the possible causes, trying to understand his point of view and taking action to solve the problem might get more difficult by older age. This indicates a decline in mental flexibility. Visual or hearing impairments can also cause cognitive decline to be felt more prominent than it actually is. However, this changes never affect the individual's daily day functioning. These findings are also unlikely to cause significant changes in pen and paper cognitive tests. MCI cognitive impairment is a period in continuum where the physician realizes significant changes in those tests. And the patient begins to have more difficulty in bill paying, setting up the pill box, remembering taking their medications and even carrying on household chores, in such a way that still does not affect the daily basis functioning to diagnose the patient as dementia. In amnestic MCI, scores of cognitive tests are prone to poorer than those of individuals with normal cognition and better than those of individuals with AD, mostly ranging in the normal limits. The same range could be seen when the individuals are put to verbal and visual memory tests.

Although there is no sign of cognitive decline in very early stages, certain biomarkers of which handling has been becoming more and more indispensable for detection of early disease should be mentioned. With the forecast made according to a hypothetical situation; early diagnosis is so important that even if we could not prevent progression of the disease, it has been revealed that when we delay its manifestations by 5 years to grow on, the number of AD patients would decrease by 57%, and the medicare costs reduce by almost half (Alzheimer's Assocation). Although we refer to MCI as the preclinical stage, it should not be forgotten that AD exhibits a continuum of pathology and there should be still periods before MCI. Since signs and symptoms can also be detected in MCI, but do not meet the criteria for diagnosing AD in MCI; the preclinical phase can be defined as the period in which the individual does not have any clinical signs and symptoms at all, but biomarkers related to AD pathology can be detected (Fig. 5).

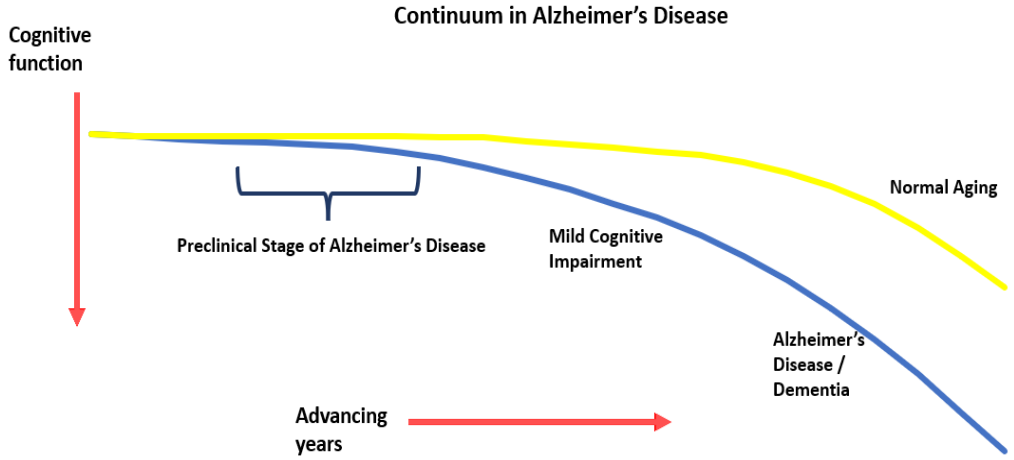

Figure 5. Clinical continuum model of AD. Conceptual preclinical AD precedes MCI. The definition of preclinical AD includes presymptomatic individuals who carries autosomal dominant mutations, asymptomatic biomarker–positive elderly individuals with the potential to develop MCI due to AD, and individuals who exhibit an insidious decline in cognitive abilities in a degree that exceeds the decline in normal aging but does not yet meet the criteria for the diagnosis of MCI. This diagram stands for a hypothetical model for the pathological–clinical continuity of AD. However, not all individuals with biomarker evidence of AD–pathophysiological process progress to clinical phases of the disease (Budson and Solomon, 2012).

So, according to this clinical continuum model (Fig. 5), there must also be a pathophysiological continuum. It is known that there is a deterioration in the processing of Aβ proteins without any measurable decline in cognitive abilities. However, if a presymptomatic individual with underlying AD pathology lives long enough, he will one day become symptomatic. Both screening findings and quantifiable chemicals/biospecimens are considered to be biomarkers which provide information regarding the stage and characteristic changes in AD. In this content, five major biomarkers are identified, which are in mostly order of development decreased 42–amino acid form of amyloid–β ($A\beta_{42}$) in cerebrospinal fluid (CSF), increased τ protein in CSF, decreased FDG uptake on PET (FDG–PET), PET amyloid imaging and structural changes, i.e. cerebral atrophy on MRI (Jack et al., 2010). Either CSF $A\beta_{42}$ or PET amyloid imaging are substantial biomarkers indicating brain amyloid plaque deposits. C–PiB is currently one of the leading trackers for imaging amyloid accumulations in vivo with PET amyloid imaging. In vivo C–PiB uptake imaging noteworthily congrues with regional quantitative analysis of Aβ accumulation in post–mortem studies (In patients subjected to ante–mortem PiB–PET imaging and autopsy). On the other hand, lower than normal level of $A\beta_{42}$ in CSF might display an association with clinical AD diagnosis, and is harbinger of well–known pathological findings at autopsy (Schoonenboom et al., 2008). Another important association seen in almost all patients is that unusually low $A\beta_{42}$ levels in CSF match with PiB–PET findings.

Although high levels of τ protein in CSF is not entirely specific for AD, elevated levels of τ correlate positively with clinical severity of disease, with phosphorylated τ being more

important for AD. This means that the greater τ concentration is encountered, the more intensified cognitive impairment takes place in the MCI–AD continuum. Briefly, increased CSF τ concentration is a well–known indicator of neuronal injury and also associated with ischemic or traumatic brain injury, but a more detailed delineation of that issue is out of the intended scope of this chapter. Higher than normal level of τ in CSF is forerunner of NFTs pathology findings at autopsy. Cerebral glucose consumption as assessed by FDG–PET is an effective biomarker for local neuronal network integrity. Cerebral glucose consumption measured by FDG–PET positively correlates with synaptophysin protein level which is considered to be an indicator of well–being of synaptic density (Rocher et al., 2003). In the framework of Alzheimer's disease, decreased FDG uptake on PET imaging means that functional synaptic capability is impaired. So much so that even if the atrophy caused by AD is rectified hypothetically, the use of glucose per gram tissue has been found to decrease in the AD neuropathology–specific topography of the brain (Ibáñez et al., 1998). Lastly, although the atrophy seen on MRI is not specific to AD, it is known to correlate with disease severity and cognitive decline. When these biomarkers are put on in a temporal order, Aβ deposits are mentioned in the first place, while signs and symptoms of cognitive impairment are not yet seen (Fig. 6). As for signs and symptoms of cognitive decline become evident mainly with the emergence of biomarkers of neurodegeneration. Thus, in the early stages of the disease, we can although detect decreased FDG uptake with PET and obtain images confirming Aβ deposition, encounter reduced Aβ levels in the CSF, but not yet detect signs of atrophy in advanced conformity with age on MRI. In case of NFTs, the formation and increase of NFTs does not entirely precede cognitive impairment, as we mentioned for Aβ plaques. Either of individuals with NFTs or those with Aβ plaque deposits can display normal cognitive abilities. However, NFTs seen in asymptomatic individuals are more specific to the entorhinal cortex and these individuals tend to be in Braak stages I and II (Braak and Braak et al., 1997). NFTs are much more common in symptomatic individuals and are not unique to the entorhinal cortex, instead more widely distributed in brain. However, even individuals with extensive Aβ plaque deposits can be asymptomatic.

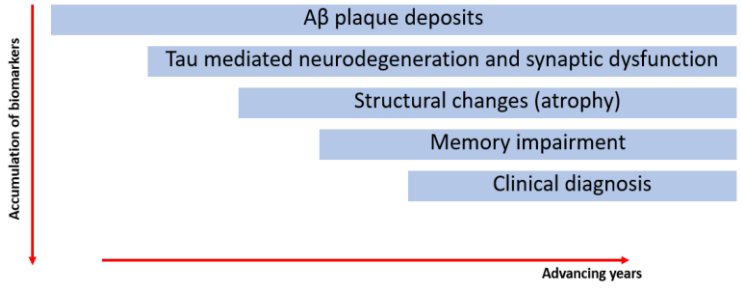

Figure 6. Aβ accumulation is determined by measurement of $A\beta_{42}$ in CSF or by PiB–PET. Tau measurement in CSF, or FDG–PET reveal the neurodegeneration and synaptic dysfunction. The degree of atrophy is determined by MRI (Jack et al., 2010).

5. Conclusion

Understanding that Alzheimer's disease is a continuous process may present us with different options for intervention. For example, the view that decreased FDG uptake detected in PET leads to neurodegeneration brings to mind possible vascular or metabolic interventions. In this case, we may find ourselves focused on treating AD by looking for ways to protect the vascular health of our central nervous system, rather than trying to find drugs that inhibit neurodegeneration. On the other hand, conditions such as MCI are becoming almost as important as AD. The diagnosis of MCI gives the person a chance to both regulate his present and future and adapt lifestyle modifications to his daily life. We should not forget that the question of "will I have AD?" is being asked more and more each day by growing elderly population has been covering a greater place in the practice of clinicians.

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CLINICAL RELEVANCE OF FERTILIZATION FAILURE AND NOVEL METHODS IN IVF

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1. Reproductive System

The reproductive system categorized as male and female reproduction in humans. The reproductive system in men includes a pair of testes, genital excurrent ducts, different accessory glands, and lastly penile. The two main functions of the testes are spermatogenesis and steroidogenesis. Spermatogenesis is the process of sperm cell development or in other word the production of the sperm cells which is called gametes. Rounded immature sperm cells undergo successive mitotic and meiotic divisions (spermatocytogenesis) and a metamorphic change (spermiogenesis) to produce spermatozoa. And secondly steroidogenesis which means synthesis of the androgens, also called sex hormones. Androgens, mostly testosterone which is substantially produced in Leydig cells that are located in the interstitial spaces of the testis are necessary for spermatogenesis and have crucial role in embryogenesis of the male embryo into phenotypic male fetus, and lastly responsible for sexual dimorphism. Accessory sex glands such as the seminal vesicles, prostate, and bulbourethral glands are taking place in male reproduction system by producing a several types of secretions that are attending to sperm to form semen.

On the other hand, female reproductive system counts in internal sex organs and external genital structures. The internal reproductive organs located in the pelvis and the outer genitalia participate in the anterior part of the perineum known as the vulva. The inner female reproductive organs are made up of pairs of ovaries, pairs of uterine/fallopian tubes, a single uterus and a vagina. External genitalia include mons pubis, labia majora and minora, clitoris, vestibule and vagina opening, hymen and external urethral orifice. Mammary glands can also be included as their functional status is directly linked to hormonal activity in the female reproductive system. Female reproductive organs exhibit cyclical monthly changes in both structure and function. These changes constitute the menstrual cycle and the appearance of the initial menstrual cycle in the maturing individual is referred to as the menarche. When the menstrual cycle becomes infrequent and eventually disappears, this change is called menopause. The menstrual cycle is mainly controlled by two hormones secreted by the adenohypophysis of the pituitary gland which are called follicle-stimulating hormone (FSH) and luteinizing hormone (LH), and by two ovarian steroids which are called estrogen and progesterone.

2. Processes of Fertilization and Implantation

Fertilization and implantation are the natural life processes in the reproductive system, which is achieved by the fusion of male and female gametes (egg and sperm) to form a zygote. The process of fertilization in humans takes place in the ampulla of the uterine tube, and then it is implanted in the internal layer of the womb/uterus. After release from the ovary, the egg can survive for about 12-24 hours. After these above mentioned processes if the egg has not fertilized, it degenerates and sheds off from the uterine lining. Contrary to this, the sperm can

live for about 72 hours. After the ejaculation the sperm cells are coming out into the vagina, and then sperms enter into the uterus through the cervical canal, and finally remaining surviving sperms swims upwards to the uterine tube to be more precise into the ampulla to fertilize the egg. The fertilization process is based on the principle of combining the haploid chromosome set of male and females to make it a single diploid cell called a zygote. In case of the absence of the fertilization, there will be no zygote formation.

The secondary oocytes released from the mature Grafian follicle of the ovary captured by fimbriae (small finger-shaped projections at the end of the fallopian tubes, through which the eggs move from the ovaries to the uterus) of the fallopian tube and get forward into the ampulla, where it is going to be fertilized by sperm within 24 hours after the release. Surrounded by multiple sperm cells, the oocyte will only be fertilized by a single sperm. The secondary oocyte completes its meiosis-II after the penetration of the sperm cell into the oocyte. Following this process, the secondary oocyte is referred to as the egg. The fertilization process happens in a few steps, including chemical and physical events. For instance; sperms incapacitation undergoes acrosomal reactions and releases chemicals called sperm lysins that are found in the acrosome. As a result of the acrosomal reaction, the membrane of the sperm and secondary oocyte are fused and subsequently the components of the sperm enter the oocyte. Calcium ions also play a significant role in the acrosomal reaction process. The optimal pH level, temperature and concentration of calcium and magnesium are the most important factors in acrosomal reaction. Immediately after plasma membrane fusion, the oocyte exhibits cortical reactions. These granules are located under the oocyte membrane, which fuses with the plasma membrane and releases cortical enzymes from the zona pellucida to the plasma membrane. Following this process, zona pellucida is toughened up by the cortical enzymes that prevent polyspermy (penetration of more than one sperm into the oocyte). Post-entrance of the sperm cell, the paused second meiotic division is completed by the secondary oocyte. This process gives rise to a haploid egg and a second polar body. The head of the sperm cell that holds the nucleus separates from the whole sperm and is called a male pronucleus. As a result, the tail and the second polar body begin to degenerate. The nucleus of the ovum is referred to as the female pronuclei. After this stage, the male and female pronuclei fuse together and their nuclear membrane degenerates. In brief, the fusion of the chromosomes of male and female gametes is called karyogamy. Now, after all these processes of the fertilization ovum takes the name zygote. The process of the entrance of sperm into the oocyte triggers the metabolism in zygote. Hereby, protein synthesis and cellular respiration are enhanced in this stage. Instantly after the fertilization, the cells start to divide and gradually multiply within 24 hours in the uterine tube, and this detached multicellular structure is called a zygote. Afterwards, between 3-4 days it migrates to the uterus, and at this moment we refer to it as an embryo. At this stage, an embryo which is in progress of the development undergoes through various stages and attaches itself to the endometrium and this process is referred as implantation.

3. Infertility

Infertility is a disease of the male or female reproductive system defined by the failure to achieve a pregnancy after 12 months or more of regular unprotected sexual intercourse. Infertility affects millions of people of reproductive age worldwide, and has an impact on their

families and communities. There are many factors that cause male and female infertility, such as genitourinary anomalies, trauma, exposure to chemicals and being in an extremely hot environment for a long time. However, the factors that cause infertility in idiopathic infertility cases are not known.

4. Advanced Sperm Selection Techniques to Improve IVF and ICSI Outcomes

Approximately 50% of infertility cases are associated with a male factor. Assisted reproduction techniques (ART) tries to help to infertile patients' sperm to fertilize an egg and give normal birth with healthy offspring. However, the effectiveness of some techniques is still under the process of improvement. After the copula, while millions of spermatozoa are inseminated, only a few hundred sperm cells collide with oocyte for fertilization and reach the ampulla. This process shows that the sperm with the best structure and properties is naturally selected to support the development of the embryo.

Considering the risks of defective sperm resulting in reduced potential of the oocyte fertilization and even the development of congenital anomalies due to the challenges in selection of the sperm cells with good quality and characteristics, we can imagine how important the sperm cell selection is. For successful in vivo or in vitro fertilization, sperm must overcome natural fertilization barriers. However, Intracytoplasmic Sperm Injection (ICSI) technique that has been used during in vitro fertilization (IVF) bypasses natural barriers. The success of fertilization in this technique is strongly influenced by the quality of the sperm used for insemination. ICSI is considered absolutely required in the case of male factor infertility with an abnormal semen analysis. ICSI is an advanced assisted reproduction procedure used in an embryology lab during an IVF treatment in which a single sperm cell is injected directly into a woman’s oocyte in order to create a fertilized egg.

The outer membrane of a sperm cell is very important in terms of their functionality as it is involved in some basic processes such as cellular metabolism, capacitation, oocyte binding and acrosomal reaction. The sperms are encapsulated in an extensive layer that provides the membrane its characteristic negative charge. Based on this, new techniques were developed to separate X and Y carrying and healthy pure headed sperms. Later, some other researchers started to modify and enhance the effectiveness of these techniques. These techniques are based on either the collection of charged sperm cells that adhere to the wall of a centrifuge tube or migration in an electric field. In both techniques, subsequent analysis of selected samples presents the huge rate of the sperm cells with high quality and higher DNA integrity. The procedure, known as the Zeta method, allows the selection of sperms with a lower DNA fragmentation than the "HA-coated plate selection" method. Despite the fact of these promising results, there are only a few published studies available related to the Zeta method selected sperm cells in ICSI patients.

The human body presents small channels containing dynamic fluid. Similar to these channels, developed microfluidic technology serves as a physiological platform for restructuring fluid channels and flows in living organisms. This technology is quantitatively controlled in a biophysical and biochemical environment, and the experimental results are visualized using optical microscopy. Moreover, this microfluidic technology provides the possible simulation of

the journey of spermatozoa through the female reproductive tract, while allowing the quantitative assessment of the dynamics of spermatozoa motility when male gametes move in the biophysical and biochemical environment. Thus, this technology can help to develop new methods of gamete selection with minimal damage.

5. ROSI/ROSNI in IVF

Round spermatids are the earliest formed haploid male germ cells at the stage of before their development into tailed spermatozoa. The use of round spermatids in IVF has been suggested for infertile men who are unable to produce spermatozoa. This procedure is either called round spermatid injection (ROSI) or round spermatid nucleus injection (ROSNI) depending on the type of material used (whole round spermatid or only nucleus of the round spermatid). Several studies showed that the efficiency of ROSI became higher in recent years; however, the efficiency rate of the ROSI in comparison to the ICSI technique is low. Even the efficiency rate of the ROSI is lower than ICSI; ROSI technique gives hope that it could help azoospermic men to have their own genetic child's.

Although difficulties with the ROSI technique still persist and the overall low success rate of this technique continues to limit its use in clinical practice, recent studies show that outcomes have been significantly improved compared to previous studies. There are also a number of strategies available to improve the quality and effectiveness of round spermatids. One of these strategies is known as in vitro germinal cell maturation. Sertoli cells (SCs) transplantation in the testicles is also another strategy to overcome the male infertility. This strategy increases the number of testicular cells, sperm count and motility in azoospermia. As well, short-term germ cell co-culturing with SCs improves spermatogenesis. The stimulating factors produced by SCs in the co-culture system also have an impact on the differentiation of spermatogonial stem cells. For this reason, Sertoli Cell-Conditioned Medium in azoospermia is also another strategy which has the ability to recover the spermatogenesis.

6. Improved Techniques for Oocyte Stimulation in IVF

Poor oocyte response after stimulation for IVF is still one of the most important problems in reproductive medicine. Since the quality of the gametes affects the ability of the embryo to develop, it is very important to evaluate the morphological features of the oocyte in the embryological laboratory. Oocyte maturation consists of synchronous nuclear and cytoplasmic maturation processes that determine oocyte quality. Ovarian stimulation can be affected by intrinsic factors such as; oocyte growth ability, age, body mass index, lifestyle-related factors and by external factors such as; IVF laboratory procedures (oocyte retrieval, denudation, freeze-thaw, preparation procedures for ICSI), culture conditions (temperature, pH), and environmental conditions (light, air quality, humidity).

Several clinical trials have examined the role of androgens in improving poor oocyte response in IVF. On the other hand, certain studies argue against the use of androgenic supplements in improving fertility rates. Based on a meta-analysis, it was reported that clinical pregnancy and live birth rates increased following transdermal testosterone administration in patients with low response. In another experimental study, the paracrine regulation of steroidogenesis in theca cells by co-culturing theca and granulosa cells were evaluated and it showed that

steroidogenesis is increased in theca cells. According to another research, a new protocol has been drawn up. In this protocol; to achieve intraovarian androgenization using the various mechanisms, they enhanced serum androgen levels by applying a daily transdermal testosterone gel. Then, they increased intrafollicular androgen levels by injecting hCG twice a week. And finally, an aromatase inhibitor called letrozole, has been used daily to prevent the androgen aromatization of estrogen with its daily application. Oral estradiol and vaginal progesterone have been favored for menstrual cycle control.

7. Preferred Embryo Selection Method to Enhance Embryo Implantation in IVF

The selection of embryos with the highest potential for implantation remains the main challenge of today's IVF labs. In this sense, various invasive and non-invasive methods have been developed to assess the morphokinetic, metabolic and chromosomal profiles of the embryo. According to current knowledge, frame-by-frame imaging is a promising non-invasive technique for facilitating embryo selection. Nowadays, this method is commonly used to identify embryos with high implantation potential to increase pregnancy rates, and to reduce the chance of multiple pregnancies by reducing the number of transferred embryos. In terms of the invasive techniques in embryo selection, blastocyst biopsy combined with complex chromosome analysis allows the identification of euploid embryos with minimal impact on the developmental potential of the embryo. This shows us that advances in technology and molecular biology allow the selection of embryos with high implantation potential in order to enhance pregnancy rate and abstain from multiple pregnancies.

8. Endometrial Scratching Method in IVF

It is known that one of the main problems underlying failed implantation is related to the receptivity of the endometrium, and therefore remains an important topic in the field of IVF. In this regard, recent researches have focused on the development of a variety of strategies to improve endometrial receptivity. Endometrial scratching (ES) is a technique used to improve the capability of an embryo to implant in the inner lining of the uterus, called endometrium after intrauterine insemination (IUI) or embryo transfer. In short, this technique involves endometrial scarring, in order to improve the receptivity of the uterus to the embryo. The ES is an inexpensive mechanical procedure for wounding the endometrium, which does not cause much discomfort to patients. This procedure can be performed using a variety of instruments such as a soft plastic endometrial biopsy catheter, Karman's cannula and vacuum aspirator, Novak's suction curette, and hysteroscopy. Mostly, in the luteal phase of the cycle preceding IVF, the endometrium is commonly scratched by using a 3mm in width small catheter known as the Pipelle®. Usually, the catheter is pushed forward through the cervix to the fundus, and then moved back and forth, and finally the process is completed by rotating the catheter to create a scratch on the endometrium in order to stimulate the endometrium.

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EFFECTS OF CAPSAICIN THE DEFENSE INDUSTRY FROM DNA PROTECTION

Sibel Bayıl OĞUZKAN

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1. Introduction

The main phytochemical in hot peppers are capsaicinoids. Among the capsaicinoids, 69% contain capsaicin, a phenolic compound responsible for the characteristic taste and pungency of hot peppers. Other bitterness substances are 22% dihydrocapsaicin, 7% nor dihydrocapsaicin, 1% homocapsaicin and homodihydrocapsaicin.

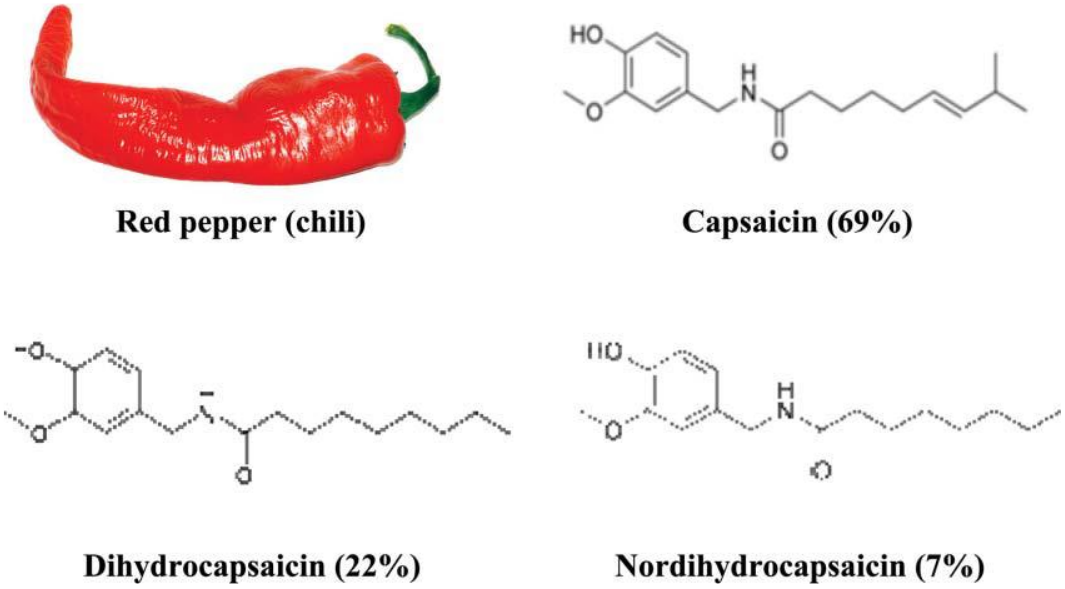

Figure 1. Red pepper and major capsaicinoids (1).

