QSAR STUDIES OF 1,2,4-TRIAZOLES

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The QSAR Method

The QSAR method is an application developed using data analysis tehcniques to design new bioactive compounds especially new effective drugs. With quantitative structure activity relationship (QSAR) method, the relationship between chemical structure and biological activties can be determined by using some descriptors (Tropsha, 2010).

The quantitative structure activity relationship (QSAR) method was founded by Corwin Hansch and until today, ıt has developed, diversified (Cherkasov et al., 2014). Actually, a study of several alkaloids using equations was published by Crum-Brown and Fraser in 1868, and it is noteworthy for being the first generation description of a quantitative structure-activity connection. The study of Cantor on the narcotic activity of several substances marked the beginning of systematic QSAR. The numerous research conducted throughout the development of the QSAR approach has led to its current status. The Hammet Technique was modified in 1956 to account for the steric, resonance and polar effects of the substituent in aliphatic molecules (Muhammad et al., 2018). Nowadays, various QSAR techniques are used and QSAR has become one of the most widely used techniques to analyze the physical and biological characteristics of compounds. This method has developed over 60 year by ongoing advancements, multidisciplinary discoveries, and community-driven innovations (cherkovs et al., 2014). The QSAR models have a wide range of applications for determining the potantiel effects of chemical substances on ecological and human health. In fact, indirectly, the QSAR method is fruquently used in academic, industrial and governmen ınstıtutes worldwide. In addition, pharmaceutical chemistry is most significant application of the QSAR.

One of the numerous goals of QSAR studies is to predict the bioactivity of compounds by describing their physicochemical characteristics. Another goal is to evaluate and understand how a chemical reaction in a chain of substances works.

These purposes can be listed as follows.

- The production of pharmaceuticals for use in human health and agriculture is quite expensive and takes roughly 10 years (Tüzün, 2013). In other words, QSAR techniques have the potential to significantly reduce the time and effort needed for the designe of new medications.

- In drug designe processes, drug candidates are tested on experimental animals, who endure excruciating suffering. Animal experiments might be minimized using QSAR technıques.

- The chemical contamination is another serious problem. The amount of experimental investigations in industrial and pharmaceutical chemistry is decreased as a result of QSAR research (Puzyn et al., 2010).

The quantitative structure-activity relationship (QSAR) approach is computer application that link a collection of structural or property descriptors of a chemical substance to determine its biological activity.

A theoretical molecular descriptor associates topological, geometrical, and quantum chemical indices of molecules. The molecular descriptors used in QSAR/ QSPR model development are generally releated to structural and quantitative properties such as size, shape, symmetry, complexity, branching, cyclicity, stereoelectronic character of molecule (Hawkins et al., 2001). The QSAR model found process consists of data preparation, data analysis and model validation. These processes are very important for any QSAR modeling. In the first step, a molecular dataset is chosen, molecular descriptors are calculated and the QSAR technique is chosen for the statistical methods of data analysis and correlation. In the second step for QSAR model process, descriptor set is designed according to biological activity. There are several different computer programs and methods that used for this step. In all of the methods, biological activities serve as the dependent variables, while descriptors serve as the independent variables. The third step in the construction of a QSAR model, the model validation process, determines predictive potential and consequently, its capacity to define the biological activities of untested substances (Golbraikh et al., 2003).

Internal and external validation are the two different types of validation techniques utilized in QSAR models. In each stage of internal model validation, one compound from the datas set is randomly discarded, and the remaining compounds are then used to build the model. The resulting model is used to forecast the deleted compound's action. Also the effectiveness of the generated model's predictive power are evaluated via external validation (Muhammad et al., 2018)

Many computational approaches in used QSAR prosess are depend on the complexity of the data. These processes include two-dimensional (2D), three-dimensional (3D), and higher dimensional techniques. The conformational configurations of atoms in space are insensitive to 2D-QSAR, and 3D-QSAR provides knowledge about the positions of atoms in three spatial dimensions. Comparative molecular field analysis, often known as CoMFA, is a technique that uses effective 3D-QSAR models. The CoMFA method is a QSAR technique constructed to link a molecule's geometric, steric, and electrostatic characteristics with its biological functions. In 3D-QSAR methods, the active conformation is a minimal energy conformer but 4D-QSAR method is quite different from 3D-QSAR methods, The active conformer of each compound in the investigated chemical series is defined as the minimal energy conformer within the values, and all conformers are taken into consideration when calculating activity in 4D-QSAR (Tüzün 2013). In the 4D-QSAR genetic algorithms provide a collection of automatically docked orientations and conformations for each molecule.

Table 1. Various stages of QSAR model development (Veerasamy et al., 2011)

1. Prepearing The Molecules for The QSAR Study
• Partial charges
• Conformations
• Aignments
• Training and Test Set
2. Calculte Values for All Descriptors for All ligands in Training Set
• Traditional 2D
• 3D (CoMFA,CoMSIA)
• 4D-QSAR
3. Select Descriptors
• By Hand
• Stepwise MLR
• Simulated Annealing
• Genetic algorithm

> **4. Create Model Using Training Set**
> - Multiple Linear regression
> - Principal Compenent Analysis
> - Partial Least Squares
> - Neural Networks
>
> **5. Validation**
> - (Internal, external)

In 5D and 6D-QSAR, respectively, the fifth (protein flexibility) and sixth (entropy) dimensions are seen as the induced-fit possibilities of ligands following binding to the active site and solvation models (Veerasamy et al., 2011).

In medicinal chemistry investigations, the concept of molecular similarity is frequently used for new sentenceses. Molecules with similar properties may show similar bioactivity. In short, molecules with same chemical or structural properties generally react similarly in biological assays. It is crucial for this approach to perform that the right molecular parameters (descriptors) and analytical techniques (metrics) be chosen for the calculation of molecular similarity.

Pharmacophores are bioactive molecules used in drug design that are ordered geometrically to (at least conceptually) complement the receptor site. These configurations of molecular characteristics are thought to be important for biological activity. Pharmacophore models are typically formed from six different feature types: hydrogen-bond donors, hydrogen-bond acceptors, basic groups, acidic groups, aromatic groups, and hydrophobic groups (Glen & Adams, 2006).

1,2,4-Triazoles

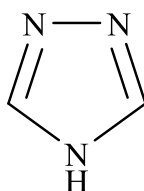1,2,4-Triazoles are aromatic heterocylic compounds with three nitrogens and two carbons

Figure 1. The Structure of 1,2,4-Triazole

According to investigations of the literature, heterocylic compounds exhibit a variety of biological features and are found in many drugs. The triazoles are substances with heterocylc structure and the ability to generate their many derivatives. For this reason, it has become the

focus of new drug candidate studies for the treatment of many diseases such as various cancer diseases (Dixit et al., 2006). For example, 1,2,4-triazol Schiff Base derivatives have demonstrated anti-fungal (Odds et al.,1985; Chai et al., 2011), anti-microbial (Çiftçi et al.,2018; Manap, 2022), anti-oxidant (Kardaş et al., 2016), activities; methal based triazole derivatives have demonstrated anti-oxidant, anticancer (Deswal et al., 2022) anti-fungal (Rodriguez-Fernandez et al., 2006), and anti-bacterial (Al-Radadi et al., 2020; Sumrra et al., 2020), anti-tümör (El-Metwaly et al., 2020). In addition , triazol and its derivatives are found in a variety of medications, including alprazolam, trazodone (an antidepressant), rizatriptan (an antimigrane medicine), and hexaconazole (an antifungal medication) (hyptonic, sedative and tranquilizer drug) (Lass-Flörl, 2011).

Some QSAR Studies of 1,2,4-Triazoles Derivatives

In reported study, 1,2,4-triazole-5-substituted carboxylic acid bioisosteres were synthesized and tested for in vitro URAT1 inhibitor activity (IC50) by the using 3D-QSAR method. This study results especially shown that all of 19 new triazole compounds, N-(pyridin-3-yl)methanesulfonamide derivative of triazole displayed highly potent URET 1 inhibitor for treatment of gout diseas (Wu et al., 2019).
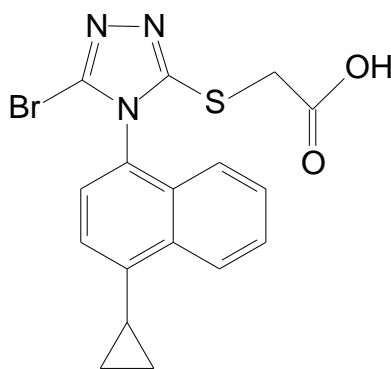