Phytochemicals such as capsascinin are known to have as many anti-oxidant and cancer-protective effects as chemotherapy drugs. Most of these bioactive substances have anti-cancer properties; It performs by stopping the progression of the cell cycle and stimulating tumor cell apoptosis (2). Red peppers contain different amounts of capsaicin.

Sweet peppers, also called bell peppers, are the most commonly known chili peperlaar in the family Capsicum annuum. Sweet peppers contain much lower amounts of capsaicin compared to hot peppers (3). Capsaicins are also important in the pharmaceutical industry due to their neurological effects as alcoioids (4). There are many studies on capsaicin antioxidants in the literature and it is well known that it has antioxidant properties (5).

2. Pepper Production

While China ranks first in the world with 16.023.500 tons of pepper production in a total area of 709.150 hectare (ha) in the world; Mexico ranks second with a production of 2,379,736 tons in an area of 136,132 ha. Turkey produces 2,072,132 tons of pepper in an area of 96,000 Ç(2018) data, the total amount of red pepper production is 179,264 tons, of which

approximately 35.28% is grown in Şanlıurfa, 30.62% in Gaziantep, 16.45% in Kilis, 9.82% in Kahramanmaraş and 1.94% in Hatay. The types of peppers grown in our country are table; kapya (for oil), bell, çarliston pepper. As a dryer; domestic peppers are such types as ornamental peppers. In addition, Hungarian pepper, Greek çarli, Chilean pepper, Jalapeno and Coarse bell (California Wonder) pepper types from block peppers with less production value are also grown. The fact that Turkey has a different ecological structure allows pepper varieties to be grown almost everywhere except for very cold regions (6). According to the official data of TUIK 2019; Tomato paste is cultivated in kapya with 879,775 tons of production and 308,417 (ha) cultivated area, Bell with 393,109 tons and 143,626 (ha) cultivated area and 313,149 (ha) cultivated area and Çarliston with 115,568 tons of production in 27,425 (ha) cultivated area (7).

According to The Observatory Of Economics Complexity (OEC) data, pepper, which is the 573 rd most traded product with a trade of 3.8 billion dollars, accounts for 0.021% of world trade.

The leading exporting country of the processed pepper sector was India with approximately 1.2 billion dollars according to 2020 data. In the same year, the leading importing country was the United States of America (USA) with 648 million dollars of imports (8).

3. Uses of Capsaicin

Capsaicin is the main bitterness component found in Capsicum species. Capsacin is used as a spice and flavoring. However, capsaicin is also used for medical and therapeutic purposes due to its pharmacological and physiological effects. In addition, capsaicin is also used against pests such as insects and mites, especially in organic agriculture, and some pathogenic fungi and bacteria (9). Hot pepper, which is consumed as a spice in many parts of the world, is widely used in the field of medicine due to the capsaicin it contains. Plants that are medically important have been used for the treatment of diseases among the people for centuries. Capsaicin has many applications in industry. Capsaicin is a homovalinic acid derivative and a fat-soluble phenol (10). Capsaicin is used extensively today in the fields of food, health and cosmetics. The most common use of capsaicin product is in the food sector due to its bitter properties. In addition, sauce production is among the fastest growing sectors of the Turkish economy. The demand for sauces is increasing with demographic consumption trends. When the two data are evaluated, the use of capsaicin in sauce and tomato paste production is an indication that the prevalence of commercial use will increase. Another use of capsaicin due to its antioxidant, painkiller and anti-tumor properties is in medical products. Capsaicin components reduce the transmission time of pain impulses by reducing substance P, which plays an active role in the transmission of pain in the central nervous system. In this way, it shows pain relief properties. Therefore, capsaicin is used locally to relieve the pain caused by herpes and shingles and to help reduce the pain caused by muscle, nerve and joint disorders. However, it has an important use in the cosmetic sector due to its nourishing and anti-hair loss properties (11).

Although the relationship with capsaicin cannot be proven by official data, it has been reported that in countries such as Thailand, where pepper consumption is high, cases of cancer caused by the digestive system are less common than in countries where consumption is relatively low. Research in Japan and China reveals that natural capsaicin components inhibit the development of cells with leukemia. Capsaicin is used as a raw material for tear gas used to intervene in

social events or for personal defense. It has also been found to be used in the wood industry as a preservative against sphaeropsissapinea and leptographiumprocerum fungi that cause wood discoloration. Another identified use of capsaicin is that it can be considered as an alternative to toxic paints. In an environmental risk assessment, it was shown that capsaicin is an alternative substance that can be used instead of toxic paint, especially on boats (12).

Another sector in which capsaicin is widely used is the agricultural sector. Capsaicin increases the endurance of the plant due to the fact that it causes an increase in some defense enzyme levels such as chitinase protein. Capsaicin is used against some pathogenic fungi and bacteria as well as its removal feature for pests such as insects and mites, especially in organic agriculture. It has been observed that it is effective for 2 months in removing pests such as aphids, red spiders, which have significant damage to natural pesticides, from the plant. Capsaicin prevents seed germination and prolongs germination time. For this reason, it is used effectively in agriculture, especially in the prevention of weeds. It is seen that capsaicin product is also used in livestock activities that can be evaluated within the scope of the agricultural sector. It has been found that especially if capsaicin is added to the chicken ration, it has stimulating effects on the metabolic activities of chicken. In this way, as a result of increased enzyme movements and fat burning, more efficient offspring and eggs can be obtained in chickens (13).

4. Health Effects of Capsaicin

Capsaicin is a secondary metabolite, the most important phenolic component synthesized from peppers, which allow plants to adapt to biotic and abiotic stress conditions (infection, injury, water stress, cold, and high light) (14). In living systems, the oxygen consumed during catabolism can be transformed into various radicals with high efficiency. The most important target of these molecules, known as reactive oxygen species, is DNA in the carcinogenesis process. Irreversible DNA damage can lead to carcinogenize, aging, and other degenerative diseases (15). Oxidative damage from free radicals may be responsible for the onset and progression of many chronic diseases, such as cancer, inflammation, and cardiovascular disease. In recent years, the antioxidant properties of natural compounds have been determined by examining the potential antioxidant components they contain (15,16). There are studies on the antioxidant effect of capsaicin in the literature and it is well known that it has antioxidant properties (17). Since capsaicins are alcoioid class compounds, they have a neurological effect and are therefore important in the pharmaceutical industry (18). Many studies have shown that capsaicin has potential antimutagenic and anticarcinogenic activitis (19). Capsaline has also been reported to selectively induce apoptosis in cancerous cells. (20) In addition, a positive relationship is reported between pepper consumption and the prevention of gastric cancer, pancreatic cancer and lung cancers in epidemiological studies (21).

One of the most effective radicals in metabolism is the hydroxyl and hydrogen peroxide radical, which can easily attack nucleotides and cause permanent damage to the structure of DNA, the most important inherited nucleotide (22). In the presence of H_2O_2, exposure of DNA to UV rays causes open-circular DNA to break and form linear DNA (linDNA; one or more fractures in both chains) (23). In the meantime, genetic disorders may occur as a result of breaks in the

DNA chain. Irreversible DNA damage can lead to carcinogenize, aging, and other degenerative diseases (24).

It is known that UV rays reaching the earth with the destruction of the stratosphere layer have negative effects on living things. UV rays cause serious diseases resulting in skin cancer and skin aging. Topical application of enzymatic and non-enzymatic antioxidants is an effective approach to protect the skin against the harmful ethics of UV rays (25). In fact, human skin has a number of mechanisms that will reduce the harmful effect of VIS (visible rays) and UV rays. However, high levels of exposure to UV rays can lead to a decrease in the amount of cellular antioxidants and ultimately to UV-induced oxidative DNA damage caused by reactive oxygen species. In addition to UV rays, free radicals can also cause DNA damage. For example, hydrogen peroxide, a type of free radical, causes DNA damage by converting guanine to 8 hydroxyguanine (26). Many studies have found that capsaicin has a protective effect on genetic material. Many studies have found that capsaicin has a protective effect on genetic material. Capsaicin extracted from green peppers grown in the Southeastern Anatolia region has been found to have a very good level of DNA-protective activities in different solvents and has been shown to have a protective effect on DNA even at low concentrations (27).

5. Capsaicin in the Defense Industry

Tear gas, pepper spray or OC gas, OC spray (OC="Oleoresin Capsicum") is a tear gas used in police work, riot and mayhem checks, personal self-defense, protection against animals such as bears and dogs (which may contain chemical compounds that cause uncontrolled tear flow in the eyes, irritating the eyes due to pain and even temporary blindness) (Bear Spray Vs. Dogs: How Effective Is It?", 2009 and Tbotech.com. "Pepper Spray", 2015).

According to the Scoville bitterness test, which is used to measure the bitterness of peppers and is the first test, the amounts of red pepper varieties and capsaicinoits were determined according to pepper types. The bitterness rate is directly proportional to the amount of capsaicin and contrary to what is known, capsaicin is also found in sweet bibes (Bayıl Oğuzkan, S and Uğraş, 2019).

Pepper spray production, the active ingredient of which is capsaicin, is generally produced from red chile pepper and cayenne pepper throughout the world. In a study in which red pepper varieties and capsanoites were investigated as scoville units, the highest capsphenoid content was found in Haberano, which grows on the Yucatan Peninsula, and the lowest was found in new Mexican peppers (Kadakal and et al., 2001). Therefore, pepper spray can be produced from different types of peppers with the appropriate purification method without even the need for Haberano pepper, which has the highest capsaicin content.

Pepper spray is produced in three different spray formats among itself.

1- OC (Oleoresin Capsicum): It is the most common and known form of tear gas. The active ingredient is capsaicin. Other auxiliary materials are filler materials. Capsaicin is not a water-soluble substance. Victims are advised to move their eyelids frequently to produce more tears and not rub their hands on their eyes, faces.

2- CS (Orthochlorobenzalmalonitrile): It is known as tear gas. It can be used alone or with OC. CS is a very effective type that is most popularly used. It makes victims passive and is active enough to cause vomiting.
3- CN (Alphachloroacetapheone): It is a form of gas bomb used by military and police organizations for defense purposes. It can lead to temporary loss of balance and skin problems. The effects of CN gas last longer than CS.

When we compare these three forms of gas spray, it is known that OC, whose active ingredient is close to 95%, is in more organic form than the others and does not leave long-term damage. For this reason, we can say that the use of spray forms with capsaicin active ingredient is important for defense and for the humane treatment of both victims and victims. In recent years, the production and use of plant-based organic weapons, the active ingredient of which is capsaicin, has become widespread.

It is known that capsaicin extracts obtained from pepper were encapsulated and started to be used as weapons. The effects of capsaicin, which has a wide range of uses for both defense industry and medical purposes, are examined in this section. Although it is important to improve both the cultivation areas and the production conditions of pepper, which is also very common in dietary consumption, we think that different methods should be developed for the production of the active substance. In addition, not only the benefits of dietary intake but also the importance of capsaicin, which is used at a simple level as a means of personal defense, is discussed in this article.

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ROLE OF MICRORNAS IN BREAST CANCER: MOLECULAR INVESTIGATIONS

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1. Introduction

According to the International Agency for Research on Cancer (http://www.iarc.fr/), in 2020, breast cancer is the most common cause of death in women that include 4.4 million. It is a heterogeneous cancer type that have a particular gene expression profile (Aliya et al., 2022). To make an effective treatment of this cancer, it is important to understand the processes and mechanisms that are involved in the development of this cancer including malignancy (Kim & Cho, 2022). It is also required to find the actual findings of resistant coupled with cancer drugs and chemotherapies (Punekar et al., 2022).

It is known that miRNAs are important regulators of whole mRNA functions during normal and abnormal conditions, particularly in different cancers (Seneff et al., 2022). The irregularities of miRNAs in all cancers especially in breast cancer are associated with development, inhibition, metastasis and drug resistance (Najafi et al., 2022). So, these miRNAs can be targets for modulation of gene expressions for effective treatment of breast cancer. Recent literature is supporting this topic because they are secreting from exosomes and body fluids (Tenchov et al., 2022). It is also shown that the circulating miRNAs expression level is totally different in healthy people and cancer patients (Shi et al., 2022).

In this chapter, we summarize the major functions of miRNAs in breast cancer development from benign to metastasis and discuss the clinical applications of modulating miRNA associated to mRNA and finally find the available miRNAs relationship with breast cancer.

2. miRNAs Biosynthesis

MiRNAs are 20-25 base pair sequence (non-coding RNAs) which control post-transcriptional gene regulation (Xiong et al., 2022). RNA polymerase II is primarily responsible for miRNA transcription as lengthy primary transcripts known as pri-miRNAs, which are distinguished by hairpin topologies (Marquardt et al., 2022). Such pri-miRNAs are converted by the RNase III enzymes Drosha and its co-factor DGCR8 to 70-100 base prototype miRNAs (pre-miRNAs) in the nuclei (Nguyen et al., 2021). The mirtron process, in which introns are spliced and debranched by lariat debranching enzyme, as well generates a variety of pre-miRNAs (Campos-Melo et al., 2022). A component made up of both the RNase III enzyme Dicer and the transactivating response RNA-binding protein cleaves them into miRNA:miRNA duplexes after they have been exported to the cytoplasm by Exportin-5, a member of the Ran-dependent nuclear transport receptor family (TRBP) (Takahashi et al., 2015). In addition to forming a protein complex with Dicer in place of TRBP, the RNA editing enzyme adenosine deaminase working on RNA 1 can also enhance the processing of miRNAs (Ota et al., 2013).

3. Breast cancer and miRNAs

It is well documented that miRNAs are crucial for the growth of tumors. According to the molecular subtypes of tumors, they express differently, and the open spot of particular miRNAs categorize to tumor abnormalities (Oliveto et al., 2017). It is crucial that the amplification of specific genes results in the up- or down-regulation of miRNAs, which then silences or amplifies tumor suppressor genes (Meng et al., 2013). Therefore, deregulation of miRNA expression has an impact on cancer progression-related activities such metastasis, tissue invasion, and apoptosis escape.

Several miRNAs **(Table 1)** have been described as crucial regulators of tumor genesis, metastasis, and chemoresistance in breast cancer and have been identified as tumor suppressors or oncogenes. Conceptually, the four stages of tumor formation are: (i) tumor genesis, (ii) therapy resistance and tumor progression, (iii) malignant conversion, and (iv) tumor advancement.

Table 1. List of miRNAs that are targets particular genes to perform specific functions in breast cancer

Sr#	Functions	miRNAs	Targets	References
1	Enhance apoptosis	miR-155	TP53	Mikamori et al., 2017
2	Inhibition of cell cycle	miR-15a	CCNE1	Luo et al., 2013
3	Increase apoptosis	miR-155	TP53INP1	Mikamori et al., 2017
4	Influence cell cycle	miR-222-3p	SOCS3 / Jak2/Stat3/Bcl-2	Feng et al., 2017
5	Influence on cell cycle	miR-21	PTEN	Zheng et al., 2017
6	Downregulatıon of MDR1 in breast cancer	miR-200c	MDR1	Safaei et al., 2022
7	Inhibition of cell cycle	miR-20a-5p	SRCIN1	Guo et al., 2019
8	Inhibit growth/invasion	miR-590-5p	Skp2	Tong & Jin, 2022

9	Tumor supressor	miR-497	Septin 2	Cai et al., 2022
10	Regulation of immunity	miR-190	IL-1R1	Yu et al., 2018
11	Tumor supressor	miR-381	FYN, ERK, p38	Mi et al., 2018
12	Tumor supressor	miR -590-5p	PITX2	Gao et al., 2019
13	Regulation of expression	miR -150-5p	E-cadherin	Lu et al., 2019
14	Regulation of expression	miR-370-3p	NF- κB	Ren et al., 2021
15	Inhibition of cell cycle	Mir-7	*KLF4*	Okuda et al., 2013
16	Inhibition of cell cycle	miR-130-3p	*RAB5B*	Kong et al., 2018
17	Tumor supressor	*miR-4319*	*E2F2*	Chu et al., 2018
18	Tumor supressor	miR-155	CD44/ CD90/ ABCG2	Zuo et al., 2018
19	Inhibition of cell cycle	*miR-29a*	EGR1	Wu et al., 2019
20	Regulation of gene espression	*miR-9*	*Nanog/CD133* / *Oct4*	Cheng et al., 2018
21	Regulation of gene expression	*miR-221*	*Nanog/CD133* / *Oct4*	Cheng et al., 2018
22	Regulation of cell cycle	miR-195	FASN, HMGCR, ACACA, CYP27B1	McAnena et al., 2019
23	Tumor supressor	miR-206	NOTCH 3	Chaudhari et al., 2022

24	Regulation of cell cycle	miRNA-32	CPT1A	Zheng et al., 2022
25	Regulation of cell cycle	miR-8084	ING2, p53-BAX	Gao et al., 2018
26	Regulation of cell cycle	miR-484	PAX-5	Harquai et al., 2019
26	Regulation of cell cycle	miR-708-3p	ZEB1/ CDH2/ VIM	Lee et al., 2018
27	Regulation of cell cycle	miR-142-3p	Bach-1/CXCR4/MMP9/VEGFR	Mansoori et al., 2019
28	Regulation of cell cycle	miR-3178	Notch1	Kong et al., 2018
29	Regulation of cell cycle	miR-1266/miR-185/ miR-30c	BCL2L1	Ostadrahimi et al., 2018
30	Regulation of cell cycle	miR-655	COX2	Majumder et al., 2018
32	Regulation of cell cycle	miRNA-29b	AKT3 SPIN1	Li et al., 2017
33	Regulation of cell cycle	miRNA-100	VEGF	Pakravan et al., 2017
35	Regulation of cell cycle	miRNA-4530	VASH1	Zhang et al., 2017
36	Regulation of cell cycle	miR-1469	PI3K/ AKT	Zhang et al., 2019
37	Regulation of cell cycle	miR-425-5p	PTEN	Zhang et al., 2020
38	Regulation of cell cycle	miRNA-96-5p	FOXO3	Yin et al., 2020
39	Regulation of cell cycle	miR-206	DEPDC1	Zhang et al., 2019

40	Regulation of cell cycle	miR-205	TG2	Seo et al ., 2019
41	Regulation of cell cycle	miR-345	KISS1	Kaverina et al., 2017
42	Regulation of cell cycle	miR-503	L1CAM	Xing et al., 2018
43	Regulation of cell cycle	miR-532/502	SET8	Cantini et al., 2019
44	Regulation of cell cycle	miR-143/145	CIAPIN1	Deng et al., 2018
45	Regulation of cell cycle	miR-132/212	PTEN	Xie et al., 2018
47	Regulation of cell cycle	miR-137	SRC3	Guo et al., 2019
48	Regulation of cell cycle	miR-663b	TP73	Jiang et al., 2018
49	Regulation of cell cycle	miR-196a	HOX/FOX	Milevskiy et al., 2019
50	Regulation of cell cycle	miR-18a	MYBL2	Luengo-Gil et al., 2019
51	Regulation of cell cycle	miR-186-3p	EREG	He et al., 2019
52	Regulation of cell cycle	miR-26a	E2F7	Liu et al., 2018

3.1. Tumor Genesis

Cancer-initiating cells (CSCs) are in charge of the growth and spread of tumors (Ghanei et al., 2020). The cells have many physiological traits in common with typical somatic stem cells, such as their ability to divide asymmetrically as well as the potential to pump tiny compounds (Steinbichler et al., 2018). In a study, they revealed that breast samples' CD44+/CD24/low Lineage cells exhibit an exceptionally significant tumor-seeding potential (Abraham et al., 2005) while, in another study, some researchers said that Let-7 is a master regulator of CSC characteristics such self-renewal capacity and tumor-seeding capacity (Thammaiah & Jayaram, 2016). According to Acikgoz et al, breast malignant tissues' CD44+/CD24/low cell populations

exhibit strong tumorigenesis and epithelial to mesenchymal transition (EMT) characteristics (Acikgoz et al., 2022). The genetic factors and molecular processes driving that development of severity as well as the ensuing systemically dissemination by affected tissues are important to understand since EMT is frequently seen throughout metastasis and invasion (Nathanson et al., 2022). Therefore, the loss of epithelial markers like E-cadherin, up-regulation of mesenchymal markers like N-cadherin and vimentin, loss of cell-cell adhesion, cell polarity, and the development of cell invasive capacities are all characteristics of the EMT type (Hamidi et al., 2022). Cavallari et al. observed that miR-205, miR-200a, miR-200b, miR-200c, miR-141, and miR-429, are specifically associated with poor prognosis in different cells undergoing EMT (Cavallari et al., 2021). The miR-200 regulator was demethylated either by ten eleven translocation (TET) group, and miR-22 promotes the formation of CSC traits like EMT and just a metastasis nature by suppressing the miR-200 group (Karami Fath et al., 2022).

3.2. Therapy Resistance and Tumor Progression

Locally as well as remotely recurrent malignancies frequently demonstrate development of resistance to therapy, similar to how breast tumors or tumor-initiating cells may display inherent resistance to cancer treatments (Ji et al., 2021). The development of the cancer and the patient's outcome are intimately tied to therapy resistance (Mehraj et al., 2021). The significance of miRNAs in breast cancer therapeutic resistance is still poorly defined (Javdani et al., 2022). The activities of some miRNAs for controlling therapy resistance in vitro are described here, however their involvement in therapy resistance in breast cancer models in vivo has not yet been shown (Garrido-Cano et al., 2021). For example, in tamoxifen-resistant MCF-7 cells, ERa-negative breast cancer cells, and HER2- or ERa-positive primary breast cancer tissues, levels of miR-221/222 was shown to be up-regulated (Kalinina et al., 2021). Additionally, paclitaxel-resistant MDA-MB-435 breast cancer cells exhibited up-regulation of miR-221/222 and miR-125b (Shahrzad et al., 2021). It showed strong relationship between miRNAs and target genes in breast cancers (Zhang et al., 2022). When relative to the primary culture, doxorubicin-resistant MCF-7 cells (MCF-7/DOX) were shown to have a substantial percentage of down-regulated and up-regulated miRNAs (Yang et al., 2021). For illustration, down-regulated miR-127, miR-34a, miR-27b, and let-7 have been linked to higher levels of the anti-apoptotic targets, including BCL6, NOTCH1, CYP1B1, and K-RAS (Filkowski, 2010) whereas up-regulated miR-206, miR-106a, miR-21, and miR-214 have been linked to lower levels of the target proteins, including ERa, RB1, and PTEN etc (Llobat & Gourbault, 2021).

3.3. Malignant Conversion

The role of miRNAs in the regulation of metastatic processes is crucial in breast cancer. For instance, miR-10 showed a greater level of expression in metastatic disease than in non-metastatic breast cancer, therefore, it is known as a critical regulator of breast cancer metastasis (Harquail et al., 2012). Some miRNAs, such as miR-126, miR-206, and miR-335, shown their function as breast cancer metastasis suppressors (Tavazoie et al., 2008). While miR-206 and miR-335 prevent the invasion of metastatic cells, miR-126 contributes to the decrease of breast cancer tumors (Negrini & Calin, 2008). The breast cancer that is connected to the transcription factor GATA3 in metastasis is suppressed by miR-29b upregulation (Chou et al., 2013). But GATA3 is necessary for maintaining the differentiation of luminal epithelial cells, and miR-

29b depletion is associated with a poor prognosis in patients with breast cancer (Chou et al., 2013). In another studies, miR-29b suppresses a network of pro-metastatic regulators linked to angiogenesis, collagen remodeling, and proteolysis to prevent the spread of breast cancer (Yan et al., 2015).

3.4. Tumor Advancement

The CXCL12 chemokine gene is directly targeted by the miRNAs including miR-127, miR-197, miR-222, and miR-223, which prevent breast cancer cells from proliferating and induce or maintain a latent state in breast cancer cells (Takahashi et al., 2015). In another study, interleukin-4 produced from CD4+ T cells activates tumor-associated macrophages, which then deliver miR-223 to breast cancer cells (Cocks et al., 2021). Through direct targeting of myocyte enhancer factor 2C, miR-223 causes the nuclear accumulation of b-catenin, which leads to the development of angiogenesis and invasiveness (Cocks et al., 2021). In another example, high levels of miR-105 secretion and expression are linked to highly metastatic breast cancer cells. By inhibiting the production of the tight junction protein ZO-1 in distant tissues, miR-105, which is produced by cancer, damages tight junctions (Llobat & Gourbault, 2021). As a result, breast cancer cells that overexpress miR-105 exhibit extremely active spreading behavior and increase vascular permeability (Takahashi et al., 2015).

4. Conclusion

We have outlined the functions of miRNAs in the biology of cancer in this chapter, concentrating on breast cancer. A growing amount of research has shown that the patient's health and tumor stage are related to the aberrational expression patterns of miRNAs in breast cancer. Additionally, there are various subtypes of breast cancer, each of which has a distinct molecular profile and functions, and these subtypes are determined and regulated by certain miRNAs. Profiling miRNA expression in breast cancer comprehending the molecular processes behind miRNA expression and release are crucial areas of study in both fundamental and applied research.

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IMPACTS OF COVID-19 ON TURKEY

Cavide DEMİRCİ

Büşra ZENCİR

1. Introduction

COVID-19 emerged in late December 2019 in Wuhan, China. This disease has been defined by the World Health Organization (WHO) as a new type of coronavirus. (Wang, Wang, Chen and Qin, COVID 2020). The virus, which showed a high contagiousness, spread all over the world, especially in Europe, in a short time. (World Health Organization [WHO], 2020). The pandemic, with symptoms such as cough, fever and severe acute respir atory tract infection, had fatal consequences and threatened the world.(Ministry of Health, 2020). According to research,80% of cases have survived the disease without requiring serious medical attention.However, in severe cases, the disease can turn into pneumonia and artificial respiration methods may be needed. However, in serious cases, it has shown that the disease can turn into pneumonia and artificial respiratory methods may be needed. It has been observed that one out of every five people in contact with the disease has a severe illness. It has been determined that individuals with chronic diseases such as diabetes, high blood pressure, lung and heart diseases and elderly people are in the risky group. Apart from the elderly, children and young people are also likely to get the infection and spread it to their environment. There have been cases where people in this age group also had a severe illness. (Johns Hopkins, 2020; TR Ministry of Health, 2020b). The negative effects of the global epidemic have been seen in many areas such as economy, sociology, psychology, education, starting from the field of health. The extent of this negative effect has increased day by day and has given concern.The rate of transmission and spread of the infection caused by the 2019-nCoV virus is much faster than other viral infections seen in the history of the world. (Ergül, Altın Yavuz, Gündoğan Aşık & Kalay,2020).

Governments had to take radical measures such as social distancing (social isolation), quarantine practices, martial law, travel and education restrictions to control the spread of the epidemic. (Bourouiba, 2020).

The first case in Turkey was detected on March 11, 2021. (Dikmen&Bahceci,2020). After the first case of COVID-19 was seen in Turkey, priority was given to health and safety measures, and it was decided to suspend education in all schools and universities. (MEB,2020). As the spread of the epidemic within the country and its consequences worsen; all domestic and international flights were suspended, scientific, cultural, artistic and similar meetings and activities were postponed, employees in public institutions and organizations were either given administrative leave or were given the opportunity to practice flexible working methods, (remote working) inter-city travels are subject to the permission of the governorship, a curfew has been declared for individuals over the age of 65 and under the age of 20, and a curfew has been declared at regular intervals for all individuals living in 30 metropolitan cities. (TC Official Newspaper, 3 April 2020, no: 89780865-153). With the "Additional Circular on Parks, Recreation, Picnic Places within the Scope of Combating the Coronavirus Epidemic" published

by the Ministry of Interior, from 28-29 March 2020 until the spread of the virus have been prevented; All kinds of activities carried out by the citizens on the beaches, recreation areas and picnic areas in the settlements on weekends have been prohibited. It has been reported that these measures can also be applied on weekdays by looking at the effectiveness of the bans and the province-district situations. (Çınar and Oğuz, 2020: p. 7).

Since June 2020, some measures have been applied by stretching, but since the beginning of 2021, the measures have been tightened again. (Erdoğdu Koçoğlu, Sevim, 2020). As in the whole world, these measures taken in Turkey have affected both social life and sectors such as education, economy and health.

2. Education During the Pandemic in Turkey

After the first case was announced in Turkey on March 11, 2020, face-to-face education was suspended in universities and all schools affiliated to the Ministry of National Education. While a holiday was announced for a few weeks in educational institutions at the beginning, it was foreseen that schools would not be able to open in the spring term, with the increase in the number of cases added to the news of death. In order not to interrupt the education and training process, the distance education process has started in Turkey as in many countries. In order to manage this process and the crisis, the Council of Higher Education (YÖK) took action quickly and took decisions in terms of transforming the education process into distance education in the spring term of 2020. (YÖK, 2020a; YÖK 2020b). With these explanations, face-to-face education was suspended at all education levels , it was decided to switch to distance education, postpone local and central exams, and introduce web-based exams in measuring and evaluating student achievement**.**

Distance education started on March 23, 2020 in primary and secondary education institutions. Cooperation between the Ministry of National Education and the Turkish Radio and Television Corporation (TRT) was established. With the cooperation of these two institutions, three different television channels were created to support distance education. In addition, the Ministry of National Education increased the capacity of EBA, the education platform in Turkey, and provided support to distance education. (Ozer, 2020). Education in Turkey was carried out by using different applications through distance education. In higher education, education was interrupted for a short time in the first place, then it was reported that the spring semester would be completed with distance education in 2020. (YÖK, 2020).

For EBA TV, 3 different channels and 6 different frequencies were broadcast on TRT, and lesson videos were broadcast on the basis of branches suitable for each class. (EBA, 2020). Thus, distance education started with “EBA TV Primary School”, “EBA TV Secondary School” and “EBA TV High School”. Classes are planned as 20 minutes each, with a 10-minute activity zone in between. As of Monday, 13 April 2020, online classes were applied to 8th and 12th grades via the EBA platform, and implemented in all grade levels as of April 23, 2020. (MEB, 2020). In online class application, teachers and students had the opportunity to exchange class online.

Online classes were defined by school administrators at certain times and announced to teachers and students, ensuring that students and teachers were ready during the online classes. With the

"whiteboard" application displayed on the screen during the online class, teachers were able to teach using the blackboard and share documents with their students**.** In addition, they were able to share tests, videos, messages or other documents with students through the EBA platform. (MEB,2020)

Crisis management features were observed when the applications made in the field of education management in Turkey during the COVID-19 process. Following the school closures, to ensure teachers,students,parents and administrators were least affected by the crisis, the following were done. Information guides for adults were prepared to help children in order to maintain psychological stability during pandemic period. A psycho-social support line was set up and online activities were done. (MEB, 2020). The infrastructure of the existing digital education platform EBA (Education Informatics Network) was strengthened, and distance education activities were supported through this platform and online classes were implemented. In addition, in order to support students' access to this education portal, cooperation with GSM operators was provided to students up to 8 GB of free internet access. (Ozer, 2020). This showed that the pandemic crisis reduced the impact on the educational organization and that crisis management plans and practices were made in education management.

3. Health Services During the Pandemic in Turkey

With its geographical location at the transition point between Asia and Europe, Turkey could not escape being affected by the Covid-19 pandemic, which spread through social contact. The late arrival of the pandemic in Turkey enabled the government to benefit from the experiences of other countries, thus strengthening the hand of the relevant actors in combating the disease. Turkey, with the transformation in health since the beginning of the 21st century, has made serious progress in the field of health, started to take precautions before the pandemic started, and met the disease with various plans. While many countries suffered from shortages of drugs, medical supplies and medical devices with the pandemic, Turkey helped many countries with these materials. It showed a successful state reaction against the pandemic with the domestic respirators it produced and the health facilities with the capacity of a significant number of intensive care patient beds, which it completed in a short time. In particular, the public coverage of health expenditures originating from Covid-19 and the provision of state assurance against the disease were another aspect of the success of Turkey's pandemic management. (Yorulmaz, Kıraç & Aydoğdu, 2021: p. 166).

Various action plans were prepared in order to take the necessary precautions in the field of health in our country, reference hospitals that played a special role in this process were established, and isolated rooms were arranged in these hospitals. A sufficient number of materials such as masks and disinfectants that may be needed for virus protection were provided. The local virus diagnosis kit has been developed and it has been possible to detect the virus in 1.5 hours (Duran, 2020: p 16).

Turkey is one of the countries with the lowest death rate per million people. The countries with the highest number of recovered patients are Turkey, Australia, China, Luxembourg, Germany and Austria. and South Africa**.** However, the countries with the highest test averages per million

inhabitants are Austria, Denmark, Estonia, Germany, Portugal, Russia, Belgium and Spain. (Tekin, 2020 p.347).

Since March 11, 2020, when the COVID-19 virus was detected in the country, healthcare professionals have played a very important role in the diagnosis and treatment of the disease with a combative, self-sacrificing, solution and help-oriented approach. During the epidemic, hospitals became the most risky institutions in terms of health and safety. These risks can be expressed as physical, chemical, biological factors and psycho-social structure, which are the natural consequences of the working environment. As health workers were directly related to human health as a requirement of their work, their stress and anxiety levels increased intensely. (Yılmaz et al., 2021: p 977-978).

Within the scope of the precautionary policy throughout Turkey, the practice of "stay at home" became active. This practice, which was carried out voluntarily at the first times when the virus spread, later turned into a curfew at regular intervals, covering 30 metropolitan cities and Zonguldak provinces, and entrances and exits to these cities with private vehicles were prohibited. (Kutlu, 2020: p. 335). Certain restrictions were introduced in order to make the stay-at-home practice operative: Measures such as holding sports competitions without spectators until the end of April, then postponing all competitions, adjourning cases that were not urgent in judicial proceedings, and restricting visitors to hospitals that have a high risk have been taken. The temporary postponement of activities such as national and international scientific congresses, meetings and conferences that would be held in April and May greatly benefited in preventing the spread of the virus among the masses. (Çınar and Oğuz, 2020: p. 6).

4. Economy During the Pandemic in Turkey

Almost all countries in the world, whether developed or developing, had to take a series of protective measures in order to contain the rapidly increasing spread. These strict measures, ranging from the ban on travels, the closure of workplaces, social isolation to curfews, brought most sectors of the economy to a standstill, and even caused some to come to a standstill. All sectors, mainly domestic and international flights, transportation services, railway services, sports, education, trade and service organizations, were adversely affected by the COVID-19 pandemic. The economies of most economically strong countries faced the threat of high inflation and rising unemployment due to excessive spending on the treatment and rehabilitation of COVID-19 patients and their families, as well as support for struggling businesses. This pandemic in the world led to a recession that negatively affected many interconnected sectors such as agriculture, commerce, industry, transportation, finance and banking, health, airlines and energy markets.

On March 18, 2020, with the Economic Stability Shield program, measures were taken against the shrinking markets, while at the same time, measures were started to be taken for commercial activities that allowed the spread of the disease and require contact. Between 15-18 March 2020, 149,382 workplaces temporarily suspended their activities across the country. In this way, it was possible to provide service without allowing customers to sit. With a circular dated March 24, 2020, the working hours of the markets and the number of customers shopping in the

markets were regulated. With the Economic Stability Shield Package dated March 18, 2020, a number of measures were taken. (Turan&Çelikyay,2020).

In our country, the number of visitors in the first two months of 2020 increased in January (16.11%) and February (3.78%) compared to the same periods of the previous year. This trend created an expectation that the 2020 season would be more intense compared to previous years. However, the first case of the unexpected global pandemic COVID-19 was detected in our country on March 11, 2020. In parallel with the increase in the number of cases both in our country and in other countries, travel bans entered into force one after another throughout the World. (Atay, 2020: pp. 168-169). In our country, the effect of the pandemic in provinces such as Antalya, Muğla and Nevşehir, whose economy is largely dependent on tourism, was much more negative than in other provinces. The tourism establishments and the people employed in these provinces were adversely affected by the process. The post-pandemic process needs to be managed very well by the public and private sectors, especially in destinations whose economy is dependent on tourism. It was necessary to take steps to minimize visa and similar travel barriers, facilitate travel opportunities, and encourage travel to our country. (Atay, 2020: p. 169).

5. Conclusion and Discussion

Many countries adopted various methods of intervention to prevent the spread of the coronavirus pandemic. The rapid policy decisions taken by our country included the most effective and exemplary implementations of these interventions for other countries. (Çetin,2020)

During the pandemic process, schools and universities rapidly implemented distance learning systems, but schools with little or no experience in distance learning, as well as schools and especially teachers who did not prepare distance learning resources, faced difficulties in using online applications. (Zaharah and Kirilova, 2020). In countries that wanted to continue education uninterrupted, it was seen that teaching opportunities supported by different technological infrastructures were used and distance education was used as the main source of learning. (Can, 2020).

Since the first months of 2020, all countries of the world have taken a series of measures in order to continue their education activities effectively despite the Covid-19 pandemic. With the recommendation of the Scientific Committee and the decision of the Ministry of National Education, distance education was started all over the country in order to prevent the spread of the pandemic. Especially in Turkey, with the break given to face-to-face education on March 16, 2020, the distance education process, which started on March 23, 2020, changed the communication and interaction of teachers with students , the way teachers conducted their lessons, and there was a transition to an online-based education. In this process, teachers, like students and parents, tried to keep up with digital education. It can be said that important developments regarding the technological and pedagogical field knowledge and experiences of teachers emerged, with many teachers turning to internet programs that enabled them to reach their students, such as online meeting tools, during the pandemic process. (Red Red, 2020).

From the very beginning of the distance education process, technical problems that prevented distance education from working effectively took up a great place. Since the whole process started very quickly without extensive preparations, it was inevitable to experience some problems with EBA when millions of students and teachers started using it. Due to the technical problems experienced in EBA and the inadequacy of the lessons on TV, some private schools started to continue their education on their own digital platforms. (Akbulut, Şahin, & Esen, 2020).

Distance education negatively affected the interactions between students-students / students-teacher. Because in virtual classroom environments, teachers and students could not communicate as easily as in formal education. In virtual lessons, teachers were not even sure if students were present in the lesson, as students did not have to turn on their cameras or microphones. Despite the efforts made, there were students who could not get full efficiency from distance education. (Akbulut, Şahin & Esen, 2020).

It was observed that there were many problems in the education made over EBA TV. The problem became more serious than we thought and affected a student body of 18 million and their families. (Şimşek, 2020).

Despite the efforts of all education stakeholders trying to keep up with this process, which covered all education levels, from pre-school to higher education; The process brought with it some problems on the basis of students, teachers and families. These problems (Impey, 2020; Oyedotun, 2020; Panesar et al., 2020) primarily affected students on a global scale. (UNESCO, 2020).

The uncertainty created by Covid-19 and the slowdown in economic activity continue in 2022. However, the pressure on the economy has weakened compared to March 2020. Nevertheless, the risks associated with such situations that may arise in the future must be properly evaluated. (Münyas, 2021).

When evaluated in terms of the Turkish economy, especially the movement restrictions economic activity have created a serious burden on the Travel restrictions ended passenger mobility, distance education module was introduced in education, sports and artistic activities were suspended, and the accommodation industry came to a standstill. In terms of the labor market, the remote working module was introduced, the physical working system of the market was changed within the framework of social and physical distance rules, and production was suspended at some production points. Contraction in export revenues and tourism revenues, changes in household consumption behaviors, contraction in industrial production index and gross fixed capital formation signaled a contraction for the next quarter. In short, COVID-19 has affected all aspects of social life, especially economic and social, and brought the processes other than basic services to a standstill. (Noble, 2021).

The pandemic has affected everyone; However, studies have revealed that the pandemic affects people whose jobs are not suitable for working online, those who work in the private sector or self-employed, the poor with low income, low education and women more negatively than others. (Bozkurt,2020) In addition to the policies put into effect by our government against the Covid-19 epidemic, which has completely changed our entire life order, many institutions,

organizations and non-governmental organizations have tried to create awareness to be protected against this epidemic with various studies they have carried out. (Turkoglu & Yilmaz, 2021).

Turkey has shown a successful performance, especially in the health sector, in the fight against COVID-19, and continues to do so. Thanks to the steps taken both in the health sector and through other sectors in Turkey, both the case contamination and the rate of increase have been brought under control, and the diagnosis and treatment processes have been carried out effectively. As a result, the death rate remained at a very low level. (İşlek, Özatkan, Utku, Arı, Çelik & Yıldırım, 2021).

The Scientific Committee and Operations Center were established 31 days before the World Health Organization's virus pandemic declaration, and 1 million boxes of Hydroxychloroquine were taken and stored before the first case was seen. Before the first case was seen, Turkey took all the necessary precautions and measures in a timely manner, preventing huge loss of life. Before the first case was seen, the information about the 14 rules to be followed in order to protect from the virus was broadcast in the media both as a public service announcement and in all news channels, with the participation of the members of the Science Board, the public was informed. Quarantine measures taken on time; Timely home quarantine of people aged 20 and under and over 65 has helped protect those aged 65 and over most affected by the virus against the risk of death. It is among the important decisions that prevent the spread of the virus and prevent great loss of life to stay at home, which can be a hidden carrier in the spread of the virus. Undoubtedly, Turkey has prevented great loss of life with the decisions it took at the first moment of the epidemic in China, and especially thanks to the Scientific Committee it formed and the decisions taken by the committee. (Wrestler, 2020).

The number of daily tests, the distribution and increase of the number of cases, the course of the cases, the intensive care occupancy rates, the number of intubations, the number of deaths were followed up day by day. In addition, these numbers are transparent and accurately recorded on a daily basis, reported to WHO and disclosed to the public. (Akgun, 2020).

6. Suggestions

The most important reason for trying different approaches in universities is that institutions are not ready for distance education processes. In-service training can be given to academics on using computer and internet-based technologies.

Free and unlimited internet service can be offered to all students and parents to be used on certain platforms. Satellite internet can be provided in rural areas where internet is limited. Informative broadcasts and posts can be made to increase parent support. Methods that can be used to motivate students can be announced through publications and shares.

It can be ensured that the distance education system to be used by the institutions is simple, plain, understandable and easy to use. It can be ensured that universities establish a solid infrastructure on distance education support services and provide continuous support to students.

YÖK can develop a national distance education system that can be used by all universities in Turkey. Quantitative and qualitative studies can be designed by taking the opinions of all stakeholders (teaching staff, students, distance education process manager) for the evaluation of emergency distance education at universities during the pandemic period. Training can be given to all stakeholders in distance education in a way that covers certain standards.

Rich content can be prepared in order to increase students' interest in the live lesson. For assessment processes, an exam environment such as face recognition that only the relevant student can access can be created.

With the current situation in Turkey, we can say that four factors are very important in digitalization in education; 1. Technological infrastructure, 2. Developing the online education skills of educators and increasing their capacities, 3. Producing quality online education content, 4. Producing effective assessment and evaluation systems for online education. (Avcı&Mediterranean, 2021).

In order to eliminate the negative effects of the pandemic on the Turkish economy, it may be necessary to use monetary policy together with fiscal policy and other political instruments. Permanent policies should be produced for fragile sectors and programs such as agricultural support packages can be implemented. (Arabcı&Yücel,2020).

The tourism sector is a very important sector for the Turkish economy. Because the share of tourism revenues in GDP in Turkey in 2018 is 3.8%. The number of registered people employed in tourism is over 1 million in 2018. (TUIK, 2020). Therefore, there is a need for an additional economy package for the tourism sector. In particular, the measures to be taken for employment and the intervention of the state in the tourism sector may also positively affect the trust of the people employed in tourism in the sector. (Spring&İlal,2020).

Although the effect of the Covid-19 epidemic has tended to decrease in recent days, the epidemic is not over yet. Even if Covid-19 leaves our country completely, it is necessary to act carefully against the risk of a pandemic that may develop again. In the next period, more importance should be given to preventive and preventive health services in our country, and permanent solutions should be produced that will be an alternative to pandemic control policies with health investments and planning. Studies should be carried out to increase the health literacy of the society. (Turkoglu & Yilmaz, 2021).

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SECTION 2
LIFE SCIENCES

GREEN CHEMISTRY

ACTIVITY BASED COSTING, ITS ADOPTION AND USEFULNESS IN ELECTRONIC HEALTH RECORDS IMPLEMENTATION: A CASE OF BAREWA CLINICS, KANO, NIGERIA

WATER - A WONDER CHEMICAL IN THE WORLD

RECENT DEVELOPMENTS AND FUTURE PROSPECTS OF CAPACITORS

GREEN CHEMISTRY

Faeeza Hazim HASAN

1. Introduction

Green Chemistry is that the style of chemical merchandise and processes that cut back or eliminate the employment or generation of risky substances.

inexperienced Chemistry applies across the life cycle of a chemical product, together with its style, manufacture, use, and supreme disposal. inexperienced chemistry is additionally called property chemistry

2. Importance of Inexperienced Chemistry

1. Prevents pollution at the molecular level.
2. could be a philosophy that applies to any or all areas of chemistry, not one discipline of chemistry.
3. Applies innovative scientific solutions to real-world environmental issues.
4. leads to supply reduction as a result of it prevents the generation of pollution.
5. Reduces the negative impacts of chemical merchandise and processes on humanhealth and therefore the atmosphere.
6. Lessens and generally eliminates hazard from existing merchandise and processes.
7. styles chemical merchandise and processes to cut back their intrinsic hazards.

3. Chemistry & Society

3.1. Pharmaceutical

Drugs (pain killers, antibiotics, heart and hypertensive drugs), disinfectants,vaccines, dental fillings, anaesthetics, contraceptives.

3.2. Agriculture

Fertilizers, pesticides.

3.3. Food

Preservatives, packaging and food wraps, refrigerants. Transportation: gas and diesel, chemical action converters to cut back exhaust emissions. Clothing: artificialfibers, dyes, waterproofing materials.

3.4. Safety

Polycarbonate materials for crash helmets.

3.5. Sports

Composite materials for rackets, all weather surfaces workplace inks, photocopying toners.

3.6. Homes

Paints, vanishes and polish, detergents, tormenter killers.

3.7. Chemical Disasters

1956: Minamata disease was initial discovered in Minamata town in Japan. it absolutely was caused by the discharge of alkyl mercury within the industrial waste from a chemical works.

1961: Itai-itai illness was caused by Cd poisoning thanks to mining in Toyama Prefecture in Japan.

1976: The Seveso disaster was associate industrial accident that occurred in an exceedingly tiny chemical manufactory close to Milano in Italy. It resulted within the highest far-famed exposure to a pair of,3,7,8-tetrachlorodibenzo-p-dioxinin residential population.

1984: The Bhopal disaster was associate industrial catastrophy that came about at a chemical plant owned and operated by Union inorganic compound (UCIL) in Bhopal Republic of India leading to the exposure of over five hundred,000 people. it absolutely was caused by alkyl Isocyanate (MIC) gas.

1986: The urban center disaster was a nuclear accident at the urban center nuclear plant in land. It resulted in an exceedingly severe unharness of radioactive materials. Most fatalities from the accident were caused by radiation poisoning.

1989: Exxon port, associate cargo vessel hit a reef associated spilled an calculable minimum ten.8 million United States of America gallons (40.9 million litres) of fossil fuel. This has been recorded jointly of the biggest spills in us history and one amongst the biggest ecological disasters.

4. History of Green Chemistry

1. In 1990 the Pollution hindrance Act was passed within the us. This act helped producea procedure for addressing pollution in an ingenious and innovative method. This sealed the thanks to the inexperienced chemistry conception.
2. Paul Anastas and John Warner coined the two-letter word “green chemistry” and developed the twelve principles of inexperienced chemistry.
3. In 2005 Ryoji Noyori known 3 key developments in inexperienced chemistry: use of critical dioxide as inexperienced solvent, binary compound oxide for clean oxidations and therefore the use of gas in uneven synthesis.

5. Concepts of inexperienced Chemistry

- Green Chemistry, or sustainable/ environmentally benign.
- Chemistry is that the style of chemical merchandise and processes that cut back or eliminate the employment and generation of risky substances.

6. Green Chemistry Focuses on to

- Minimize:

- Waste
- Energy use
- Resource use (maximize efficiency)

❖ Utilize renewable resources

7. Global Recognition of Green Chemistry

Global Recognition of inexperienced Chemistry:

Australia: The Royal Australian Chemical Institute (RACI) presents Australia's inexperienced Chemistry Challenge Awards.

Canada: The Canadian inexperienced Chemistry laurel wreath is associate annual award givento somebody or cluster for promotion and development of inexperienced chemistry

Italy: inexperienced Chemistry activities in Italy centre on inter-university syndicate called INCA. In 1999, INCA has given 3 awards annually to business for applications of inexperiencedchemistry.

Japan: In Japan, the inexperienced & property Chemistry Network (GSCN), fashioned in 1999,is a company consisting of representatives from chemical makers and man of science.

UK: within the uk, the Crystal Faraday Partnership, a non-profit cluster based in 2001, awards businesses annually for incorporation of inexperienced chemistry.

USA: us Environmental Protection Agency (EPA).

8. Nobel Prize in Green Chemistry

1. The honor Committee recognized the importance of inexperienced chemistry in 2005 by grant Yves Chauvin, Robert H. Grubbs, and Richard R. Schrock the honor for Chemistry for "the development of the metathesis methodology in organic synthesis.
2. Frances Arnold won in 2018, it for the directed evolution of enzymes, a way she has pioneered over the past twenty five years and has accustomed pursue new avenuesat intervals inexperienced chemistry and to engineer reactions fully new nature.

9. Green Chemistry and Property Development

❖ The United Nations defines property development as 'meeting the requirements of gift while not compromising the power of future generation.

❖ Green chemistry focuses on the way to attain property through science and technology.

❖ To higher perceive and solve the problem of environmental pollution, several approaches and models are developed for environmental impact assessments.

❖ Some of those approaches and models are no-hit in predicting impacts for hand-picked chemicals in hand-picked environmental settings.