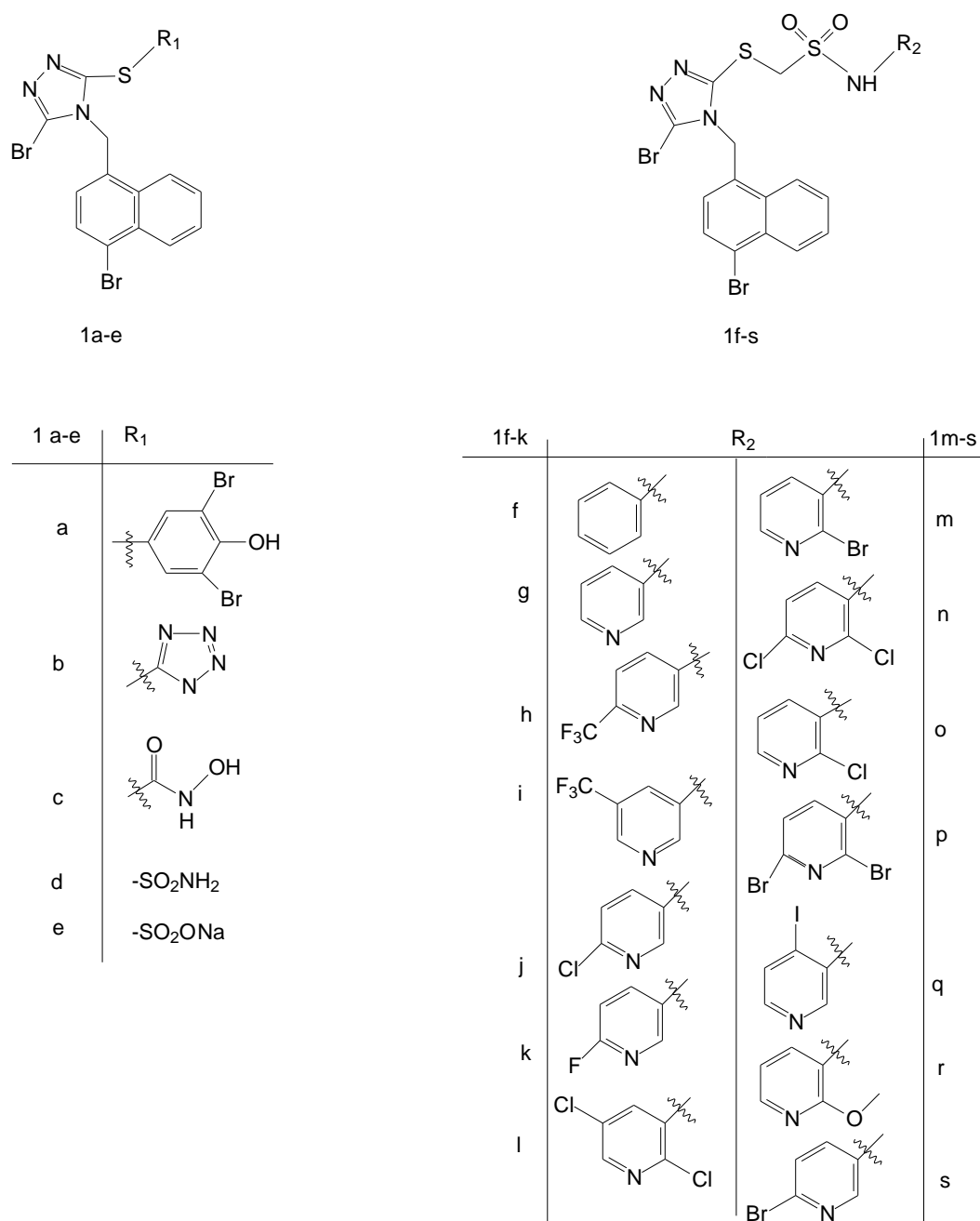**Figure 2**. Lesinurad (structure of approved URET1 inhibitor) (Wu et al., 2019).