- ❖ These models have joined air and water quality aspects to purpose and nonpoint sources and are terribly helpful for the event of emission management and compliance ways.
- ❖ However, a number of the approaches and models were aimed primarily at evaluating the number of pollutants that would be discharged into the atmosphere with acceptable impact, however didn't specialize in pollution hindrance.
- ❖ However, a number of the approaches and models were aimed primarily at evaluating the number of pollutants that would be discharged into the atmosphere with acceptable impact, however didn't specialize in pollution hindrance.
- ❖ The conception of end-of-pipe approaches to waste management ablated, and methods like environmentally acutely aware producing, eco-efficient production, or pollution hindrance gained recognition.

10. The Benefits of Green Chemistry

- Economical
- Energy efficient
- Lowers cost of production and regulation
- Less wastes
- Fewer accidents
- Safer products
- Healthier workplaces and communities
- Protects human health and therefore the atmosphere

11. Why Will We Would Like Inexperienced Chemistry?

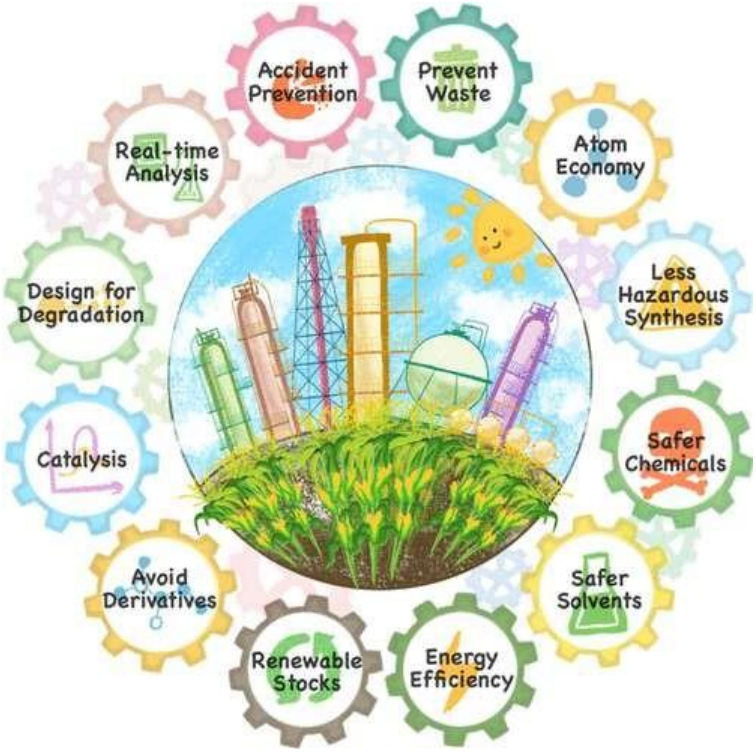
- Chemistry is undeniably a really outstanding a part of our daily lives.
- Chemical developments bring new environmental issues and harmful surprising aspect effects, that end in the requirement for ‘greener’ chemical merchandise.Eg. DDT.
- Green chemistry appearance at pollution hindrance on the molecular scale it's an especially vital space of Chemistry thanks to the importance of Chemistry in our world these days and also the implications it will show on the environment.

- The inexperienced Chemistry program supports the invention of a lot of environmentally friendly chemical processes that scale back or perhapseliminate the generation of risky substances.

- This program works terribly closely with the twelve principles of inexperienced Chemistry.

12. Principles of Green Chemistry

- There are a unit twelve principles of inexperienced Chemistry that area unit usefulwithin the property of the atmosphere all of those area unit mentioned below well, that however these principles area unit useful in property.



1. **Prevention.** Prevention. it's higher to forestall waste than to treat or finish off waste once it's shaped.
2. **Atom Economy**. Atom Economy. artificial ways ought to be designed to maximise the incorporation of all materials employed in the methodinto the ultimate product.

3. **Less Hazardous Chemical Synthesis**. Less risky Chemical Synthesis. Whenever practicable, artificial methodologies ought to be designed to use and generate substances that possess very little or no toxicity to human health and also the atmosphere.

4. **Designing Safer Chemicals**. Chemical merchandise ought to be designed to preserve effectuality of the perform whereas reducing toxicity.

5. **Safer Solvents and Auxiliaries**. the utilization of auxiliary substances (solvents, separation agents, etc.) ought to be created supererogatory whenever doable and, when used, innocuous(harmless)

6. **Design for Energy Efficiency**. Energy necessities ought to be recognized for his or her environmental and economic impacts and may be reduced. artificial ways ought to be conducted at close temperature and pressure.

7. **Use of Renewable Feedstocks**. Use of Renewable Feedstocks. A stapleor feedstock ought to be renewable instead of depleting whenever technically and economically sensible.

8. **Reduce Derivatives**. supererogatory derivatization (Blocking cluster, protection/deprotection, temporary modification of physical/chemical processes) ought to be avoided whenever doable.

9. **Catalysis**. chemical change reagents (as selective as possible) area unitsuperior to ratio reagents.

10. **Design for Degradation**. Chemical merchandise ought to be designed in order that at the top of them perform they are doing not move theatmosphere and instead break down into innocuous degradation merchandise.

11. **Real-time Analysis for Pollution Prevention**. Analytical methodologieshave to be compelled to be more developed to permit for real- time in-process observation and management before the formation of riskysubstances.

12. **Inherently Safer Chemistry for Accident Prevention**. Substance and also the variety of a substance employed in a activity ought to be chosen thus on minimize the potential for chemical accidents, as well as releases, explosions, and fires.

13. Examples of Green Chemistry

New syntheses of nonsteroidal anti-inflammatory and sertraline.

- Integrated circuit production.
- Removing Arsenic and salt from pressure treated wood.
- Many new pesticides.
- New oxidants for bleaching paper and disinfecting water.
- Getting the lead out of automobile paints.
- Recyclable furnishings.
- Replacing VOCs and chlorinated solvents.
- Biodegradable polymers from renewable resources.

In the finish we will say that inexperienced chemistry isn't an answer to any or all environmental issues however the foremost elementary approach to preventing pollution

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ACTIVITY BASED COSTING, ITS ADOPTION AND USEFULNESS IN ELECTRONIC HEALTH RECORDS IMPLEMENTATION: A CASE OF BAREWA CLINICS, KANO, NIGERIA

Adewale A. ADEKIYA

1. Introduction

Traditional costing systems have worked well for many decades and may continue to be useful today to value inventory and measure the cost of goods sold. However, practitioners are facing various challenges using the traditional costing systems in today's competitive environment. In the present globalize world, cost and management accountants are now expected to be team players in key internal decisions in such areas as product development, profitability analyses, improvement in quality of products and processes, and the evaluation of overall company performance (Welfle & Keltyka, 2002).

According to Garisson, Noreen & Brewer (2009) activity costing (ABC) is a costing method that is designed to provide managers with cost information for strategic and other decisions that potentially affect capacity and therefore "fixed" as well as variable costs. It is ordinarily used as a supplement to, rather than as a replacement for a company usual costing system. This infers that most organizations that use ABC have two costing system – the official costing system that is used for preparing external financial reports and the activity based costing that is used for internal decision making and for managing activities. As a strategic cost management tool, activity-based costing (ABC) plays a vital role. The ABC (activity-based costing) model has revolutionized costing systems (Johnson and Kaplan, 1987). Under ABC, product costs are not strictly isolated to manufacturing costs and are expanded to include non-manufacturing costs such as selling, marketing, distribution, and administrative that can be directly traced to the product through activities (Garrison et al, 2006). This may result in improved resource allocation consistent with strategic objectives and budget surplus (Zaman, 2007). ABC has reportedly helped many organizations to better manage their business activities when combined with total quality management and business process re-engineering (Adams, 1996).

One of the greatest misconceptions about ABC is that the system is not applicable to service organizations (Compton, 1996). On the contrary, the utility of ABC has expanded beyond the manufacturing sector to improve the accuracy of non-manufacturing costs, as well as enabling profitability analysis for customers and other business functions (Chenhall & Langfield, 1999). As a result, the utilization of ABC has been evident in areas such as database marketing (Doyle, 2002) the financial industry (Dodd & Lavelle, 2002) the healthcare industry (Federowics et al, 2010). Telecommunications, transport, wholesale, distribution and Information services sectors (Kennedy & Affleck, 2001). Substantial changes have been witnessed in the services sector within this last two decades. This is due to emergence of new competitors as a result of deregulation, which has also given companies greater freedom in setting prices and determining the mix of products to offer. Well managed services firms with a good understanding of their markets, customer's data base and information technology can become more profitable in a deregulated and more competitive environment (Maiyaki, 2011). This equally applies to the

health sector in which thousands of patient databases must be kept to maintain an updated patient profile. Though ABC is a relatively new phenomenon in the health care sector. It is a comprehensive approach that the health care field can use to analyze the cost-effectiveness of implementing an electronic health record system (Federowics et al, 2010). The total cost to implement an EHR includes obvious costs, such as licensing fees, and hidden costs, such as impact on productivity. Unlike the traditional accounting method, ABC includes all of the organization's expenditures and is less likely to miss hidden costs.

The Nigerian health sector is currently witnessing an upsurge in demand which could be related to a steady rise in population. This is evidenced in the establishment of numerous private health care facilities in order to provide for the shortcoming of limited government owned hospitals that are available. An efficient health services delivery in a modern day's health administration system with a large population of patients would require an electronic health records. Federowics et al. (2010) maintained that there is an empirical evidence that health organizations are more likely to be more productive after the application of ABC to their electronic health records system in that health care managers can benefit by using ABC to analyze the effects of electronic health record investments on productivity and efficiency. However, since the rate of adoption of ABC is still relatively low in the Nigerian business environment, there seems to be lack of evidence on its applicability in the health sector. This paper examine the concept of ABC and its associated benefits in the implementation of an electronic health records within the Nigerian healthcare sector with a specific focus on Barewa clinics in Kano metropolis.

2. Literature Review

2.1. The Need for Activity Based Costing (ABC)

Traditional cost accounting, which mainly allocates overhead cost on the basis of one single cost driver such as direct labor or output volume, systematically distorts product costs in modern manufacturing and service environments in which overhead costs are a significant portion of product costs. Thus, incorrect product cost information can lead to poor decisions (Wang, Du, Lei and Lin, 2010). An alternative managerial philosophy and its associated measurement systems, namely, activity-based costing (ABC), has been offered to overcome some of the failures of standard costing for improving managerial decision making. ABC has been acknowledged to provide cost information for more precise cost allocation (Sheu, Chen and Kovar, 2003).

2.2. Benefits of Activity Based Costing

The benefits associated with the adoption of activity based costing could be explained as diverse and enormous. For instance the costing methodology known as ABC yields cost information that may be significantly different than what is provided when the traditional absorption cost method is used. According to Chea (2011) ABC analysis enables managers to slice into the business many different ways by product or group of similar products, by individual customer or client group, or by distribution channel and gives them a close-up view of whatever slice they are considering. It also give exact information on what activities are associated with specific part of business and how those activities are linked to the generation of revenues and

the consumption of resources. By high-lighting those relationships, ABC helps managers understand precisely where to take actions that will drive profits (Cooper and Kaplan, 1991). In addition, managers can use ABC to analyze many other aspects of their company's operations. They can compare the profits that various customers, product lines, brands, divisions or regions generate and thus use this as a basis of taking critical internal decisions, spanning across functional areas that involve not only products, but also distribution and customer related decisions related to selling price and production. Performance improvement, which can be seen in terms of time, cost, and quality has been shown to be having close relationship with activity based costing in that ABC has a moderate impact on time, a significant impact on quality, and a substantial impact on cost (Gering, 1999). Bidanda et al. (2003) pointed that most companies do not recognize that their traditional costing systems provide unreliable and distorted cost information until their profitability and competitiveness have deteriorated. In other words, the adoption of activity based costing offers many advantages over the traditional means of costing.

3. Examples of Companies that have successfully Adopted and Implemented Activity Based Costing

Insteel industries manufactures a range of products such as concrete reinforcing steel, industrial wires and bulk nails for the construction, home furnishing, appliances and tire manufacturing industries. The company implemented an activity based costing system at its manufacturing plant in Andrew South Carolina, USA and immediately began using activity based costing to make strategic and operating decisions. In term of strategic decision, Insteel dropped some unprofitable products, raised prices on others and in some case even discontinued relationship with some unprofitable customers and later realized that taking such simple actions does not improve profit. It can either redeploy its freed up capacity to increase sales or eliminate its freed up capacity to reduce costs. Insteel chooses to redeploy its freed up capacity and used its activity based costing system to identify which new business opportunities to pursue. In term of operational improvement, insteel revealed that its 20 most expensive activities consumed 87 percent of the plant $21.4 million in costs. Almost $4.9 million was being consumed by non-value adding activities. Teams were formed to reduce costs on this activity and within one year, overall non value adding activities costs have dropped from 23 percent to 17 percent of total cost. This signifies a drop of $2.5 million in total cost.

Kemp LLC, headquartered in Minneapolis, Minnesota, produces dairy products such as milk, yogurt, and ice cream. The company implemented an ABC system that helped managers understand the impact of product and customer diversity on profit margin. The ABC model captured differences in how the company entered orders from customer, how it packaged orders, how it delivered orders and the time spent by each drivers at each customer's location. Kemp ABC system helped the company acquire a large national customer because it identified the specific manufacturing, distribution and order handling costs associated with serving this customer. The ability to provide the customer with accurate cost information built a trusting relationship that distinguishes Kemps from other competitors. Kemp also used its ABC data to transform unprofitable customers into profitable ones. For instance one customer agreed to accept a 13 percent price increase to eliminate two low volume products and to begin placing

full truckload orders rather than requiring partial truckload shipments thereby lowering Kemp costs by $150,000 per year.

Owen and Minor, a $3billion medical supplies distributor in California offers an activity based billing option to its customers instead of charging a fixed amount for items that are ordered by customers, the charges are based on activities required to fill the order as well as on the cost of the item ordered. This charges encourage customers to reduce their weekend delivery requests and results in decreased cost for Owen & minor which can then be passed on to customers in the form of lower charges for the specific items that are ordered.

Also, Providence Portland medical center (PPMC) used ABC to improve one of the most expensive and error prone processes within its nursing units. Ordering, distributing, and administering medications to patients. To the surprise of everyone involved, the ABC data showed that medications related activities made up 43 percent of the nursing unit's total operating costs. The ABC team members knew that one of the root causes of this time consuming process was the illegibility of physician orders that are faxed to the pharmacy. Replacing the standard fax machine with a much better $5,000 machine virtually eliminated unreadable orders and decreased follow up telephone calls by more than 90 percent thereby saving the hospital $500,000 per year. In total, the ABC team generated improvement ideas that offered $1 million of net saving in redeploy able resources.

3.1. Adoption Rate of Activity Based Costing

Although it has been claimed that ABC can reduce the cost allocation inaccuracies associated with traditional costing, as well as providing benefits such as improved performance. The literature however suggests that ABC is still underutilized by firms in the last two decades of its development. According to Armitage and Nicholson (1993) evidence of adoption during the early 1990's indicates an adoption rates ranging from approximately 10 percent of firms in the UK and Ireland to 14 percent in Canada. Later in the same decade, studies suggested that many firms were still using traditional costing systems, and that an approximate 20 percent adoption of ABC was apparent (Sulaiman, Ahmad, & Alwi, 2004). Research in the UK in 1995 and 1999 showed that the consideration of ABC and actual adoption dropped while reported rejections of the concept increased over four years between two studies that looked at ABC adoption (Innes et al, 2000). However in the United States of America (USA), survey results showed that 86 percent were using traditional costing systems in 1996 (Cheatham & Cheatham, 1996) whereas a more recent study (Kiani & Sangaladji, 2003) illustrated that 52 percent of respondents were implementing some stage of ABC. This trend was also evident in Australia, where Chenhall and Langfield (1998) found that an increasing number of firms were adopting ABC. Also Manufacturing firms in France increased their ABC adoption from 15.9 percent in 2002 to 33.3 percent in 2008 (Elhamma, 2012).

In recent years, some studies have been done on the adoption and implementation of the ABC methods in developing countries. For instance Anand et al. (2005) in a survey of 60 large and medium sized manufacturing companies in India found a higher adoption rate of 20 percent for activity-based costing, 13 percent for activity-based management, and 7 percenty for activity-based budgeting. Another study by Chongruksut (2005) in Thailand revealed a 35 percent rate

of adoption while that of Ruhanita (2007) in Malaysia indicated an adoption rate of 36 percent. Another study by Moalla (2007) in Tunisia as cited in Elhamma (2012) revealed an adoption rate of 23.75 percent while in South Africa, Sartorius, Eitzen, & Kamala (2007) found an adoption rate of 12 percent. Also, the study by Ngong (2010) in Cameroun, see: Elhamma (2012) uncovered an adoption rate of 9.3 percent which indicates that the developing countries of Asian pacific region are more diligent in its adoption. Unfortunately, there is unavailability of data on the adoption rate of ABC in Nigeria.

Though ABC rate of adoption is gradually increasing However, it is still apparent that its rate of adoption is surprisingly low given its proposed associated benefits. Some of the reasons given for the low adoption rate according to Garisson, Noreen and Brewer (2009) ranges from the high cost involved in the implementation and maintenance of ABC, the anticipated human resistance that characterized any proposed change program, which limit the support and participation of management, line managers and accountants in any activity based costing initiative, the difficulty associated with the interpretation of ABC data when using it to make decisions, and the ineffectiveness of reports generated from ABC in conforming to generally accepted accounting standard (GAAP). Organizations proposing the implementation of ABC are thus advised to have two costing systems which would include the traditional costing system for making external report and the other for making internal decisions.

3.2. Benefits of ABC in Implementation of Electronic Health Records

Although ABC is a relatively new phenomenon in the health care sector. It is however a comprehensive approach that can be can used to analyze the cost-effectiveness of implementing electronic health records. The total cost to implement an EHR includes obvious costs, such as licensing fees, and hidden costs, such as impact on productivity. Unlike other cost estimating methods, ABC includes all of the organization's expenditures and is less likely to miss hidden costs (Federowics et al, 2010). For example, other cost estimation methods include the costs of training staff members on a new EHR, such as by including the cost of hiring trainers and purchasing training materials. However, ABC goes further and also accounts for the cost of the staff members participating in the training instead of working. Compared with other methods, ABC offers an approach that is less likely to miss costs and thereby more likely to produce an accurate assessment of the cost-effectiveness of implementing an EHR (Federowics et al, 2010).

In a study by Federowics et al. (2010) of a 3 physician clinic in Midwest United States, it was discovered through the use of ABC that the clinic was more productive after implementation of EHR. For the analysis, fiscal year 2006 is a "before" picture of the clinic without the EHR, and fiscal year 2007 is an "after" picture of the clinic with the EHR. All operational activities were divided into seven (7) and classified as personnel, executive management, human resource & finance, building, supplies, electronic health records, and other operating expenses. The EHR expense is found by first dividing the total organization-wide investment cost of the EHR over the period for implementation. This number is then divided by the total number of physicians the EHR intends to support. This number is finally multiplied by the number of full-time equivalent physicians in the clinic.

The table below shows a breakdown of the total cost of all operational activities by categories in year 2006 before EHR implementation and year 2007 after EHR implementation.

Total Expenses

Activities	Fiscal Year 2006	Fiscal Year 2007
Personnel	$716 755	$702 274
Executive management	$36 806	$38 611
Human resource and finance	$61 344	$64 351
Building	$180 189	$179 294
Supplies	$203 183	$255 927
Electronic health record	----	$24 733
Other operating expenses	$126 749	$124 789
Total expenses	$1 325 027	$1 389 979

The total number of patient appointment for fiscal year 2006 is 3828 while the appointment for fiscal year 2007 is 4168. This as been indicated was taken from the clinic's schedule of records.

Cost Per Appointment

	YEAR 2006	YEAR 2007
Total expenses	$1 325 027	$1 389 979
No. of patient appointments	3828	4168
Cost per appointment	$346.14	$333.49

In determining the effect EHR implementation on cost, the costs per appointment both before and after its implementation were considered. This was done through the following steps.

Step 1: Determining a list of activities into which the total cost of operation will be allocated

Step 2: Allocating the appropriate amount of expenditure into each activity

Step 3: Calculating the total costs for each period. The total cost is the sum of the costs in the expense categories.

Step 4: Determining the number of patient appointments for each period

Step 5: Calculating cost per appointment for each period. This was determined by dividing the total expenses by the number of patient appointments

Step 6: Comparing the total cost per appointment before and after EHR implementation and draw conclusions.

The following equation was used to determine the percentage change in the total cost per appointment after EHR implementation:

% Change in cost per appointment

= (Cost After − Cost Before)/(Cost Before) × 100%

= ($333.49 − $346.14)/($346.14) × 100%

= −3.65%.

The decision rule for this analysis is that if the percentage change in value is positive then the clinic is less productive and if it is negative then the clinic is more productive after the implementation of the electronic health record. Therefore, with a percentage change of –3.65%, the clinic is more productive with the EHR.

4. Methodology

Through the use of non structured qualitative interview, the opinion of staffs of Barewa clinics and maternity were examined. The staff's strength amount to a total of 24 including the medical doctors working on part time basis. The simple random sampling technique was employed to interview 13 staffs including the medical director after the exclusion of staffs such as messengers, securities and cleaners due to the fact that they are not expected to be knowledgeable about ABC as a result of their low level of formal education. The questions asked ranged from if they are currently using ABC, if they had any prior knowledge of ABC, and their general perception of ABC as a costing tool. In addition to all this the medical director of the clinic was asked if the clinic is currently on the use of electronic health records and if the management of the clinic would like to implement some form of electronic health records program in the nearest future.

5. Major Findings and Discussion

A close look at the results obtained from the interview indicates that about 60% or 8 of the subjects interviewed, made up of 3 nurses and midwives, 2 lab technicians, and the rest, general staffs, had no prior knowledge of activity base costing. 3 of the staffs comprising 2 medical doctors and a nurse admitted to a limited prior knowledge of ABC but do not have any knowledge of its usefulness especially in the health sector. Also, the accountant of the clinic admitted to having an above average knowledge of ABC but that the clinic is not currently using it and is not considering its adoption in the nearest future. Reason given for this is lack of management initiative and support. The medical director however admitted to having a prior knowledge of ABC, and equally admitted that the clinic is considering the introduction of an electronic health record system but does not have knowledge of the benefits of application of ABC to health care delivery services or to an electronic health record system. He equally maintained that since their current traditional costing system takes care of all their accounting

system, he does not see a reason why another method of costing whose implementation would result in additional expenditure should be introduced.

6. Conclusion

The findings in this study are pointer to a relatively low knowledge of ABC including its overall usefulness and cost benefits. It can also be concluded that one of the challenges against the initiation or implementation of an activity based costing system is low management support which exists in form of the perceived cost or expenditure associated with its implementation.

7. Recommendations

An activity based costing system is an accounting system that is cost effective and thus can be applied in accounting operations of virtually all manufacturing and services organizations including an electronic health record system in a health care services delivery organizations. When applied appropriately, it creates an avenue for efficient use of organizational resources and thus brings out the best returns. Aside this it help organizations to single out for elimination, unproductive activities thereby resulting in a general reduction of operation cost, and can be use to take critical internal decisions related to pricing and production. It is hereby recommended that:

I. The accountants in health care delivery services must start making attempts to bring to the awareness of management, the enormous benefits associated with efficient implementation of activity based costing program.

II. Though the initial revenue required to implement an ABC program is considerable high however, this enormous investments could be recoup within some few period of time after implementation. Management of health care services are thus advised to lend out full commitment and support to staffs as regards ABC implementation most especially when the organization is currently in use of electronic health record system or considering its implementation. Such support could range from training programs on application and interpretation of ABC data, financial supports and a program of general orientation of staffs about the applicability of ABC and its associated benefits.

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WATER - A WONDER CHEMICAL IN THE WORLD

B.H.S. THIMMAPPA

1. Introduction

Water has always been an integral part of everyday life and the world around us. It is essential to almost every form of life, and all body fluids are dilute water solutions. It is of crucial importance for sustaining the specific biochemical reactions that keep us alive and hence the most significant solvent in the world for human survival. Molecular dynamics and structural fluctuations of many molecules in an aqueous medium have direct consequences on their fundamental functional roles. One of the most significant aspects of water is that it acts as an influencing factor in weather and climate. The discernible positive aspect is that it helps moderate the earth's temperature. In the hydrologic cycle, water is used and returned to the environment by evaporation and precipitation. The industrial growth of a country strongly depends on the proper use of water resources. The statement "The next big wars will be fought over water" underlines the importance of water in the future. Life as we know it would not exist without the unique and unusual properties of water. Water demand is escalating with increasing world population, increase in agricultural, industrial, and mining activities, deforestation, and changes in lifestyles, contributing to social pressure among users. The population of the planet is expected to exceed 9 billion by 2050, and severe depletion of crucial resources, including water, is predicted. Domestic water uses include drinking, bathing, laundering, cooking, housecleaning, and watering the garden**.** Industrial uses include the generation of steam, building construction, manufacture of hydrogen, oxygen, and water gas, agricultural irrigation, making steel, hydroelectricity generation, as a food additive, flame retardant material, and as an industrial solvent. Water is essential in the industry for cooling products and equipment, boiler feed, process requirements, and sanitary purposes. It can act as a solvent, transport medium, participant, and catalyst. It is also useful in navigation, recreation, mining, and ecosystem support. It is used as a powerful polar protic solvent in organic synthesis and as a moderately strong monodentate ligand in inorganic complexes in the laboratory. It is used in commercial establishments like restaurants and educational institutions such as schools and colleges. Water has an exceptional ability to dissolve a wide variety of substances, which is considered the universal solvent. This solvent property is vital in the transfer of substances in biological systems and the hydrological cycle. Water is a common ingredient in many food products; and is used as an agent for mixing or washing operations. Significant applications of ice include food processing, preservation and distribution, chemical industries, and special applications such as cold treatment of metals, medical items, and construction work. Ice is used to maintain the quality of fish, vegetables, and fruits during processing and transportation to distant places. Fisheries use water as a medium for growing fish, and transportation in the tropics is an essential use of water. Ships, steamers, and boats sailing on the surface of the sea save our time, money, and energy. Hydroelectric power stations extract energy from water. Steam is useful in cooking, energy production, and transport systems. It can be found in food processing factories, refineries, and chemical plants. Water is used as a cooling and heating medium over a wide range of temperatures, as a cleaning material, as a fire-fighting agent, and

in aquaculture. Pure clay water bottles or containers with modern designs provide a facility to keep water cold, especially during the summer. Moreover, water has a religious significance as a fundamental life element. Hydrotherapy that involves the use of water for treatment or to maintain health is a part of alternative medicine. It is essential in flushing toxic byproducts from our bodies. Thus, water is a basic necessity for life and health, and the economy in general. It is the life force that entertains us and makes our life colorful.

People contribute to water stress through excessive exploitation of surface and groundwater, pollution of water resources, and inefficient use of freshwater. Both natural and human-induced flooding can cause massive destruction of properties with social, economic, political consequences and broader consequences. Adequate water supply for all can be limited by drought, overuse, and pollution by oil spills, industrial effluents, and other waste materials. The products of human activities, when entering the environment, disturb aquatic ecosystems, and water quality is affected by pollution. Water scarcity affects plants, animals, and the entire ecosystem as it plays a critical role in the forest environment. The composition and diversity of species change drastically in forests that suffer water stress, which can lead to disastrous consequences. The world's water problems stem from a lack of sustainable water resource management. Sustainable water use involves the current and future rates of use and associated social policies for implementation to manage precious water resources. The water footprint of products, individual consumers, companies, and nations vary widely, and growing pressure on the available water supply and sanitation has a profound impact on our social, economic, and environmental health. Electricity generation in hydroelectric power plants is considered to be a process having a low environmental impact. Water used for this purpose is not consumed, and there is no generation of harmful waste or emission of toxic gases. Further, this technology avoids the negative impacts of burning tons of coal in thermal power plants while preserving fossil fuel for future generations. Many of our recreational activities are based on water. Natural waterfalls in different parts of the globe attract tourists all over the world, and artificial musical water fountains installed in gardens in different parts of the world enhance happiness quotient. A fresh and exciting nature walk along the streams in the forest, enjoying the gentle breeze has caught the attention of youngsters and senior citizens alike. The panoramic view of waterfalls in the lap of nature, a safe pool of water that adorn the local landscape, a beautiful view of the coastline, or breezy beaches provide a refreshing break from the hectic life. Water can be considered as the world's most celebrated architect, as reflected in the glacial streams, gushing waterfalls, hills, valleys, shrubs, and landscape supporting plant and animal life. Water/ice is used for recreational purposes, such as swimming, rafting, surfing, and ice-skating. Some water sports and activities such as diving, water polo, water aerobics, surfing, and boat racing are becoming popular across the world.

World water day (WWD) is observed on March 22 every year, as recommended by the United Nations, to focus on international water issues. World environmental day (WED) is celebrated each year on June 5 to raise greater global public awareness and to promote actions to protect toxic-free nature for all. The primary usefulness of water in everyday life and its influence on modern society by creating several global job opportunities in water-related activities attract youngsters to have additional career options. Some subjects deal with the study of water-related

topics. Hydrology deals with the occurrence, distribution, movement, monitoring, modeling, and properties of the water of the earth and related environmental interactions [1-5]. Limnology is a branch of ecology that deals with the study of inland waters, and oceanography is a branch of earth science that studies the ocean in great detail. The reader interested in understanding the subject matter by further reading can obtain specific information about water issues, quality, supply, and management in several dedicated websites and textbooks [6-11]. The recent developments in waterproofing technology for devices provide solutions to manufacturers regarding the actual use of electronics. The bottled water industry is rapidly growing, with a boost in sales across the globe. There are more than seventy journals publishing research studies on different aspects of water science and technology [12-13]. The top global water research institutes are working in different areas of specialization, such as membranes, desalination, drinking water and wastewater, nutrient recovery and infrastructure, and water reuse [14-15]. There is a growing body of research on different aspects of water, and it has a significant effect on how the sustainable use of water can change overall development.

Water is an essential substance in the literary ecosystem, and it is unique from multiple perspectives. It has been a source of inspiration for many centuries across the world, transforming life into literature. The people of early civilizations, such as the Indus Valley Civilization, Mesopotamian Civilization, and Egyptian Civilizations, settled near rivers as they needed water for drinking and their crops. In the historical context, water conflicts were frequent from ancient to contemporary times reflecting the immeasurable value of water. There are many idioms in the English language referring to water like a fish out of water, in deep water, test the waters, and keep one's head above water. They reflect the critical role of 'water' in history [8,16]. The images of water representing dreams, desires, love, and fears play a prominent role in many novels and other literary works. There are several quotes related to water such as "water is the driving force in nature," "life in us is like water in a river," "you can't cross the sea merely by standing and staring at the water," "pure water is the world's first, and foremost medicine," "in one drop of water are found all the secrets of the oceans." The proverbs "water is the only drink for a wise" and "water seeks its level" illustrate a practical precept. Water is of central importance in all world religions and is considered an ultimate natural fluid with multiple benefits. Water is considered one of the five fundamental elements of life as a symbol of life and cleansing in ancient philosophy and as one of the basic alchemical symbols. It has been an enormous source of inspiration for poets in different continents and countries as it touches different aspects of life and is essential for human existence on earth. Water is a powerful metaphor in the expression of poets as it is a force of nature. Many thought-provoking and visually stimulating artworks depict different aspects related to water, conveying meaningful messages. One can enjoy some spectacular digital images on different websites on various themes related to water and wastewater processes [17]. There are several movies involving water in their title or those set in or around water [18-19]. Exposure to the literature would certainly help people develop a sharing and caring mindset regarding water usage, and develop nature-friendly behavior and use of eco-friendly technologies. Water is characterized by distinct physical and chemical properties, theoretical and mathematical models, multiple applications in various fields of activity, and unique structure and bonding features.

2. Physical Characteristics

Water is a chemical with the molecular formula H_2O, and it consists of one oxygen atom bonded by two hydrogen atoms. When hydrogen burns in the air, it combines with oxygen to form water. Its enthalpy of formation is -285.8 kJ/mol, and energy is required to break the stable bonds. It has a bent or V-shaped structure with an H-O-H bond angle of 104.5^o and an O-H bond length of 0.096 nm. There are two pairs of non-bonding electrons (lone pairs) on the oxygen atom and two bonding pairs in the water molecule's electronic structure. It belongs to the C_{2v} point group with two mirror planes and only one rotational axis C_2. According to the valence shell electron pair theory, the two lone pairs strongly repel each other, resulting in the decreased bond angle from that of a regular tetrahedron, 109.5^o. The bonding in water can be considered as an sp^3 hybridization of orbitals on the oxygen atoms. Two hybrid orbitals overlap with the 1s orbital of the hydrogen atom to form two covalent bonds, while the other two contain lone pairs of electrons. It is the most abundant compound in the Earth's biosphere, with a molar mass of 18 g/mol. There are three normal modes of vibrations, symmetric stretching and bending, and symmetric stretching. It is in a liquid form at room temperature without odor, taste, or color, and it can readily transform from liquid to solid and gaseous states. Its chemical name is dihydrogen monoxide. It is a polar molecule with a significant electric dipole moment (μ) of 1.84 D and a dielectric constant of 78.39. The oxygen atom has a partial negative charge, and the hydrogen atoms have a partial positive charge. The bond dipoles, though equal in magnitude, do not cancel each other, because of a bent structure and because the water molecules have an overall dipole moment. It is an excellent solvent due to its strong solvation power, the solute-solvent (ion-dipole) attractions and because of the highest dielectric constant of all common liquids, which decreases the interionic attractions. The energy of separation between two dipoles or two ions is inversely proportional to the dielectric constant of the solvent. It can dissolve a wide range of ionic and polar covalent molecules. The table salt readily dissolves in water because of strong ion-dipole forces between the ions (cations and anions) and the polar water molecules that overcome the lattice energy of solid sodium chloride. It can form hydrogen bonds with other polar species that play a significant role in forming the solution. Compounds such as ethanol, acetone, tetrahydrofuran, and sugar dissolve in water and are completely miscible because of H-bonded interaction with the solvent. When a covalent molecule dissolves in water, the solution consists of discrete molecules dispersed throughout the medium. A few molecules such as hydrogen chloride gas, when it dissolves in a water medium contain H^+ and Cl^- ions. Water dissolves a wide range of ionic and polar-covalent substances and is the most readily available liquid on Earth. It is interesting to note that water-soluble vitamins like vitamin C are polar, while fat-soluble vitamins like vitamin A are non-polar. Commercial products like sodium chloride, bromine, and magnesium are obtained from seawater. Water in a chemical compound could exist as coordinated water, interstitial water, hydrogen-bonded water, clathrate water, adsorbed water, occluded water, absorbed water, lattice water, and zeolitic water. They differ in the degree of association between water molecules and the other components of the crystal, and several compounds may have more than one type of bonding.

Water has a melting point of 0 ^{o}C and a standard boiling point of 100 ^{o}C at atmospheric pressure. An exciting feature in the phase diagram of water is that the melting point of water decreases as the external pressure increases. The triple point of water is at 0.01 ^{o}C and 0.006 atm, at which all three phases (ice, water, and vapor) are in equilibrium. The abnormally high boiling point is due to the more considerable energy required to break the hydrogen bonds that hold the water molecules together. The boiling point is essential for many processes that involve thermal energy input, including cooking. The high pressure inside pressure cookers causes water to boil at a higher temperature (~120 ^{o}C), and the time required to cook food is reduced to half the usual time. It takes longer to cook food at higher altitudes, as the water boils at a lower temperature (~ 71^{o}C on top of the Himalayas). The density of water at 20 ^{o}C is 0.998 g/mL, and at 25 ^{o}C, it is 1.00 g/mL. It has a maximum density at 4 ^{o}C and expands upon freezing because of open framework formation, and these properties cause seasonal lake stratification. From 0 ^{o}C to 4 ^{o}C, the trapping of water molecules in the cavities of the three-dimensional ice structure continues to make water progressively denser. Beyond 4 ^{o}C, the density of water decreases with increasing temperature because of the higher contribution of the thermal expansion process. It has the second-highest specific heat capacity of 4.186 Joule/gram°C. This helps in moderating the temperature by preventing extremes in the geographical regions and stabilizing the temperatures of organisms by absorbing the heat formed in the cells and transporting it to the skin where it can be lost. Thus, water keeps the temperatures of the oceans constant and maintains our normal body temperature. Similarly, the efficiency of water heating systems in the house depends on this high specific heat of the water. Water can absorb much heat to enhance the average kinetic energy by breaking many intermolecular hydrogen bonds, with only a slight increase in temperature. It can give off a substantial amount of heat while its temperature decreases only slightly. Large water bodies absorb heat in the summer season while they release heat in the winter season, to effectively moderate the local ecosystem's climate. Energy used in the evaporation of water over land and sea each year is estimated to be 1.25 x 10^{21} KJ and thereby tends to decrease the temperature of the atmosphere. When water vapor condenses to raindrops over the land each year, 0.31 x 10^{21} KJ energy is released, leading to an increase in the temperature of the atmosphere [20-22].

It has a large heat capacity of 75.3 J/mol K, caused by hydrogen bonding between water molecules, and this results in oceans cooling more slowly than the land. It has the highest thermal conductivity of all molecular liquids, i.e., 0.6 J/s m ^{o}C, and this helps in the transfer of thermal energy within living organisms. It has a very large enthalpy of vaporization (2250 J/g), which affects our ability to regulate our body temperature by evaporation of sweat. It is essential for heat transfer in the atmosphere and oceans. Condensation of water vapor in the atmosphere releases a large amount of heat, triggering storms. The higher heat of evaporation determines the transfer of heat and water molecules between the atmosphere and water bodies. The critical temperature of the water is 374 ^{o}C, and the critical pressure at this temperature to bring about liquefaction is 217.7 atm. Supercritical water (SCW) is formed at a temperature and pressure above its critical point. At the critical point, the hydrogen bonds holding water molecules break entirely, and this phase can dissolve substances that were previously insoluble in ordinary water in the liquid phase. Supercritical water can behave both as a polar and a non-polar solvent,

making it a powerful medium to dissolve a variety of substances and carry out chemical reactions. The practical value of this beautiful property lies in its application in the eco-friendly destruction of industrial wastes. Water is transparent to visible and longer-wavelength ultraviolet light, and this enables the light required for photosynthesis to reach considerable depths in water bodies and control atmospheric temperature. The high latent heat of fusion of water than any standard liquid helps in stabilizing temperature at the freezing point of water. The surface tension of water is 72 dynes/cm at 25 ^{o}C, and this high surface tension is essential in regulating drop formation in clouds and rain.

The property of wetting is due to its ability to adhere firmly to different materials. The freezing point of pure water at atmospheric pressure is 0 ^{o}C, and this value has been fixed at zero on the temperature scale as a convenient standard temperature point. Water has a relatively low viscosity of 0.890 centipoises at 25 ^{o}C and can make a significant impact on the rate at which blood is pumped around our bodies. The ionic product of water (Kw) = $[H_3O^+][OH^-]$ is 1.00×10^{-14} mol^2 dm^{-6} at 25 ^{o}C, and water is an inferior conductor of electricity. The ionic product of water has to be constant, and human plasma has to be electrically neutral. This mechanism protects plasma pH from severe deviations. The refractive index of water is 1.333 at 25 ^{o}C, and it has the least bending effect of light, among other liquids. Its dependence on temperature and wavelength has several applications in biomedical optics and optics of tissues, as it is the most crucial component of intercellular fluid and blood plasma.

The human baby at birth contains nearly 80 % water, while the healthy adult human body contains about 70 % water by weight. It carries nutrients to the cells and takes away waste products as a major component of blood. The three principal categories of water in the human body include intracellular fluid (ICF ~ 55 %), extracellular fluid (ECF ~ 37.5 %), and plasma (`7.5 %). Water deficiency will result in dehydration, and excess body water can cause water intoxication. Its distribution and availability vary widely over the surface of the earth, and over 70 % of the Earth's surface is covered by water. The total amount of freshwater on Earth is 2.5 % of the total water present, making it one of the most precious resources. The world's water consumption data provided by the United Nations in different categories involves agricultural 70 %, domestic 10 %, and industrial 20 %. The purification of water is necessary to get rid of contaminants that can affect our health, and it is now a significant industry with many plants operating at a water processing capacity of the megaton-per-day scale. The transformation of seawater to produce potable water through a large-scale desalination process is of enormous importance to meet the needs of the increasing world population. Apart from making the easy availability of water, it is essential to introduce other changes to meet the growing consumer demands of a changing world, including an active policy approach to enhance and strengthen the green infrastructure. The most commonly used small-scale methods to obtain freshwater include ultrafiltration, distillation, ion-exchange techniques, ultraviolet sterilization, and multistage reverse osmosis processes. The selection of a particular treatment method or a combination of techniques depends on the source of the water, the end-use envisaged, and the quantity required. The infrastructure required for optimal utilization of available water must be constructed to meet future sustainable development challenges on the path. Globally, the response of people to practical green solutions will be a crucial indicator of the future.

There are three hydrogen isotopes (^{1}H, ^{2}D, ^{3}T) and three oxygen isotopes (^{16}O, ^{17}O, ^{18}O), and in principle, 18 different types of water are possible with slightly different properties. These are also known as isotopologues. The three common types of water are natural water (H_2O), heavy water (D_2O), and tritium water (T_2O). Heavy water (D_2O) is used as a coolant and a neutron moderator in nuclear research reactors. It reacts more slowly than ordinary hydrogen because of its extra mass. THO, HDO, and D_2O occur naturally in ordinary water in deficient concentrations. The existence of tunneling behavior of water is unprecedented, and in this new state, the water molecules are delocalized around a ring, assuming an unusual double-top-like shape [23]. This discovery provides an opportunity for researchers to take a different approach to water-related phenomena. Hard water contains low percentages of $Fe^{2+,}$ Ca^{2+}, Mg^{2+} or Mn^{2+} ions in dissolved form, usually present as bicarbonates, chlorides, sulfates, and nitrates, due to contact of rainwater with soils and rocky substances on its way to the oceans. It does not give lather with soap, a qualitative indicator of the hardness of the water. The total hardness of water can be quantitatively estimated by complexometric titration using EDTA. Temporary hardness caused by carbonates and bicarbonates can be removed by boiling, while permanent hardness caused by sulfates and chlorides can be removed by treating zeolites. Drinking water purification is the single most effective way required to prevent waterborne diseases such as cholera, typhoid, and dysentery. Water disinfection is an essential step in water treatment to make it fit for human consumption, in addition to other physical, chemical, or biological processes. Conventional surface water treatment includes coagulation, flocculation, sedimentation, filtration, and disinfection steps to obtain clean water. The buildup of boiler scales in hot water heating systems clogs the pipes and reduces the efficiency of heat transfer as well as the flow of water through the pipes. Hard water is responsible for the boiler scale, which may result in a boiler explosion, in extreme cases. Wastewater corrosion can result in a loss of water carrying capacity of pipes, structural failures, and degradation in the quality of water transported. Water conditioning and wastewater treatment include removing particulate matter, organics and inorganics, hardness and other scale-forming substances, corrosive contaminants, pathogenic bacteria, viruses, and protozoans. Hard water can be softened on a large-scale by the lime-soda process and small-scale by ion-exchange methods. The lime-soda process involves treating water with lime, CaO, and soda ash, Na_2CO_3, precipitating Ca^{2+}, and Mg^{2+} into $CaCO_3$ and $Mg(OH)_2$. The ion exchange procedure involves passing the hard water through a bed of ion-exchange resin. The Na^{+} ions available on the resin are exchanged with Ca^{2+} ions, and the resin is regenerated by flushing it with a concentrated solution of NaCl. Zeolite water softening process, using Zeolite bed, operates on alternate cycles of softening run and regeneration run, where calcium and magnesium ions are removed from the water, and the exhausted Zeolite bed is regenerated for reuse.

3. Chemical Properties

It is of interest to note that water participates in making and breaking bonds in different types of reactions including, simple dissolution, acid-base reactions, redox reactions, hydration and dehydration reactions, ionic dissociation, solvolysis, and ligand chemistry [24-28]. Water is amphoteric and it has the unique ability to act as either an acid or a base and can participate in

acid-base reactions [Proton donor: $NH_3(aq) + H_2O(l) \rightarrow NH_4^+(aq) + OH^-(aq)$; Proton acceptor: $HCl(g) + H_2O(l) \rightarrow H_3O^+(aq) + Cl^-(aq)$]. The autoionization reaction of water can be written as $H_2O(l) \rightarrow H^+(aq) + OH^-(aq)$. At room temperature, this ionization process is extremely rapid in both directions, and at any given instant, a tiny fraction of molecules undergo ionization. Moreover, the H^+ ion in water interacts strongly with the non-bonding electron pairs of liquid water molecules to form hydronium ions [$H^+(aq) + H_2O(l) \rightarrow H_3O^+(aq)$]. The electrolysis of water by electrical energy input decomposes it into hydrogen and oxygen as per the overall electrochemical reaction $2H_2O(l) \rightarrow 2H_2(g) + O_2(g)$. In this electrolytic production, hydrogen is produced at the cathode and oxygen at the anode, and this is the basis of the fuel cells used in hydrogen-powered vehicles [Anodic oxidation: $2H_2O(l) \rightarrow O_2(g) + 4H+(aq) + 4e^-$ Cathodic reduction: $4H^+(aq) + 4\ e^- \rightarrow 2H_2(g)$].

Limestone caves are formed by the dissolving action of underground water containing CO_2 that is slightly acidic on $CaCO_3$ in the limestone [$CaCO_3(s) + H_2O(l) + CO_2(aq) \rightarrow Ca(HCO_3)_2(aq)$]. Calcium oxide (lime) reacts with water to produce calcium hydroxide (slaked lime) [$CaO(s) + H_2O(l) \rightarrow Ca(OH)_2(aq)$]. Chlorine reacts with water to form aqueous solutions of hypochlorous acid, an active oxidizing agent and hydrochloric acid [$H_2O(l) + Cl_2(g) \rightarrow HOCl(aq) + HCl(aq)$]. The usefulness of chlorine water lies in its antibacterial action due to hypochlorous acid and its use as a bleach. Most metal oxides that dissolve in water react to form metal hydroxides, i.e., Metal oxide + water → Metal hydroxide [$BaO(s) + H_2O(l) \rightarrow Ba(OH)_2(aq)$]. The basicity of metal oxides is due to the reaction of the oxide ion with water [$O^{2-}(aq) + H_2O(l) \rightarrow 2OH^-(aq)$]. The alkali metals react vigorously with water, forming hydrogen gas and alkali metal hydroxides [$2M(s) + 2H_2O(l) \rightarrow 2MOH\ (aq) + H_2(g)$]. Among the alkaline earth metals, Magnesium reacts with steam to form magnesium oxide and hydrogen [$Mg(s) + H_2O(l) \rightarrow MgO(s) + H_2(g)$]. Calcium and other elements down the group react with water at room temperature to form respective hydroxides [$Ca(s) + 2H_2O \rightarrow Ca(OH)_2(aq) + H_2(g)$]. The transition metal, iron reacts with steam to give iron oxide and hydrogen gas [$3Fe(s) + 4H_2O(l) \rightarrow Fe_3O_4(s) + 4H_2(g)$].

Steam reacts with red-hot coke to produce the product water gas [$H_2O(g) + C(s) \rightarrow H_2(g) + CO(g)$]. Non-metal oxides react with water to form acids containing oxygen [$CO_2(g)+ H_2O(l) \rightarrow H_2CO_3(aq)$]. Another non-metal compound, ammonia dissolves in water to form ammonium and hydroxide ions [$NH_3(aq) + H_2O(l) \rightarrow NH_4^+(aq) + OH^-(aq)$]. This ammonia solution acts as a weak base. Non-metal chlorides react with water forming acidic solutions [$SiCl_4(l) + 2H_2O(l) \rightarrow SiO_2(s) + 4HCl(aq)$]. The electrochemical corrosion reaction involves the reaction of water and oxygen to give hydroxide ions at the cathode: [$O_2(g) + 2H_2O(l) + 4e^- \rightarrow 4OH^-(aq)$]. Water reacts with certain metal salts to form hydrates [$CuSO_4 + 5H_2O \rightarrow CuSO_4{\cdot}5H_2O$]. Plaster of Paris forms a paste on mixing with water and then hardens into a solid mass, used in making casts and sculptures. [$(CaSO_4)_2{\cdot}H_2O + 3H_2O \rightarrow 2CaSO_4{\cdot}2H_2O$]. Some hydrates lose their water of crystallization spontaneously at room temperature on exposure to air in a process called 'efflorescence' [$Na_2CO_3{\cdot}10H_2O(s) \rightarrow 10H_2O(g) + Na_2CO_3(s)$]. Deliquescence is the process in which a substance absorbs water from the air to form a solution [$NaOH(s) \rightarrow Na^+(aq) + OH^-(aq)$]. Deliquescent substances are used as drying agents; for instance, anhydrous calcium chloride is used in desiccators for storing materials that pick up moisture. Water decomposes

into hydrogen and oxygen in the ratio of 2:1 by volume when electrolyzed by direct current [$2H_2O(l) \rightarrow 2H_2(g) + O_2(g)$]. Some practical applications of this chemistry include the use of cold or hot packs as an immediate first aid product as they will help to reduce inflammation, and they function by dissolving salt into the water. Commercial instant cold packs often use either ammonium nitrate or urea as their salt component, while hot packs use either magnesium sulfate or calcium chloride. When these chemical ingredients dissolve in water, heat is either released in an exothermic reaction or absorbed in an endothermic reaction [An endothermic process: $NH_4Cl(s) \rightarrow NH_4^+(aq) + Cl^-(aq)$; An exothermic process: $MgSO_4(s) \rightarrow Mg^{2+}(aq) + SO_4^{2-}(aq)$]. The double replacement reaction of water with calcium dicarbide produces acetylene gas and calcium hydroxide solid, i.e. $CaC_2(s) + 2H_2O(l) \rightarrow C_2H_2(g) + Ca(OH)_2(s)$. Iron(III) salts react with water to form hexaaqua iron(III) complex, i.e., $FeCl_3(s) + 6H_2O(l) \rightarrow [Fe(H_2O)_6]^{3+} + 3Cl^-(aq)$]. Hydrolytic cleavage takes place when phosphorous oxide, P_4O_{10} reacts with water [$P_4O_{10}(s) + xH_2O \rightarrow 4H_3PO_4(aq)$]. Similarly, aluminum chloride undergoes hydrolysis when it reacts with water [$AlCl_3(s) + 6H_2O(l) \rightarrow [Al(H_2O)_6]^{3+}(aq) + 3Cl^-(aq)$]. The solution of aluminum chloride is very acidic. This property is because of a small but highly charged Al^{3+} ion that draws electrons in the O-H bonds of water towards itself to enable them to become proton donors. The following equilibrium is established. [$[Al(H_2O)_6]^{3+}(aq) + H_2O \rightarrow [Al(H_2O)_5(OH)]^{2+} + H_3O^+$].