Figure 3. Structures of 1a-e and 1f-s compounds synthesized in study (Wu et al., 2019)

In "A review synthesis, evaluation and qsar study of substituted 1, 2, 4-triazole nucleus" study, Singh et al. collected data of triazole derivatives and investigated QSAR analysis. The QSAR regression data were obtained to predict the anticancer biological activity against the human pancreatic cancer cell line (Panc-1) of 1,2,4-triazole derivatives. According to obtained results, triazole compounds with different R grup may be used as descriptor for the development of predictive QSAR models (Singh et al., 2020).
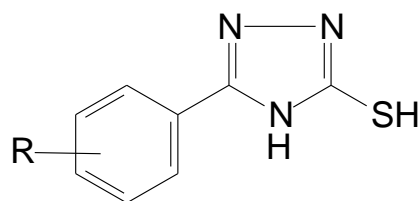
Figure 4. Structure of 1,2,4-triazole-3-thiol derivatives containing different R group (Singh et al., 2020).

Adegoke et al. synthesized 1,2,3-triazole-pyrimidine derivatives and investigated anticancer activities of 1,2,3-triazole-pyrimidine derivatives against human esophageal carcinoma (EC-109) by using the DFT-QSAR method. The results obtained from QSAR method were compared with experimental values. The evaluated results shown that the experimental and predicted inhibition efficiency (IC 50) of 1,2,3-triazole-pyrimidine gave good correlation results for generated a novel QSAR model equation for human esophageal carcinoma (EC-109) through multiple linear regression (Adegoke et al., 2020).
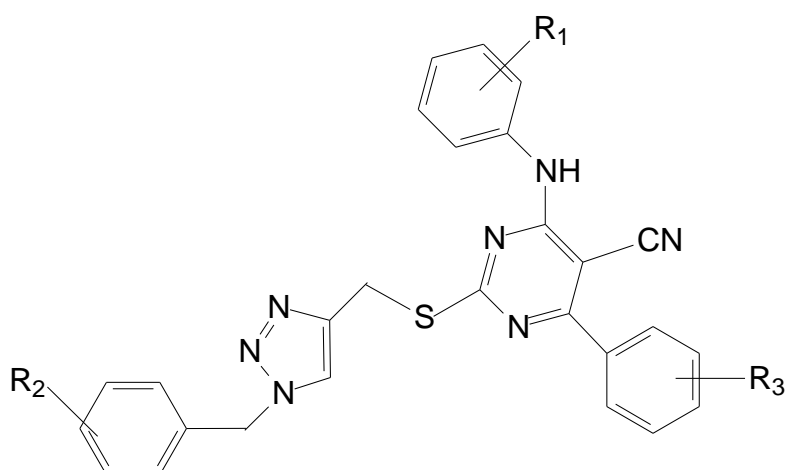
Compounds	R_1	R_2	R_3	Compounds	R_1	R_2	R_3
1	p-OCH$_3$	o-Cl	H	11	o-CH$_3$	o-Cl	H
2	m-CF$_3$	o-Cl	H	12	o-F	p-CH$_3$	H
3	o-Cl	o-Cl	H	13	p-CH$_3$	p-CH$_3$	H
4	p-Cl	o-Cl	H	14	o-Cl	p-CH$_3$	H
5	m-Cl	o-Cl	H	15	p-CH$_3$	o-Cl	H
6	o-OCH$_3$	o-Cl	H	16	p-CH$_3$	o-Cl	p-CH(CH$_3$)$_2$
7	m-CH$_3$	o-Cl	H	17	o-OCH$_3$	o-Cl	p-CH(CH$_3$)$_2$
8	m-NO$_2$	o-Cl	H	18	p-CH$_3$	o-Cl	p-CH$_3$
9	o-F	o-Cl	H	19	p-CH$_3$	o-Cl	m,p,o-triOCH$_3$
10	p-F	o-Cl	H	20	p-CH$_3$	o-Cl	p-Cl

Figure 5. Structure of 1,2,3-triazole pyrimidine derivatives with different R_1, R_2 and R_3 grups (Adegoke et al., 2020).