Water reacts with some organic compounds to form different products. Water reacts with butyl chloride, producing butyl alcohol and hydrochloric acid [$C_4H_9Cl(aq) + H_2O \rightarrow C_4H_9OH(aq) + HCl(aq)$]. The direct hydration of alkenes produces alcohol, and ethanol is manufactured by reacting ethene with steam [$CH_2{=}CH_2(g) + H_2O(g) \rightarrow CH_3CH_2OH(g)$]. The reaction involves breaking the π bond in the alkene and an O-H bond in water, as well as the formation of a C-H bond and a C-OH bond. Carbon dioxide dissolves in water to an extent, forming carbonic acid that lowers the pH of the water, and this is responsible for the popping sensation of carbonated soft drinks [$H_2O(l) + CO_2(g) \rightarrow H_2CO_3(aq)$]. Industrial manufacture of sulfuric acid by the contact process involves the reaction of water with oleum to form concentrated sulfuric acid in the final step [$H_2S_2O_7(l) + H_2O(l) \rightarrow 2H_2SO_4(l)$]. The production of sulfuric acid is an indicator of the industrial strength of a nation. Concentrated sulfuric acid removes water of crystallization from copper(II) sulfate pentahydrate [$CuSO_4.5H_2O(s) \rightarrow CuSO_4(s) + 5H_2O(l)$]. Common dehydrating agents used in organic syntheses include concentrated sulfuric acid, concentrated phosphoric acid, and hot aluminum oxide. Acid anhydrides react with water to give the carboxylic acid [$(CH_3CO)_2O(l) + H_2O(l) \rightarrow 2CH_3COOH(aq)$]. Acyl halides undergo nucleophilic substitution readily with nucleophiles such as water [$CH_3COOCl(l) + H_2O(l) \rightarrow CH_3COOH(aq) + HCl(g)$].

The carbon dioxide in the atmosphere reacts with water in the raindrops to produce H^+ ions [$H_2O(l) + CO_2(g) \rightarrow H^+(aq) + HCO_3^-(aq)$]. Nitrogen dioxide reacts with water to give a mixture of nitrous acid and nitric acid [$H_2O(l) + NO_2(g) \rightarrow HNO_2(aq) + HNO_3(aq)$]. Water reacts with sulfur trioxide, formed by oxidation of sulfur dioxide, to form sulfuric acid [$H_2O(l) + SO_3(g) \rightarrow H_2SO_4(aq)$]. This acid rain produced by polluted air present in the atmosphere damages marble structures, architectural monuments, and statues all over the world. It can leach minerals as the rain percolates through soil and rocks [29-31]. In agriculture-intensive areas of the world,

water contains significant quantities of sulfate and nitrate ions, partly due to the widespread use of nitrogenous fertilizers containing these ions. Water vapor is the most important greenhouse gas in Earth's atmosphere that trap heat, which makes the Earth warmer and vibrates in response to the absorption of infrared radiation (3756, 3657, & 1595 cm^{-1}). Water plays an important role in the rusting of iron, and it is an electrochemical process that requires the presence of oxygen, water, and an electrolyte. Water-line corrosion is a special type of corrosion when water is stagnant in a steel tank for a long time. This corrosion results from differential aeration leading to the formation of oxygen concentration cells and corrosion take place just below the water level.

Hydration, hydrolysis, dehydration, redox, and acid-base reactions occur during the breakdown and the reassimilation process to transform foodstuffs into specific metabolites in living systems. All the body's critical functions, including the reactions of metabolism and the transfer of chemical energy, depend on the presence of a proper amount of water. Proper intake of water per day varies depending on the climate, dietary habits, body structure, and physical activities, and we need to drink about three liters of water every day. Water containing traces of dissolved salts of Ca, Na, Mg, and Fe are essential for good health, and water is the medium for the transport of nutrients. The surface-active properties of soaps and detergents are attributed to their structure, having both hydrophilic and hydrophobic parts. The water-soluble polymers such as cellulose, polyoxyethylene, polyvinyl alcohol, polyvinyl pyrrolidone, polymethacrylic acid, polyphosphoric acid, and polysilicic acid have a significant commercial impact, and they are used as food sources, blood plasma substitutes, cosmetics, and as diluents in certain medicines. The role of water in human life, its contributions to humankind, and the research opportunities available for discoveries have a profound positive impact on consumers of different categories, and water shortage can have severe economic consequences. The world of water chemistry would require more rigorous experimental investigations and precise calculations based on different models to discover new phenomena that occur in water mediums and to have a better understanding of the impact of climate change or global warming on natural water resources. Acidification of water supplies due to the dissolution of toxic metals such as Cd, Al, Pb, and Hg from the soil, sediments, metal pipes, and soldering materials is a potential public health hazard. The functions crucial to producing pure water include hazardous waste reduction, breakdown of pollutants, developing adequate sewage water treatment systems, the cycling of nutrients, recharging catchment systems, and re-establishing natural ecosystem services. Further, understanding water variability, conducting laboratory and field studies of water, establishing aqueous reaction mechanisms, performing real-time estimates of ice pack thickness in the Arctic, and implementing long-term water supply measures to help prevent drought-induced migration of people or drought-caused failure of agriculture.

4. The Place of Water in Nature

Water is present as solid ice in polar icecaps and glaciers in the Arctic and Antarctic zones and as liquid water in other places on the earth, in rivers and lakes [32-34]. Water vapor is always present in the atmosphere to different extents. About 71 % of the Earth's surface is covered with water, and the oceans contain about 96.5 % of the total water content of the Earth. The

conversion of carbon dioxide and water into carbohydrates takes place by the process of photosynthesis.

$$6CO_2\,(g) + 6\,H_2O(l) \xrightarrow{h\nu} C_6H_{12}O_6(aq) + 6O_2(g)$$

It is the most important reaction in the world, and the energy released in the reverse reaction called respiration is essential to keep us alive. We depend on plant photosynthesis to supply the bulk of our energy needs, as we do not have the capacity for using solar energy directly. Glucose dissolves as a molecule due to its ability to form hydrogen bonds with water molecules. Water is a liquid at room temperature because of hydrogen bonding, and it plays a prominent role in our daily lives. The properties and functions of biological molecules materialize in a water medium. Oceans, rivers, lakes, and ponds would exist, and it would rain as an integral part of the water cycle in nature. Water is the most abundant and widespread solvent on Earth and an aqueous solution that occurs in nature, such as biological fluids and seawater, contains many solutes in different concentrations [35-42]. Water would rise through the capillary tubes in the roots and stems of plants because of high surface tension, and they can obtain salts required for their growth as water can dissolve ionic substances. Ponds and lakes freeze from the surface downwards as solid ice is less dense than liquid water, making a layer of ice on the top in the winter. This phenomenon helps the aquatic plants, fish, and other water-living organisms to survive in the warmer water below the ice in winter. In the solid state, hydrogen bonds have directional nature with specific orientations in the rigid ice crystal lattice, whereas, in the liquid state, they are continuously formed and broken. Water expands as it freezes into ice, and in the ice, the strong hydrogen bonds hold the molecules in a relatively open tetrahedral network structure. Water with weak bonds between its particles clings to the walls of the container and curves upwards. Essential ionic compounds are absorbed into the bloodstream from the aqueous solution in the intestines of animals. Cells in the human body require water to regulate their volume and osmotic pressure to enable biological structures to perform bodily tasks such as transporting nutrients and waste and serving as physical barriers. Small fluctuations in different body systems can build up and cause profound changes over time. Fish and other lake-dwelling organisms obtain nutrients and oxygen dissolved in water. The amount of dissolved oxygen in water is about 9 ppm when it is completely saturated with air at 1 atm and 20 ^{o}C. Water vapor consists of discrete water molecules, and intermolecular H-bonding chances are small due to the mobility of molecules at high temperatures. It is continuously generated by evaporation in the atmosphere and moves upwards, leading to cloud formation by condensation. The amount of water vapor in the air is known as humidity, and it is measured by hygrometers. The local climate is influenced by evaporative cooling and enhanced relative humidity due to the transpiration process. Unfavorable micro-climatic conditions, unseasonal rains, hot weather, or high humidity can affect certain crops and shake people’s confidence. Water vapor is effective at absorbing the thermal radiation from the Earth's surface, and it is known to be present outside the solar system in small quantities. Extraterrestrial liquid water is a topic of wide interest as it is one of the prerequisites for extraterrestrial life. In the solar system, the asteroid Ceres has large amounts of ice on its surface and also an atmosphere. Thus, water is a precious, life-sustaining resource for the community required for drinking, livestock, irrigation, and

industries. As water is crucial for our survival, and to fulfill the needs of the plant and animal kingdoms, pollution of local water sources, development of water-intensive industries, climate change, and lack of legislation can lead to threatening consequences. While adapting modern water treatment techniques, judicious use of water and proper water policies can lead to water as a path to growth. The procedures for obtaining necessary approvals and the regulatory framework need to be streamlined to have an enabling policy framework.

5. Water for Humanity and Observations

There is a need to recognize the biological, environmental, and industrial importance of water in the real world around us and to make reasoned choices on water consumption [43-48]. The amount of freshwater available to meet our industrial, domestic, and agricultural purposes is relatively limited. Of the 2.5 % freshwater, less than 1 % is available as surface water or groundwater, and the remaining portion of this freshwater is locked in glaciers and polar ice caps. The remaining part of the total volume of water on earth (96.5 %) is found in the oceans. Further, water must be treated to obtain the quality of water suitable for drinking purposes. The total hardness should be less than 400 mg/L, and chloride ion concentration should be less than 250 mg/L. As part of the water purification system, chlorination produces a group of by-products called trihalomethanes (THMs) that are suspected carcinogens. The WHO has prescribed a concentration limit of 100-200 µg/L on the total quantity in potable water. A study on the health effects of arsenic in drinking water in some parts of the world indicates a lung and bladder cancer risk. The environmental protection agency (EPA) of the USA issued the standard for arsenic in public water supplies to less than 10 µg/L. Today, the water of several rivers is polluted by industrial and domestic wastes and even dead bodies. The types of water pollution could include physical (suspended matter, thermal, solid waste) chemical (nutrients, toxic inorganic materials, persistent organic pollutants), microbiological (oxygen demanding, pathogens). Water pollution is a major global problem and one of the main problems of ecology [49-64]. This issue has to be tackled by local bodies and the government by implementing preventive measures, corrective steps, and promoting local recycling of water at all levels. Ten people out of a hundred lack access to clean and safe drinking water, and accessing it through local social enterprises via a network of subscribers for a nominal charge in a locality would make a difference in people's lives. Physical water scarcity arises as a result of inadequate natural water resources to meet the requirement of a geographical location. In contrast, economic water scarcity is a result of poor management of water resources. It is the latter type to be addressed in several countries facing a clean water crisis, and the limited availability of water impacts business. The joint effects of such a water crisis include reduced agricultural production, cost escalation of commodities, and economic pressures or political stresses. Climate change and water scarcity could adversely impact forest biodiversity and multiple forest products, which in turn would severely impact local communities dependent on forests for their livelihoods and as a source of raw material for a wide range of domestic and commercial applications. The change in a forest ecosystem can serve as a kind of early warning system for environmental problems and could have unpredictable consequences. Water acts as a vital social lubricant in the economic chain through its use in the industrial sector, agriculture, and tourism industry. It is essential to recognize the economic value of water in addition to its

ecosystem service, and all human beings should have access to clean water at an affordable price. Importantly, the goal of water for humanity will be achieved within the broad framework of science, technology, and product, and how we apply science practices more broadly.

The human population explosion on a global scale and increased human activities and development have resulted in multiple applications of the three typical phases of water [65-74]. Water is becoming an increasingly scarce resource, and the overexploitation of groundwater resources in the recent past has resulted in the drying of water tables, leading to several emerging water-related science, technology, and management issues. Increased depletion of groundwater, declining surface water sources, decreased replenishment, and excess evaporation due to global warming have caused many water-related issues and concerns [75-76]. The shortage of water harms ordinary citizens' lives, and the potential of distributing fresh water of good quality to all will positively impact societies. Snow measurements from Cryostat show that the Antarctic ice layer is losing 159 billion tons of ice each year, and more than a billion people depend on mountain snowflakes for their water needs. As the climate changes, snowfall may decrease in the future. Water conservation, harvesting, recycling, and the clean water act are essential parts of positive activities to restore the required amount of water for different domestic, industrial, and agricultural purposes.

There is a need to create awareness among the general public on rainwater harvesting, green belt development, and water conservation techniques. Conducting training, awareness, and sensitization programs for people will help maintain the sustainability of water resources. The right combination of recharging water bodies and reliable, responsible, and socially useful water delivery models are expected to make the desired positive impact on the ground. It is essential to improve water quality by regulating domestic sewage, runoff from agricultural lands and livestock areas, and industrial wastewaters from food-processing plants and paper mills. The service-specific regulations governing water use must specify the requirements relating to storage, packaging, transport, delivery, recycling, optimized utilization, distribution network, and regulated water tariff structure. Regulatory requirements are essential to have control over the introduction of toxic wastes from domestic, agricultural, and industrial sectors. Integrated wastewater management, large-scale public water transport systems, waste management legislation, and proper implementation aspects will inspire the next generation for a shared future. Adaptation of global water quality standards involves significant technological development challenges as well as several management changes. Conflict resolution regarding water disputes involves negotiations seeking a fair and reasonable settlement, which is acceptable to all and causes minimum damage to the environment. In the broader context, it is more important to strike a balance between water conservation and social development goals and arrive at river water-sharing agreements with neighboring countries. Water supplies must be affordable to all as it is the basic need of every human being.

Further, progress in equipment, technology, and purification methods will stand the next generation in good stead. Funding for not-for-profit water-related research activities and application-oriented research programs should be encouraged by the government. The research outcome will help us better understand the benefits of water and social issues associated with its supply to enable us to make intelligent decisions in the future. An association of the

government with non-profit organizations for constructing and maintaining water purification plants, and managing water supply projects in different areas can make a substantial socio-economic impact. Building a state-of-the-art water treatment plant based on reverse osmosis technology in different locations can save millions of people from waterborne diseases in the world. Progressive and eco-friendly policies and practices in implementing effective water management to achieve tangible results will allow the government to fulfill its commitment to a greener tomorrow gradually. Advanced wastewater treatment, disposal and analysis, water processing and distribution systems, and recycling and reuse of wastewater from various industries are necessary due to the contamination of water by hazardous wastes. The industries that require large quantities of water include tanneries, breweries, distilleries, refineries, aluminum, copper and zinc smelting, thermal power plants, and units engaged in the production of fertilizers, textiles, paper, sugar, cement, iron and steel, pesticides, petrochemicals, pulp and paper, dyes and dye intermediates, aerated drinks and packaged drinking water. Engineering systems for water purification include physical and chemical processes such as volatilization, dissolution, precipitation, hydrolysis, complexation, redox reaction, and photochemical reactions. Evaluation of water for public distribution involves a battery of determinations such as dissolved oxygen content, biological oxygen demand, determination of dissolved constituents, and testing for the presence of various forms of harmful microorganisms. A few general principles may be observed in water conditioning and industrial wastewater treatment: increasing industrial reuse, pollution control, recovery of by-products, and the use of green chemistry and engineering principles in the manufacture of pulp and paper, petroleum, and chemical and allied products. The discovery, development, and commercialization of low-polluting processes, green manufacturing methods, and additional research efforts in environmental protection should be encouraged by funds and grant programs by the governments. The green movement has lit the spark for water struggle in several places, and water harvesting and environmental conservation efforts directed towards meeting the challenge of water shortage have improved the situation dramatically. The millennium development goal of safe drinking water has reached the international target. Setting up a drought and flood monitoring and management cell (DFMMC) to recommend dynamic short-term and long-term plans, and concrete steps to encourage massive afforestation, protecting natural forests, lakes and other catchments, preventing the destruction of existing forests, preventing soil erosion, recharging the tanks, rivers, and groundwater, and environmental norms to conserve, manage and reuse of water for the benefit of all is essential. Local water management committees (WMC) can promote water conservation by documenting local water resources, developing guidelines for the extraction of water, conducting discussions and awareness sessions, and removing invasive species from waterbodies. It is crucial to have intricate water purification systems that remove harmful viruses, bacteria, hardness, turbidity, pesticides, harmful metal ions, organic compounds, lead, and other impurities for domestic purposes. The adherence to waste disposal rules, efficient effluent handling, and decreasing pollution levels in lakes and groundwater sources is a collective responsibility of both government and industry. Establishing an efficient effluent treatment plant in specific industries to ensure that either less amount or no residual harmful water is released helps them to achieve minimum liquid discharge (MLD) or zero liquid discharge (ZLD) status.

There is a threefold increase in fresh water withdrawals in the past fifty years. Development at the cost of forests, rivers, and other water bodies will result in desertification and agricultural land shrinkage. Heatwave conditions can lead to exhaustion, cramps, and sunstroke, killing many people across the world every year, and they harm the ecology. With extreme heatwave conditions and acute water shortage in several parts of the planet due to global warming, the heat-related mortality rate has increased substantially. Action plans include public awareness programs, early warning systems, drinking more water, and immediate medical attention. Ecological restoration measures have to be taken on a massive scale to reduce the impacts of heatwaves sustainably. Climate change will increase the evapotranspiration rate, leading to more demand for water. This shortage will result in water conflicts between industry and communities. It is essential to implement a comprehensive water policy, making all industries, particularly water-intensive ones, recycle and reuse their wastewater back into integrated operations and install necessary pollution control equipment. Recycled wastewater in many industries can be used for maintaining gardens, washing, landscaping, and cooling towers. Saline water for the industry can be used after sedimentation, filtration, reverse osmosis, chlorination, chemical oxidation, carbon adsorption, electro-dialysis, solar desalination, multi-stage flash distillation, or other treatments. The quality and quantity of water available and the effect of impurities such as arsenic, pesticides, and fluorides on the process have to be considered while selecting a suitable location for constructing a factory. Breakthrough research outputs in energy conversion technologies or desalination technologies would make water available in large quantities at the location of industries and open prospects for further industrial development. Conservation of water through the recycling of wastewaters and their use in the agricultural sector may help prevent severe ecological degradation and prevent environmental contamination. The protection of the environment requires strict laws related to water pollution control, reasonable water quality standards, standards for hazardous water pollutants, implementation aspects, and evaluation methods for both private and public water treatment plants globally. The laws, rules, and regulations will have a direct bearing on the water usage by the contemporary aspirational society. It is better to adapt the required international regulatory standards and have an institutional mechanism to implement the law's intent. The legislative framework should also include the option of enforcing penal action against defaulters as an essential component. We have to establish water testing laboratories to check the quality of water and set up pure drinking water units to ensure the supply of potable water to millions of residents across developing countries in the world by 2025. Water quality parameters to be checked include dissolved oxygen, specific conductivity, pH, alkalinity, major ions, temperature, suspended solids, and turbidity. The principal impurities in Municipal Corporation water include suspended matter and organic substances (sediment, microorganisms), dissolved mineral matter (bicarbonates, sulfate, chlorides of Ca, Mg & Na), and dissolved gases (O_2, N_2 & CO_2). Primary water treating operations include sedimentation, coagulation, filtration, chlorination, taste, and odor removal. The optional treating operations involve the hardness removal, zeolite process, lime-soda process, fluoridation/fluoride removal, demineralization, and removal of dissolved gases.

Water is a finite resource, and water usage needs to be carefully managed to prevent its rapid depletion. A combination of physical, psychological, environmental, and social factors leads to water pressures. Several concrete steps need to be taken to prevent the future water crisis, and developing a sound long-term water supply strategy would certainly have some effect on reducing water pressures. The first step is to collect high-quality data about water resources. We have to learn lessons from hard-core environmental facts and figures of major development projects and carry out in-depth research that helps us to make a well-informed choice to avoid drought. The second step is to prevent water pollution as it means less need for purification. The third step is to ensure a clean potable water supply and better sanitation through better management practices. A global surveillance network is required to monitor the quality of water used in different parts of the world. It is important to share best practices in reliable tools and technologies to replicate the model across the world. Fourth, a public campaign to promote awareness about the dangers of waterborne diseases and the need to have public interest safeguards to promote socioeconomic development. This awareness can bring about a big change. There is a need to increase awareness about the importance of water as a marketable commodity. Creating responsible water consumption patterns by the citizens could help in avoiding water-based conflicts between states or nations. Fifth, encouraging the use of existing water and wastewater technologies as well as developing new environment-friendly technologies. We need a multipronged approach that involves collaboration among neighboring nations and states and improves system efficiency, including distribution and delivery planning, adequate infrastructure, and specific training requirements. Funding for research and development, innovative water treatment process marketing, and encouragement for creating brand equity would go a long way in establishing water conservation, management, and optimal use. Adopting water-efficient practices, technological innovations, and mandatory reuse in water-intensive industries have a major impact on the socio-economic life of local areas. Attracting private sector investments and participation in eco-friendly water purification plants, research and development efforts on water-related issues are necessary to help contribute towards sustainable development. Sixth, frame future policies on the continuous water supply and distribution systems for domestic, industrial, and irrigation purposes. It is becoming increasingly clear that manufacturing industries should follow environmentally sustainable business practices in their production activities with a focus on energy, water, and nature conservation. Geographic Information Systems (GIS) can be applied in developing water distribution system hydraulic models. Environmental impact assessment (EIA) of large water resources projects, drought assessment, and forecasting, estimating the area and intensity of rainfall, water quality management, corrective, preventive, and scheduled maintenance of water systems, reuse of water, rainwater harvesting, forest regrowth, artificial recharging of groundwater and analyses of other technical aspects play an important role in sustainable water management. Construction of modern rainwater harvesting systems such as dams, injection wells, percolation ponds/tanks, stepwells, open wells, and subsurface barriers serve as effective alternatives to rejuvenate depleted groundwater aquifers. The key to managing water issues is to initiate local water conservation and management practices, and water sharing through dams and canals and the interlinking of rivers to enable water transfer from surplus to deficit regions. Periodical data collection on water pollution levels in different nations will equip the world to

initiate and accelerate global level actions required to keep the pollution level minimum and increase the availability of pure water, under the concept of water for all. A transparent reporting mechanism will enable us to understand the actions implemented to promote a robust and meaningful water distribution system with optimum water efficiency and reuse of water, the impact of these actions on the degree of pollution, and the long-term prospects of sustainable water resources management. The beginning of change lies in each individual's mind, and we need to cultivate the habit of not wasting precious resources like water and causing pollution. Political will and delivery of services and synthetic engineering systems for drinking water are two of the numerous steps to deliver optimal results. Pricing of water should be determined based on working expenses, including the cost of operation and maintenance. Print and electronic media should present a positive and realistic image to the general public, and governments should encourage interdisciplinary research to meet the emerging challenges of the global water crisis.