In this study, Elmchichi et al. collected the data of A, B, and C type triazole derivatives to reveal the relationship between physicochemical properties and anti-cancer effects of the compounds. The researcers randomly divided these compounds two parts as learning set, test set. After that, they studied anti-pancreatic cancer activity of compounds using QSAR method which calculates 11 different descriptor with different statistical methods (Elmchichi et al., 2020).
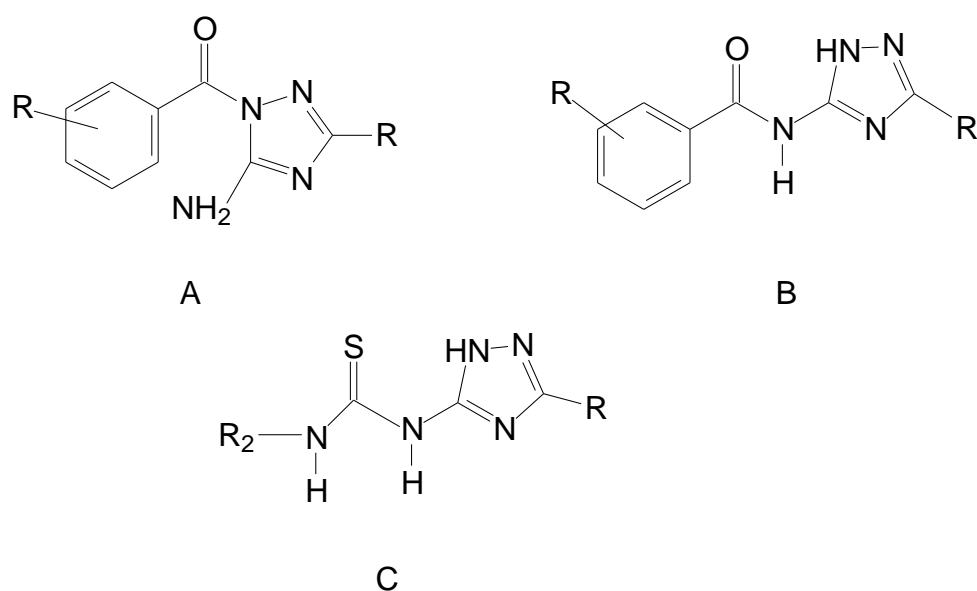

Figure 6. Structures of A, B and C type 1,2,4-triazole derivatives (Elmchichi et al., 2020)