Global climate change has attracted considerable attention from interdisciplinary researchers around the world in the last decade. The research on essential aspects of water-related topics is expected to reveal new insights on the scale of the impact and its environmental effects. The surface temperature of the earth is increased by 0.74 ^{o}C in the last hundred years. Global warming may lead to extreme hydrological events such as flash floods and severe droughts, driving many creatures to extinction. This warming will further affect the regional ecology and the life of local people, and in extreme cases, it may lead to ecological catastrophes and large-scale social disruptions. The problems of water quality, quantity, reuse, and pollution are complex. They may vary significantly from one location to another and depend on the prospective use, whether for power generation, heating/cooling, agriculture, domestic applications, or as a solvent. A broad-based approach involving sustainable agriculture, water efficiency in agriculture, sustainable tropical forestry, sustainable development, technical and commercial efficiency of water supply systems, and a sustainable business model will facilitate the sharing of water. Creating ecological awareness, change in the mindset regarding development, better water use policies, responsible consumption of natural water resources, and the use of new techniques to sustainably use water is expected to have positive impacts on the sustainable use of H_2O for humanity. It is essential to take the application and usefulness of water harvesting and conservation ideas, and nature-friendly practices to the common man through the commercialization of products. Managing water harvesting on a large-scale is crucial for consideration in terms of the added load because of high demand due to increased human activities, which will lead to a substantial increase in water level. The web of issues and concerns associated with effective water management affecting the stakeholders must be addressed through a pragmatic approach, social activism, and empowerment of people to achieve a long-term solution. We must cultivate a greater sense of universal responsibility and put it into practice for the good of humanity. Each should have the right to equal access to natural water resources and the responsibility of protecting the environment for future generations by performing all activities within existing resource constraints. There is an urgent need for intense goal-oriented action by the governmental system and all the stakeholders to foster community water management practices through a societal transformation as water is one

of the most abundant, yet depleting, a chemical in nature and essential for life on Earth. Besides, preventing water loss due to leakage and illegal drawing of both surface and groundwater in some areas should become an integral part of sustainability services to preserve this precious commodity. The bottom line is that we have to increase groundwater levels, conserve water, reduce and reuse, plant trees, and fine-tune farming practices through participative ecosystem management and have integrated and sustainable water resources management for more equitable distribution as water is the fundamental substance of life.

The first observation is the rapid loss of forest cover in the recent past in various parts of the world. It is essential to carry out forest area evaluation and detect green cover changes based on satellite data. This survey helps us better understand the relationships between human activities and the change in natural ecosystems. Afforestation on a massive scale plays an essential part in preventing an accelerated reduction of forest cover and enhancing water holding capacity. New forest areas should be added each year to sensitive landscapes to decrease soil erosion and enhance transpiration. We have to protect them from forest fires, grazing, encroachment, and illegal cutting of trees. The second observation is that coal-based power plants are responsible for much of the world's greenhouse gas emissions. It is essential to develop novel technologies and use alternative power generation technologies such as solar, nuclear, and hydropower. The third observation is that the policymakers are focusing their attention on consumption rather than savings. The government should move the focus toward spreading awareness about the judicious use of this multi-use substance and popularizing water harvesting techniques to reduce the global water footprint. The structure and operational details of water treatment and distribution systems should be comprehensive, including supplying water, infrastructure development, exceptions, and administrative matters. The fourth observation is that the determination of the water prices is ad hoc and needs some structured approach and reforms. The fifth observation is that water conflicts arise because of vested interests, and we need to emphasize the importance of developing collective responsibility, primary national interests, and long-term sustainability goals. There is a need for creating more online educational platforms to spread the message about water conservation and to disseminate articles, news, images, and videos about water. It is essential to provide mental, graphical, computational, or physical models to enhance understanding of key water chemistry concepts, acquire domain-specific knowledge, and use models to explain a specific observation or analyze new experimental outcomes. It is crucial to research issues connected with water consumption and development, to lead the people in the right direction. The social commitment of agriculture departments, civil society organizations, and corporate companies, coupled with positive initiatives can change the entire landscape and help holistic and balanced development of humanity's well-being.

The integrated organ and printing system uses water-based ink to hold cells and micro-channels to form tissues that can safely integrate into our bodies [77]. Developments in 3D bioprinters could make organs and human tissue good enough for transplant. The future of water purification could involve its treatment with ultraviolet light-emitting diode devices (UV-LED) at the point of use rather than conventional mercury lamps [78]. The recent advances in the water-based printing process involve the use of liquid, waterborne printing

inks with negligible volatile organic compound content [79-83]. A significant advance in water-based batteries includes water-in-salt lithium-ion battery technology that could change the use of battery-powered electric vehicles in the future [84]. Smart underwater micro-drones could be used to monitor or map large areas of the oceans [85]. Further advancements in air-to-water generators or advanced versions of wastewater treatment plants, and the adoption of new technologies, help expand access to clean drinking water to new consumers.

6. Conclusions

In this chapter, we have described the essential uses and different properties of water and emphasized the need to confirm, correct, apply, extend and improve water science and engineering concepts, principles and applications while solving problems related to water. Water is the critical substance for the survival of all civilizations and cultures. It has an essential role in continuing plant and animal life. It would serve to fortify people on the journey of their lives and their businesses. The businesses can be grouped into verticals like municipal water supply and wastewater treatment, industrial water, and wastewater treatment, seawater desalination, pollution control, and green power generation. The water demand grows as populations increase, placing more significant stress on finding adequate supplies to meet the demand. A focused approach by governments on implementing particular strategies on the ground will have a significant impact on achieving the national population stabilization target within a short period. Liquid water, a collection of water molecules, is a powerful symbol of hope and literary imagination. It is supporting the whole ecosystem and is crucial for our existence in the laboratory of life. It is a common substance and a unique solvent, essential for living systems. We have to learn to respect nature because of the life-giving care of the water bodies like rivers and streams. We have to invest heavily in quality education and public health, such as clean water, sanitation, and disease control. The growth of an innovative healthcare delivery model depends on the incorporation of waterborne disease prevention through better sanitation and water purification processes in its ecosystem. Funds for developing comprehensive solar power infrastructures such as solar parks and solar farms will help achieve global energy generation targets, enhancing the solar energy capacity manifold.

Water can act either as an acid or as a base. All the chemistry that makes life possible takes place in water media, and different tests involve chemical reactions in water, including the analysis of blood and other body fluids. There are some chemical reactions in water with metals, non-metals, and compounds. Water plays a pivotal role in the metabolism of foodstuffs in the stomach or oxygen transport within the body system. When raindrops come in contact with carbon dioxide in the atmosphere, water becomes acidic due to the formation of carbonic acid. Water pollution control methods and water treatment techniques used to soften hard water play an essential part in the supply of water required for domestic purposes and industrial processes. The challenges include mindset change, building better systems, achieving water security, maintaining high purity standards, reduction in water pollution levels, improvement in the quality of services, changes in technology, and fair price and transparency. The focus on innovative ideas, a proper plan, established processes, a business model, organizational structure, a strong network of mentors, better water management, access to risk capital, and a forward-looking workforce would pave the way toward sustainable global growth. Further

research and development efforts to improve the water purification and distribution system are warranted. Another direction for future research in this area is the exploration of the technical improvements in monitoring systems and the effective delivery of water fulfilling the regulations. It will be fascinating to see if the development of advanced and hybrid water technologies would significantly reduce the incidence of waterborne diseases. It is an enduring water link in the entire ecosystem that becomes important to the process of climate change. An analysis of specific geospatial data could help in overcoming the water crisis in the future by reconstructing concepts critical to the future of our society. ‘Save water-save the earth’ is a powerful message that would transform the world for the better. It is essential to realize that ‘just do it’ is not enough, but ‘do it right’ is the way to go, as many small expeditious steps in the right direction can make a great leap forward. It remains to be seen if the prospect depends on how water management plans reflect our close observation of images from contemporary situations, history, and life.

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RECENT DEVELOPMENTS AND FUTURE PROSPECTS OF CAPACITORS

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1. Introduction

The structure formed by placing a space/air or a dielectric material between the conductive plates is called a capacitor (Riaz & Kanwal, 2019). It is assumed that the capacitor will indeed be recharged by Q in a manner that corresponds to the voltage differential of V, if a voltage difference of V is supplied between both the planes (Zharin, 2010). The measure of how much a capacitor can be charged under the applied potential difference is called the capacitance of that capacitor (Pal et al., 2021).

The capacity of the space (air) capacitor is defined by the expression (Muñoz-Enano et al., 2021).

$$C_0 = \frac{Q}{\Delta V} \tag{1.1}$$

The unit of the capacitance (SI) is Farad (F), Q is the amount of charge stored in the capacitor and its unit is Coulomb, ΔV is the potential difference between the electrodes and its unit is Volt.

The capacitance value depends on the geometry of the capacitor and the characteristics of the region between the parallel plates (Ciftja, 2021).

If there is a gap between the capacitor plates, the capacitance of the capacitor is defined as

$$C_0 = \varepsilon_0 \frac{A}{d} \tag{1.2}$$

Here, A is the surface area of the electrodes, d is the distance between the electrodes, and ε_o is the permittivity of free space and its value is $8.85 \times 10^{-12} Fm^{-1}$.

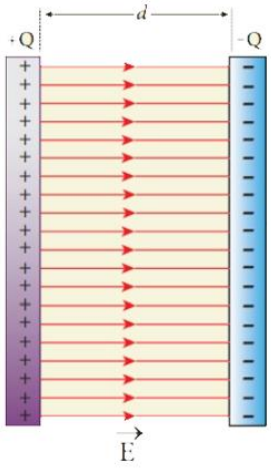

Figure. 1. Electric field lines between the parallel plates of a air capacitor (Rediansyah & Viridi, 2015).

When a potential difference is applied to the capacitor, the distance between the conductive plates must be very small in order from the surface area (d<<A) to create a uniform electric field between the conductive plates as in figure 1.

When a dielectric material is placed between the plates of the capacitor, the capacitance of the capacitor increases. C is the capacitance of the dielectric capacitor, ε is the permittivity of the dielectric material is expressed with,

$$C = \varepsilon \frac{A}{d} \tag{1.3}$$

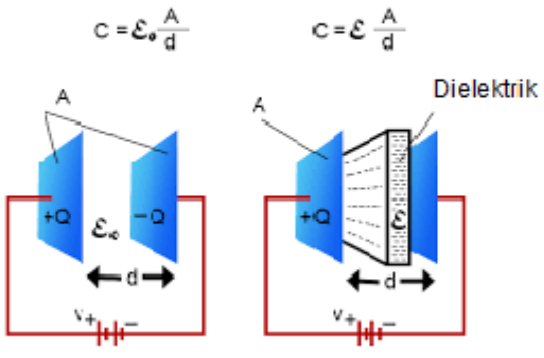

Figure 2. The capacitance of air and dielectric capacitor connected to the battery (Nishino, 1996).

The material placed between the plates of a capacitor with low electrical conductivity is called a dielectric (Matko & Milanovič, 2021). When a dielectric material is placed between the two

plates of the capacitor, the capacitance of a capacitor increases. The dielectric material provides the following contributions to the capacitor:

A distinguishing characteristic of the piezoelectric medium that changes through one materials to the next and raises capacitance by a factor of is the dielectric constant (Burke, 2021). The mechanical support provided by the insulators allows the two panels to be placed closer to one another without actually touching.

A capacitor with a capacity of C_o is linked to a cell and recharged to a potential of V_o when there is a space among its layers.

The cell is unplugged when the capacitor has been fully charged. The charge Q_o is present on the plates, and the change in voltage between the two is calculated as V_o. It is seen that when a dielectric is placed between the plates, the potential difference drops to a smaller value such as V. It will be seen that the dielectric capacitor will be more charged than the gap capacitor as in Figure 2.

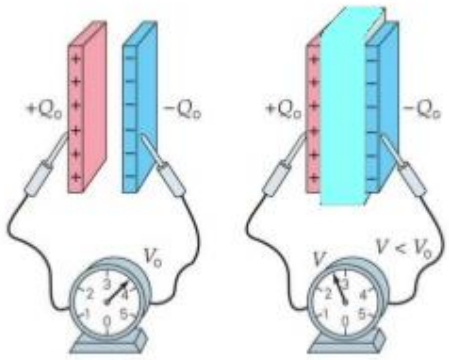

Figure 3. The charge amounts of the air and dielectric capacitor connected to the battery (Ippili et al., 2022).

When $\kappa > 1$, then $\Delta V < \Delta V_o$.

$$V = \frac{1}{\kappa} V_0 \tag{1.4}$$

The constant κ in this equation is called the dielectric constant or relative permittivity of the material between the plates (Figure 3). The dielectric constant κ is just a number and it has no dimension.

The capacitance of a dielectric capacitor,

$$C = \frac{Q_o}{V} = \frac{Q_o}{\frac{V_o}{\kappa}} = \kappa \frac{Q_o}{V_o} = \kappa\, C_0 \tag{1.5}$$

Equation (1.5) states that by placing a dielectric material between the plates of capacitor, the capacitance can be increased by a factor κ. The electrical energy stored in a dielectric capacitor is also affected. The energy stored in air capacitor is U_o and the energy stored in a dielectric capacitor is U.

$$U = \frac{1}{2}\frac{Q^2}{C} = \frac{1}{2}\frac{{Q_o}^2}{\kappa C_o} = \frac{1}{\kappa}\,U_o \tag{1.6}$$

2. Dielectric in Microscopic Dimension

The electrical structure formed by the positive (+q) and negative (-q) charges with a distance d between them is called the electric dipole (Ambroziak & Ciężkowski, 2021). Electric dipoles are represented by dipole moments.

Electric dipole moment,

$$p = qd \tag{2.1}$$

It is shown in Figure 4. Here d is the distance between the negative charge and the positive charge. The dipole moment vector is from negative charge to positive charge. The unit of dipole moment (SI) is coulomb-meter (Cm); however, the unit commonly used in atomic physics and chemistry is debye (D).

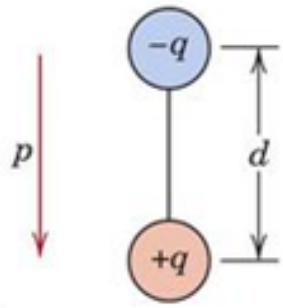

Figure 4. Electric dipole moment (Ambroziak & Ciężkowski, 2021).

When there is dielectric material between the capacitor plates, the total $\vec{E}$ electric field also decreases by the ratio of the decrease in the potential difference between the plates.

$$\vec{E} = \frac{\vec{E}_0}{\kappa} \tag{2.2}$$

Let us explain the decrease in electric field by examining an ideal dielectric material.

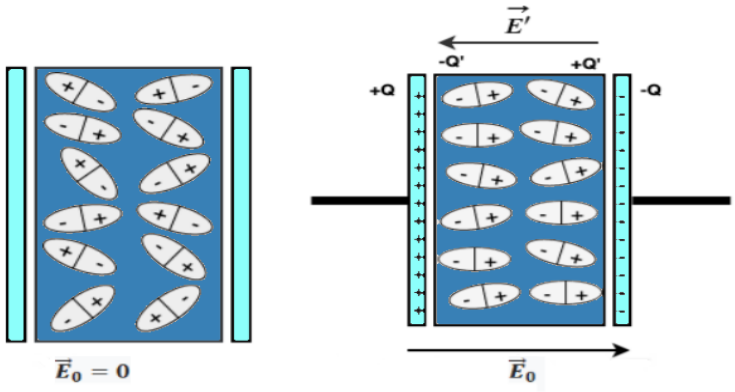

Figure 5. Distribution of dipoles under the absence and presence of external electric field (Du et al., 2022)

In in Figure 5, under the absence of electric field, dipoles are homogeneously distributed in the dielectric material. When a potential difference V_o is applied between the dielectric capacitor plates, a torque acts on the dipoles in the dielectric material between the plates. The dipoles are forced into a rotational motion in the electric field direction under the effect of torque, as shown in figure 5. The rotational motion of the dipoles depends on the frequency of the electric field and the temperature.

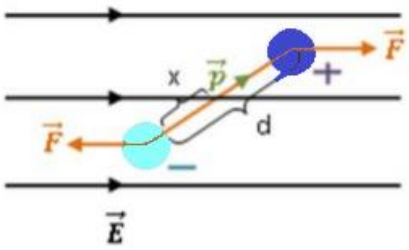

Figure 6. Torque acting on a positive and negative charge under a uniform electric field (Shoyama & Matsusaka, 2019).

Let's show this torque relationship mathematically; where $\vec{F}$ is the applied force

$$\vec{F} = q\,\vec{E} \tag{2.3}$$

Here E is the applied electric field and q is the distance between the charges. The expression $\vec{\tau}$ torque acting on the system,

$$\vec{\tau} = \vec{d} \times \vec{F} \tag{2.4}$$

The torque on the system can be calculated by using the above equation.

$$|\vec{\tau}| = \tau = |\vec{d}||\vec{F}|sin\theta \quad (2.5)$$

$$\tau = Fxsin\theta + F(d-x)sin\theta \quad (2.6)$$

$$\tau = Fd\ sin\theta \quad (2.7)$$

The applied force $\vec{F} = q\ \vec{E}$ and the distance between the charge centers d= p/q, the torque is written as

$$\tau = pEsin\theta \quad (2.8)$$

$$\vec{\tau} = \vec{p} \times \vec{E} \quad (2.9)$$

Torque is a vector quantity and its direction is inwards from the page plane as shown in figure 7.

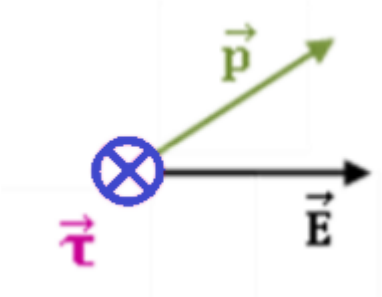

Figure 7. The torque that causes the rotational motion of the dipole (Melle et al., 2002).

By placing the dielectric material between the capacitor plates the decrease in the potential difference and the electric field $\vec{E}$ can be explained by using Gauss's Law.

Air between capacitor plates: Gauss's Law is used to find the electric field ($\overrightarrow{E_o}$) between the plates of a parallel plate capacitor when there is air between the plates. The net flux through the Gaussian Surface:

$$\phi_e = \oint \vec{E}.d\vec{A} = E_oA = \frac{Q}{\varepsilon_o} \quad (2.10)$$

$$E_o = \frac{Q}{\varepsilon_o A} \quad (2.11)$$

It is the expression of the electric field for air capacitor. Q/A is the charge per unit area, σ is the charge density. Electric field expression based on charge density

$$E = \frac{\sigma}{\varepsilon_o} \quad (2.12)$$

Dielectric material between the plates: If there is a dielectric material between the plates of the capacitor, a Gaussian surface can be chosen as in figure 8, and the electric field expression

$$\oint \vec{E}.d\vec{A} = EA = \frac{Q-Q'}{\varepsilon_o} \quad (2.13)$$

$$E = \frac{Q-Q'}{\varepsilon_o A} \quad (2.14)$$

$$E = \frac{Q}{\varepsilon_o A} - \frac{Q\prime}{\varepsilon_o A} \tag{2.15}$$

Q' is induced charge of dielectric capacitor. Q and Q′ charges are oppositely signed charges. Q – Q′ represents the charge on the specified Gaussian surface.

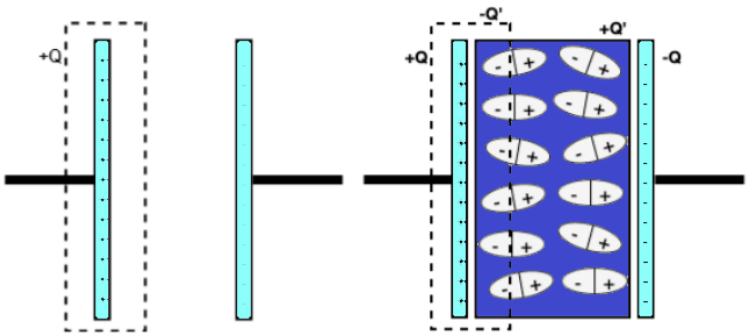

Figure 8. Selective Gaussian surface in air and dielectric capacitor (Li & Behdad, 2013).

Equation (2.15), If the magnitude of the electric field is written in terms of charge,

$$E = \frac{E_o}{\kappa} = \frac{Q}{\kappa\varepsilon_o A} = \frac{Q - Q\prime}{\varepsilon_o A} \tag{2.16}$$

$$\frac{Q}{\kappa\varepsilon_o A} = \frac{Q}{\varepsilon_o A} - \frac{Q'}{\varepsilon_o A} \tag{2.17}$$

$$Q' = Q\left(1 - \frac{1}{\kappa}\right) \tag{2.18}$$

The amount of charge induced on the surface of the dielectric is always less than the amount of charge on the plate surface $(Q' < Q)$.

If written as charge density, it becomes

$$\sigma' = \sigma\left(1 - \frac{1}{\kappa}\right) \tag{2.19}$$

When the equation (2.17) is simplified it can be written as

$$\frac{Q}{A} = \varepsilon_o\left(\frac{Q}{\kappa\varepsilon_o A}\right) + \left(\frac{Q'}{A}\right) \tag{2.20}$$

Vector representation of equation (2.20)

$$\vec{D} = \varepsilon_o\vec{E} + \vec{P} \tag{2.21}$$

Here in equation (2.21), the first term corresponds to the displacement field, the second term corresponds to the applied field between the plates, and the last term corresponds to the field due to polarization.

3. Polarization Mechanisms

The dielectric material responds to the electric field by polarizing it. Polarization results from the response of dipoles to the electric field effect. The polarization vector is related to the

neutralized charges on the surfaces of the capacitor plates (Chiu, 2014). Average dipole moment, can be written as

$$\vec{p} = \alpha\vec{E'} \tag{3.1}$$

Here α is the polarizability coefficient and E′ is defined as the local electric field. The polarization vector,

$$\vec{P} = (\kappa - 1)\varepsilon_o\vec{E} = N\alpha\vec{E} \tag{3.2}$$

This equation relates the dielectric constant κ, which is the microscopic parameter of the dielectric, to the molecular parameters N, α and E.

3.1. Electronic Polarization

Considering the structure of an atom, its nucleus consists of electrically neutrons and positively charged protons, and a cloud of randomly moving electrons. When the external electric field is applied, the nucleus of the atom and the negative electron cloud around it are separated from each other. This light charge separation makes one side of the atom slightly positive and the other slightly negative. The resulting polarization is called electronic polarization and is illustrated in figure 9. In dielectric materials, electronic polarization is observed. Electronic polarization takes place within a short time (Nunes & Vanderbilt, 1994). Electronic polarization is observed at high frequencies at approximately 10^{15}Hz. α_e represents the ability of the electron cloud to move the nucleus under the influence of the electric field, in other words it is the coefficient of electronic polarizability.

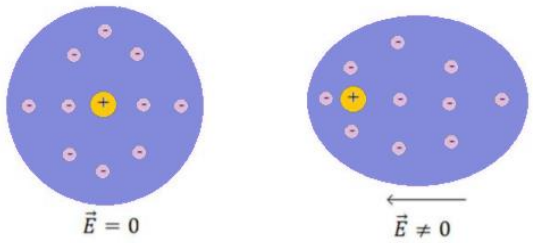

Figure 9. Electronic Polarization (Nunes & Vanderbilt, 1994).

3.2. Ionic Polarization

Ionic polarization (Kumar et al., 2020) takes place in ionic crystal elements. In the absence of an external electric field, the positive ions within the crystal cancel out the negative ions and the total charge becomes zero. When an external electric field is applied, the negative and positive charge ions are displaced, resulting in an induced polarization. Figure 9 illustrates the displacement of ions due to the electric field. The ionic polarization is represented by α_i. Since the ions that make up the crystal lattice are heavier in mass than the electrons, electronic polarization takes longer to occur. Ionic polarization generally occurs in ionic materials and is observed at low frequencies compared to electronic polarization. Ionic polarization is observed at approximately 10^{13}Hz.

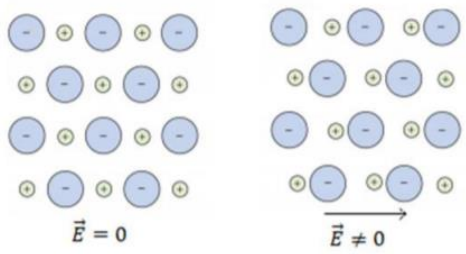

Figure 10. Ionic Polarization (Kumar et al., 2020).

3.3. Dipolar Polarization

Dipolar polarization (Shin et al., 2015) occurs in molecules that have dipoles when there is no electric field. When an external electric field is applied to these molecules, a torque acts on the dipole moments in the structure. As a result, the molecules tend to align as required by the applied electric field. When the electric field is removed, the dipoles return to their original position. This is called dipolar polarization and is represented by α_d. This polarization mechanism occurs in the range of 10^{-3}-10^{-9} seconds and is observed in the frequency range 1kHz-1MHz.

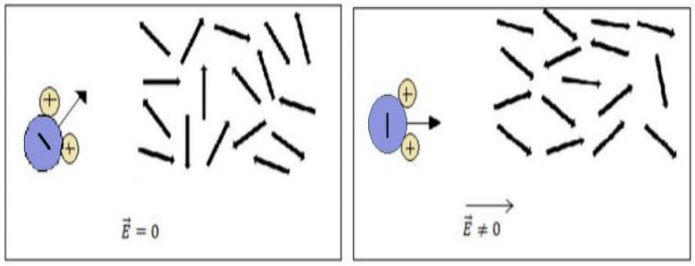

Figure 11. Dipolar Polarization (Shin et al., 2015).

3.4. Interface Polarization

When there is an accumulating of charge at an interface between two materials or between two areas inside a material as a result of an external electric field, this phenomenon is known as interfacial or space charge polarisation (Hermann & Schmidt, 2020). Interfacial polarisation is different from ionic polarisation in that it impacts free charges in addition to the bound positive and negative charges, i.e., ionic and covalently bonded structures. As a result, interfacial polarisation is typically seen in polycrystalline or amorphous substances. According to Figure 12. Due to the dielectric material's insulating qualities, the electric field will result in a charge imbalance and happen at a frequency of roughly 10-2 Hz, where α_s is the polarizability coefficient of the interfaces.