In the "Synthesis, crystal structure and 3D-QSAR studies of antifungal (bis-)1,2,4-triazole Mannich bases containing furyl and substituted piperazine moieties" study, Yan Zhang et al., reported that a series of piperazine-containing 3-(furan-2-yl)-1,2,4-triazole Mannich bases and bis-Mannich bases were synthesized and some compound's anti-fungal activities were evaluated using the CoMFA set of 3D-QSAR method. According to data reported, steric and electrostatic field are two important factor for compound's bioactivity or deactivity (Zhang et al., 2018).
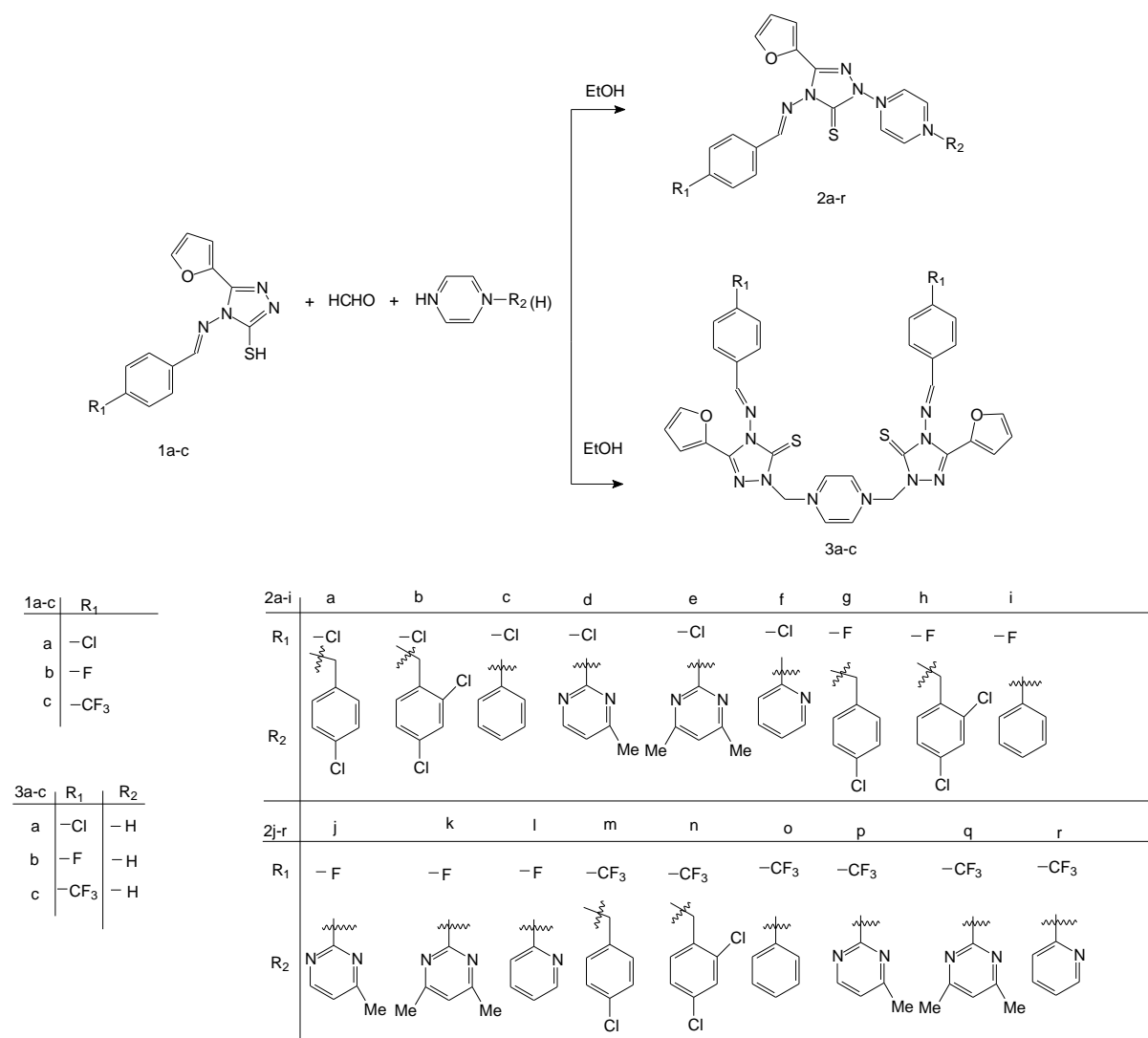
Figure 7. Structures of Schiff Bases and Mannich Bases of triazoles derivatives (Zhang et al., 2018)