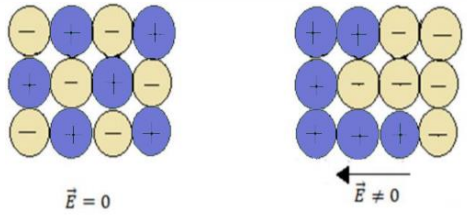

Figure 12. Interface Polarization (Hermann & Schmidt, 2020).

The polarization mechanisms of the frequency with respect to the dielectric constant and the dielectric loss are shown in Figure 13.

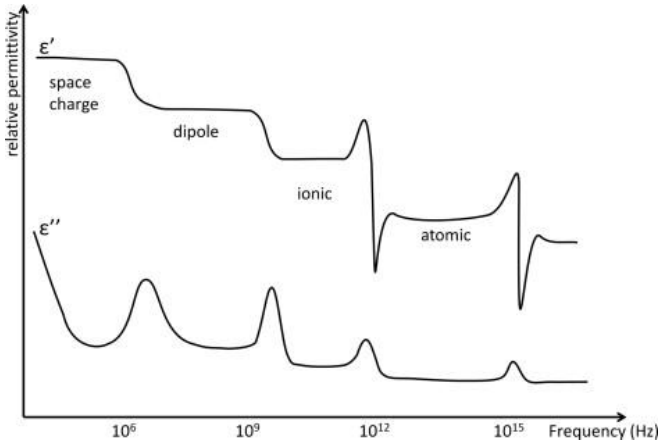

Figure 13. Polarization mechanisms according to frequency, dielectric constant and dielectric loss (Kim et al., 2021).

4. Variable Electric Field and Dielectric Loss in the Capacitor

If a potential difference with angular frequency ω is applied between the plates of air capacitor, the potential difference can be written as

$$V = V_{\circ} e^{i\omega t} \tag{4.1}$$

The charge on the surface plates of the capacitor is,

$$Q = C_{\circ} V = C_{\circ} V_{\circ} e^{i\omega t} \tag{4.2}$$

The current caused by these charges is;

$$I_c = \frac{dQ}{dt} = \frac{d}{dt}(C_{\circ} V_{\circ} e^{i\omega t}) = i\omega C_{\circ} V_{\circ} e^{i\omega t} \tag{4.3}$$

rearrange this equation

$$cos\frac{\pi}{2} + isin\frac{\pi}{2} = i \tag{4.4}$$

By substituting $i = e^{i\frac{\pi}{2}}$ in the equation (4.1),

$$I_c = e^{i\frac{\pi}{2}} \omega C_{\circ} V_{\circ} e^{i\omega t} = \omega C_{\circ} V_{\circ} e^{i(\omega t + \frac{\pi}{2})} \tag{4.5}$$

By substituting $I_\circ = \omega C_\circ V_\circ$ in above equation, we get

$$I_c = I_\circ e^{i(\omega t+\frac{\pi}{2})} \tag{4.6}$$

As you can see, there is a 90° phase difference between the loading current and the applied potential. In other words, the current is 90˚ ahead of the applied voltage. This is explained with the phasor diagram in the figure. This is valid only for the capacitor with air between the plates. The capacitor belonging to such a structure is defined as the ideal capacitor.

If a potential difference is applied to the capacitor while there is a dielectric material between the capacitor plates, energy is lost when the dielectric structure becomes polarized. In this case, there will be a loss of current due to energy loss in the dielectric and it is indicated by I_R. In a dielectric capacitor, the phase difference between the charging current and the applied voltage will be different than 90°, that is, it will be 90-δ. This situation is represented by a phasor diagram.

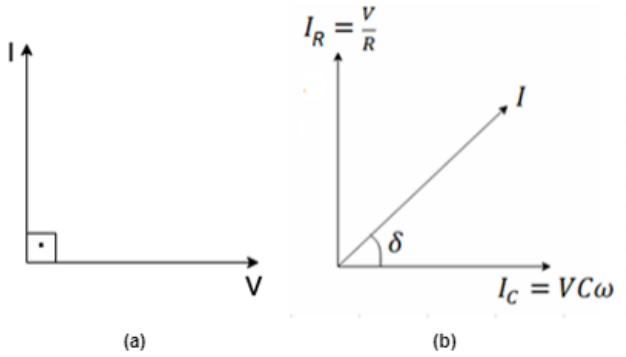

Figure 14. Phasor diagram representation of capacitor under variable electric field (AC), (a) For Air Capacitor (b) For Dielectric Capacitor (Wang et al., 2021).

Conductance is $G = 1/R$

$$I_R = GV \tag{4.7}$$

The total current of the capacitor is,

$$I = I_c + I_R = (i\omega C + G)V \tag{4.8}$$

Tangent of phase angle between charge current and total current is

$$tan\delta = \frac{I_R}{I_c} = \frac{1}{\omega RC} \tag{4.9}$$

known as the loss factor. Considering the phase difference between the charging current and the loss currents in the effect of the variable electric field, an expression that can be defined as the charging and loss components in the dielectric material can be used. For this purpose, here the dielectric complex permittivity is one of the distinguishing properties of the dielectric, and its expression is

$$\varepsilon^* = \varepsilon' - i\varepsilon'' \tag{4.10}$$

By using this expression, the total current is;

$$I = \left(i\omega\varepsilon^{'} + \omega\varepsilon^{''}\right)\frac{C_{\circ}}{\varepsilon_{\circ}}V \tag{4.11}$$

$$I = i\omega C_{\circ}\frac{\varepsilon^{'} - i\varepsilon^{''}}{\varepsilon_{\circ}}V \tag{4.12}$$

$\varepsilon^{'}$ the real component of the electric permittivity, and $\varepsilon^{''}$ the imaginary component of the electric permittivity,

κ^{*}, complex dielectric constant is defined as

$$\kappa^{*} = \frac{\varepsilon^{*}}{\varepsilon_{\circ}} \tag{4.13}$$

and the expression

$$\kappa^{*} = \kappa^{'} - i\kappa^{''} \tag{4.14}$$

$\kappa^{'}$ dielectric constant, $\kappa^{''}$ is the dielectric energy loss.

Considering the phasor diagram for a dielectric capacitor, the total current expression is,

$$I' = \frac{dQ}{dt} = \frac{d}{dt}CV_{\circ}e^{i\omega t} = i\omega CV_{\circ}e^{i\omega t} \tag{4.15}$$

$$C = \kappa^{*}C_{\circ} \tag{4.16}$$

$$I' = i\omega(\kappa^{'} - i\kappa^{''})C_{\circ}V_{\circ}e^{i\omega t} \tag{4.17}$$

$$I' = i\omega\kappa^{'}C_{\circ}V_{\circ}e^{i\omega t} + \omega\kappa^{''}C_{\circ}V_{\circ}e^{i\omega t} \tag{4.18}$$

$$tan\delta = \frac{I_R}{I_C} = \frac{\omega\kappa^{''}C_{\circ}V_{\circ}e^{i\omega t}}{\omega\kappa^{'}C_{\circ}V_{\circ}e^{i\omega t}} = \frac{\kappa^{''}}{\kappa^{'}} \tag{4.19}$$

Here it is seen from the expression of the loss factor that the dielectric constant is the ratio of the real and imaginary parts.

The currents observed in the dielectric are expressed in terms of the current density.

Current density,

$$J = \frac{I_R}{A} = \frac{\omega\kappa^{''}C_{\circ}V_{\circ}e^{i\omega t}}{A} \tag{4.20}$$

Electric field can be expressed as;

$$\left|\vec{E}\right| = \frac{V}{d} \tag{4.21}$$

$$C_{\circ} = \frac{A}{d}\varepsilon_{\circ} \tag{4.22}$$

By adding equations 4.21 and 4.22, in the current density equation 4.20, we get

$$J = \frac{I_R}{A} = \frac{A}{d}\frac{\omega\varepsilon_{\circ}\kappa^{''}E_{\circ}de^{i\omega t}}{A} \tag{4.23}$$

$$J = \omega\varepsilon^{''}E \tag{4.24}$$

$$\sigma_{AC} = \omega\varepsilon^{''} \tag{4.25}$$

Equation (4.25) is called variable field conductivity of dielectric medium.

5. The Clausius-Mossotti Equation

The polarization is dependent on the magnitude of the electric field acting on the dipoles (Duerinckx & Gloria, 2022). The value of polarization is,

$$\vec{P} = N\vec{\mu} \tag{5.1}$$

In Equation 1.56, N is the number of dipoles per unit volume, $\vec{\mu}$ is the mean dipole moment. α is Polarization coefficient, $\overrightarrow{E'}$ local electric field, Polarization can be written as

$$\vec{P} = N\alpha\vec{E}' \tag{5.2}$$

Let's examine the model of dipoles formed by non-polar molecules under the influence of an external electric field. The local field acting on a reference molecule is caused by the effect of the external electric field. It is explained by considering the model in Figure 15.

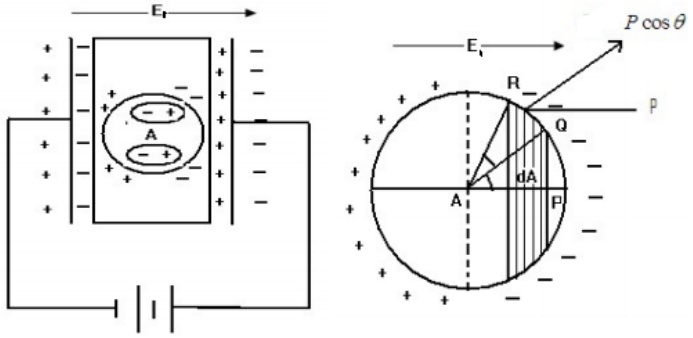

Figure 15. The local electric field that occurs in the dielectric material (Duerinckx & Gloria, 2022).

Let's suppose for the purposes of this model that a virtual sphere surrounds the reference molecule A in the physical world. $\overrightarrow{E_1}$ is the electric field between the plates, $\vec{E}_2$ is the electric field between the dipoles, and $\vec{E}_3$ is the electric field resulting from the surrounding dipoles. As a consequence, A is the electric field acting on the reference molecule.

$$\vec{E}' = \vec{E}_1 + \overrightarrow{E_2} + \overrightarrow{E_3} \tag{5.3}$$

Here $\vec{E}_1$ is taken as $\vec{E}$ since it is the external electric field and $\vec{E}_3$ electric field can be neglected since it is very small relative to $\vec{E}_1$ and $\vec{E}_2$. If we choose $\overrightarrow{dA}$ surface area within the sphere, there will be an electric field corresponding to each field. Electric fields in the horizontal direction neutralize each other. For the fairly small electric field $\vec{E}_2$,

$$d\vec{E}_2 = \frac{1}{4\pi\varepsilon_o}\frac{dq\cos\theta}{r^2} \tag{5.4}$$

$$dq = dA \times P_N \tag{5.5}$$

$$dq = dA \times P\cos\theta \tag{5.6}$$

$$dA = 2\pi r^2 \sin\theta d\theta \tag{5.7}$$

$$dq = 2\pi r^2 P \cos\theta \ \sin\theta d\theta \tag{5.8}$$

$$dE_2 = \frac{1}{4\pi\varepsilon_o}\frac{2\pi r^2 P \cos^2\theta \sin\theta d\theta}{r^2} \tag{5.9}$$

$$dE_2 = \frac{1}{4\pi\varepsilon_o} 2\pi P \cos^2\theta \sin\theta d\theta \tag{5.10}$$

Equation (5.10) is obtained. By integral the solution $\int dE_2 = E_2$

$$E_2 = \frac{2\pi P}{4\pi\varepsilon_o}\int_0^{\pi} \cos^2\theta \sin\theta d\theta \tag{5.11}$$

$$\vec{E}_2 = \frac{\vec{P}}{3\varepsilon_0} \tag{5.12}$$

$$\vec{P} = \varepsilon_0(\kappa' - 1)\vec{E} \tag{5.13}$$

$$\vec{E}_2 = \frac{\vec{E}}{3}(\kappa' - 1) \tag{5.14}$$

Get this result.

Substituting this result

$$\vec{E}' = \vec{E}^1 + \overrightarrow{E^2} = \vec{E} + \frac{\vec{E}}{3}(\kappa' - 1) = \frac{\vec{E}}{3}(\kappa' + 2) \tag{5.15}$$

By equating equation 3.2 with equation 5.15 we get,

$$\vec{P} = (\kappa' - 1)\varepsilon_0 \vec{E} = N\alpha\vec{E}' = \frac{\vec{E}}{3}(\kappa' + 2) \tag{5.16}$$

By rearranging the equation, we get

$$\frac{\kappa' - 1}{\kappa' + 2} = \frac{N\alpha}{3\varepsilon_0} \tag{5.17}$$

and this equality is called Clausius-Mossotti equation. The Clausius-Mossotti equation establishes a relationship between the dielectric constant κ' (macroscopic magnitude) and the polarization constant α (microscopic magnitude).

6. Debye Model

When an electric field is applied to a dielectric, the dipoles oscillate and rub against each other (Zhou et al., 2021). The polarization that occurs as a result of the movement of the dipoles under the influence of the electric field shows changes as a function of time. In accordance with this definition, polarization at t=0 can be written as

$$P_\infty = P_E + P_A \tag{6.1}$$

Here P_∞ is instantaneous polarization with electric field effect, and P_E is the sum of electronic polarization and P_A is the atomic polarization. As time progresses, the dipoles will rotate due to the changing direction of the applied variable electric field, and the resulting polarization will change as a function of time. At any time t, a time dependent polarization is obtained, as in the equation of total polarization.

$$P(t) = P_{\infty} + P_{(dipol)} \tag{6.2}$$

Here,

$$P_{(dipol)} = (\varepsilon - \varepsilon_{\infty})E(t) \tag{6.3}$$

Considering that the change in dipolar polarization can be proportional to the difference of the dipoles from the equilibrium position, it is assumed that the dipolar polarization will change with time. This situation is given by the equation,

$$\frac{dP_{(dipol)}}{dt} = \frac{1}{\tau}(P_{s(dipol)} - P_{(dipol)}) \tag{6.4}$$

Here, τ is the time between two equilibrium states of the dipoles after the electric field is applied, and is called the relaxation time. $P_{s(dipol)}$, is the polarization under constant electric field effect, and it can be written as,

$$P_{s(dipol)} = (\varepsilon_S - \varepsilon_{\infty})E \tag{6.5}$$

The time-variance equation of polarization is written as,

$$\frac{dP_{(dipol)}}{dt} = \frac{1}{\tau}\left[(\varepsilon_S - \varepsilon_{\infty})E - P_{(dipol)}\right] \tag{6.6}$$

If an alternating electric field is applied $\left(E = E_0 e^{i\omega t}\right)$,

$$\frac{dP_{(dipol)}}{dt} + \frac{1}{\tau}P_{(dipol)} = \frac{1}{\tau}(\varepsilon_S - \varepsilon_{\infty})E_0 e^{i\omega t} \tag{6.7}$$

Above is obtained. By integrating the equation,

$$P_{(dipol)} = ce^{-\frac{t}{\tau}} + \frac{(\varepsilon_S - \varepsilon_{\infty})E_0}{1+i\omega t} e^{i\omega t} \tag{6.8}$$

The first term of the equation explains the variable behavior, going to zero when t →∞. The second term explains its permanent state.

$$P_{(dipol)} = \frac{(\varepsilon_S - \varepsilon_{\infty})E_0}{1+i\omega t} e^{i\omega t} \tag{6.9}$$

In the case of a variable electric field, the phase difference between the applied field and the polarization vector is

$$\varepsilon^* = \varepsilon' - i\varepsilon'' \tag{6.10}$$

The complex dielectric constant is shown in the figure. The complex dielectric constant is written in terms of relaxation time.

$$\varepsilon^* = \varepsilon_{\infty} + \frac{\varepsilon_S - \varepsilon_{\infty}}{1+i\omega t} = \varepsilon_{\infty} + \frac{(\varepsilon_S - \varepsilon_{\infty})(1-i\omega t)}{1+\omega^2 t^2} \tag{6.11}$$

If the above equation is divided into real and imaginary parts, the following equations are obtained.

$$\varepsilon' = \varepsilon_{\infty} + \frac{\varepsilon_S - \varepsilon_{\infty}}{1+\omega^2 t^2} \tag{6.12}$$

$$\varepsilon'' = \frac{(\varepsilon_S - \varepsilon_{\infty})\omega t}{1+\omega^2 t^2} \tag{6.13}$$

These equations are called Debye's equations. Debye Equations reveal the effect of relaxation time on the polarization that occurs under a variable electric field in the dielectric, as shown in Figure 16.

The ratio of the real and imaginary parts gives the energy loss as a result of friction during the rotation of the dipoles.

$$\tan\delta = \frac{\varepsilon''}{\varepsilon'} = \frac{(\varepsilon_S - \varepsilon_\infty)\omega t}{\varepsilon_S + \varepsilon_\infty \omega^2 t^2} \tag{6.14}$$

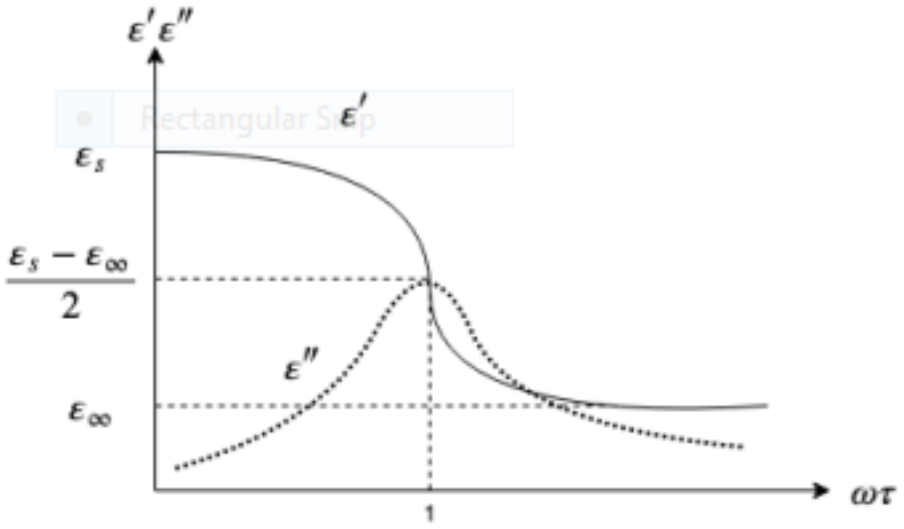

Figure 16. Debye Relaxation Graph (Gedeon, 2021).

7. Drude Model

The Drude model is also called the free electron model (Basu & Dhasmana, 2022). This model provides information about the heat capacity, magnetic permeability, thermal conductivity and electrodynamics of metals. In this model, electron-electron and electron-ion interactions are not taken into consideration and the force acting in the electric field is written as

$$\vec{F} = m\vec{a} = q\vec{E} \tag{7.1}$$

$$\vec{a} = \frac{q\vec{E}}{m} \tag{7.2}$$

Here q is the electron charge, m is the electron mass and $\vec{E}$ is the electric field and the velocity of these electrons can be written as

$$\vec{V}_S = \vec{V}_I + \vec{a}t \tag{7.3}$$

Here $\vec{V}_S$is the drift velocity and $\vec{V}_I$ is the initial velocity. If $\vec{V}_I = 0$, by rearranging the equation,

$$\vec{V}_S = \frac{q\vec{E}}{m}\tau \tag{7.4}$$

The current density is written as,

$$J = \frac{I}{A} = nqV_S \tag{7.5}$$

Here, n is the number of charge carriers per unit volume. Substituting the expression V_S in the equation,

$$J = \frac{nq^2E}{m}\tau \tag{7.6}$$

$$J = \sigma.E \tag{7.7}$$

$$\sigma.E = \frac{nq^2E}{m}\tau \tag{7.8}$$

$$\sigma_0 = \frac{nq^2}{m}\tau \tag{7.9}$$

get conductivity equation. This expression is called DC conductivity and does not depend on the electric field.

8. Alternative Conductivity

When observing the motions of bound charges under an electric field, frictional forces should also be considered (Tan et al., 2022). The force acting on electron is

$$\vec{F} = m\vec{a} = q\vec{E} + \vec{F}_d \tag{8.1}$$

$\vec{F}_d$ is the friction force between charges, given by $\vec{F}_d = -\frac{m\vec{V}}{\tau}$. If we rearrange the equation, we get

$$m\vec{a} = q\vec{E} + \left(-\frac{m\vec{V}}{\tau}\right) \tag{8.2}$$

$$m\frac{d\vec{V}}{dt} = q\vec{E} - \frac{m\vec{V}}{\tau} \tag{8.3}$$

$$m\frac{d\vec{V}}{dt} + \frac{m\vec{V}}{\tau} = q\vec{E} \tag{8.4}$$

Under the alternating field area, electric field and velocity will depend on time, it is given by

$$E(t) = E_0e^{i\omega t} \tag{8.5}$$

$$V(t) = V_0e^{i\omega t} \Rightarrow \frac{d\vec{V}(t)}{dt} = i\omega V_0e^{i\omega t} \tag{8.6}$$

As a result,

$$mi\omega V_0e^{i\omega t} + \frac{m}{\tau}e^{i\omega t} = qE_0e^{i\omega t} \tag{8.7}$$

$$V_0m\left(i\omega + \frac{1}{\tau}\right) = qE_0 \tag{8.8}$$

$$V_0 = \left(\frac{q\tau}{m}\right)\frac{1}{1+i\omega t}E_0 \tag{8.9}$$

equation (8.9) will equal the drift velocity,

$$V_0 = V_S \tag{8.10}$$

By writing the current density,

$$J = nqV_S = \frac{nq^2\tau}{m}\frac{1}{1+i\omega\tau} \quad (8.11)$$

and

$$J(\omega) = \sigma(\omega)E(\omega) \quad (8.12)$$

By substituting conductivity in this expression;

$$\sigma(\omega) = \frac{\sigma_0}{1+i\omega\tau} \quad (8.13)$$

By making the denominator of σ(ω) real, and then write it in imaginary and real part,

$$\sigma(\omega) = \frac{\sigma_0}{1+\omega^2\tau^2} - \frac{i\omega\tau\sigma_0}{1+\omega^2\tau^2} \quad (8.14)$$

The first term in equation 8.14 is the real and the second term is imaginary. And the real term is called AC conductivity.

$$\sigma(\omega) = \frac{\sigma_0}{1+\omega^2\tau^2} \quad (8.15)$$

As atotal DC and AC can be written as,

$$\sigma_{top}(\omega) = \sigma_0 + \sigma(\omega) \quad (8.16)$$

9. Conclusion

Depending on the individual technology, modern capacitor technologies typically have the possibility to provide power and energy concentrations that are quite higher than expected. Cost considerations in the consumer, commercial, and industrial sectors will play a major role in the implementation of these possibly ever-more compact designs. The development of modest, crafts-level production capabilities would enable the demonstration of cost cutting execution and technologies expansion validated over a wide range of innovative packaging applications.

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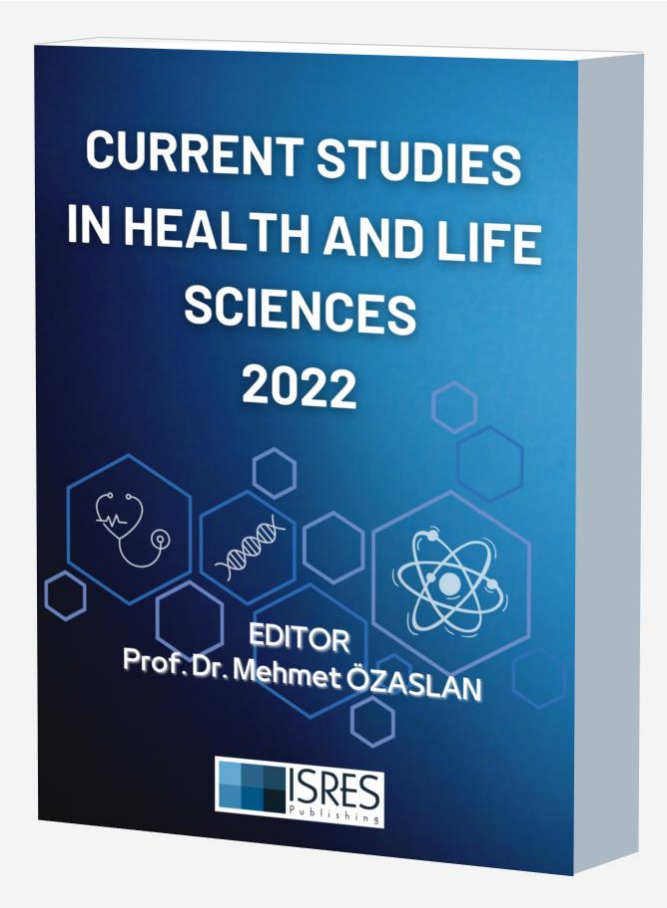

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