In this study releated 3D QSAR method of 1,2,4-triazole derivatives, Hong-jin Tang et al. investigated to analyze the SAR for 1,2,4-triazole derivatives as XOR inhibitors by select a data set of 48 3,5-dipyridyl-1,2,4-triazole derivatives with XOR inhibitory activity from the work of Nagata Osamu et al. In this study. The steric, electrostatic, and hydrophobic fields for each compounds were obtained using (CoMSIA) model and the obtained data were evaluated especially the relationship of the in terms of the bioactivity of molecule. According to results that the steric, electrostatic, and hydrophobic fields play an important role in bioactivity of compounds (Tang et al. 2016).
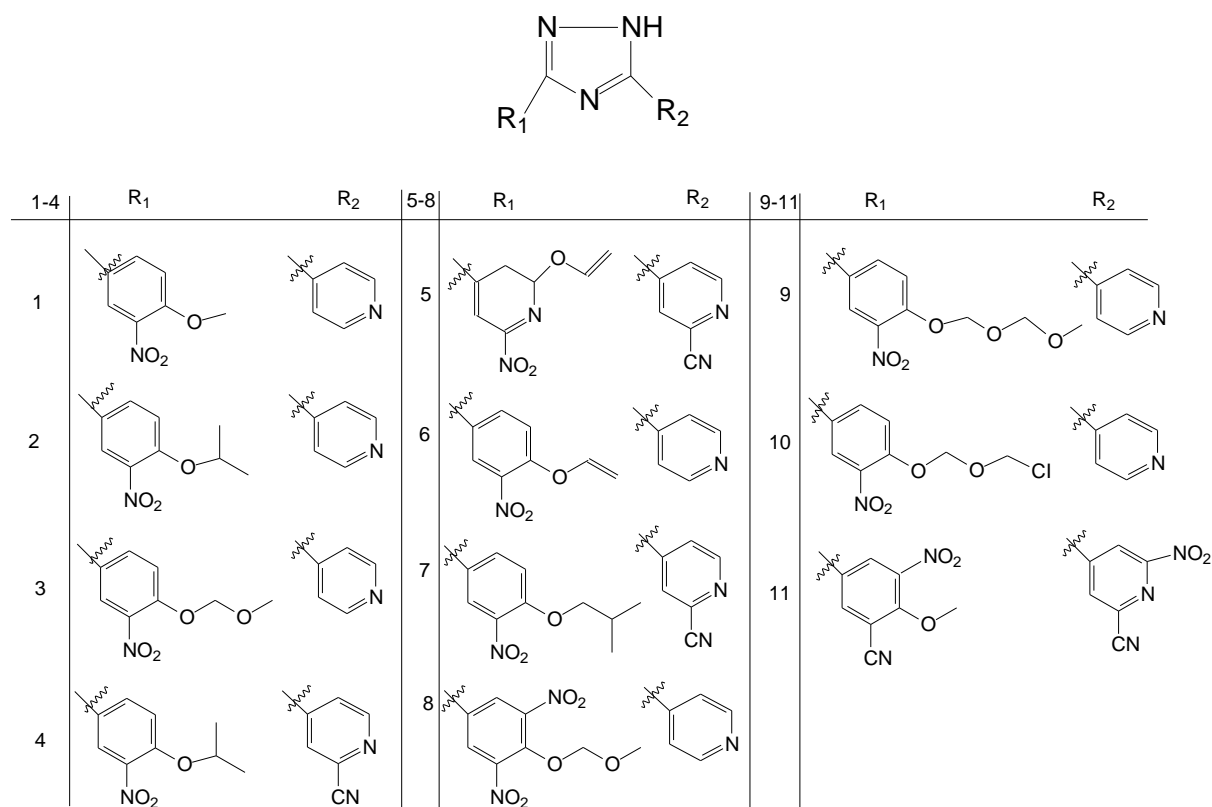
Figure 8. Structures of new designed 3,5-dipyridyl-1,2,4-triazole derivatives (Tang et al. 2016)

Mehta1 et al. used 4H-1,2,4-triazole derivatives to design of new anticancer agents by using QSAR method. In this reported work, a set of 51 molecules of 3,4,5-trisubstituted-4H-1,2,4-triazole derivatives were used for 3D-QSAR studies to designe dual tankyrase inhibitors as Wnt signaling antagonist. Two data set of triazole derivatives were used in study. First data set was training set (39 molecules) and second set was used test set (12 molecules). The data of compounds were obtained from literatüre and CoMFA, CoMSIA, and HQSAR models were applied for QSAR study. The results of study shown that QSAR methods employe for the design of different bioactive triazole derivatives (Mehta et al., 2020).
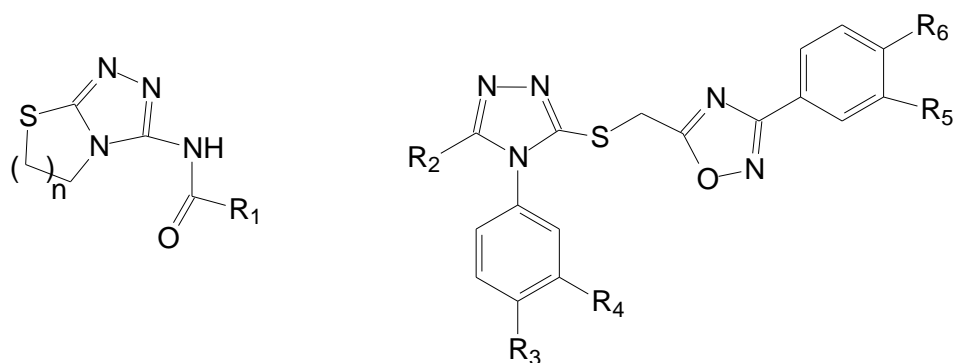
Figure 9. Training set and test set of 3,4,5-trisubstituted-4H-1,2,4-triazole derivatives (Mehta et al., 2020)

In a QSAR study of triazole derivatives, a seri of menthol derivatives containing 1,2,4-triazole-thioether were synthesized and examined anti-fungal properties against tested fungal by experimental studies. In addition, QSAR analysis studies were performed using the CoMFA /3D-QSAR method to design new antifungal compounds against fungals (Huang et al.,2021).
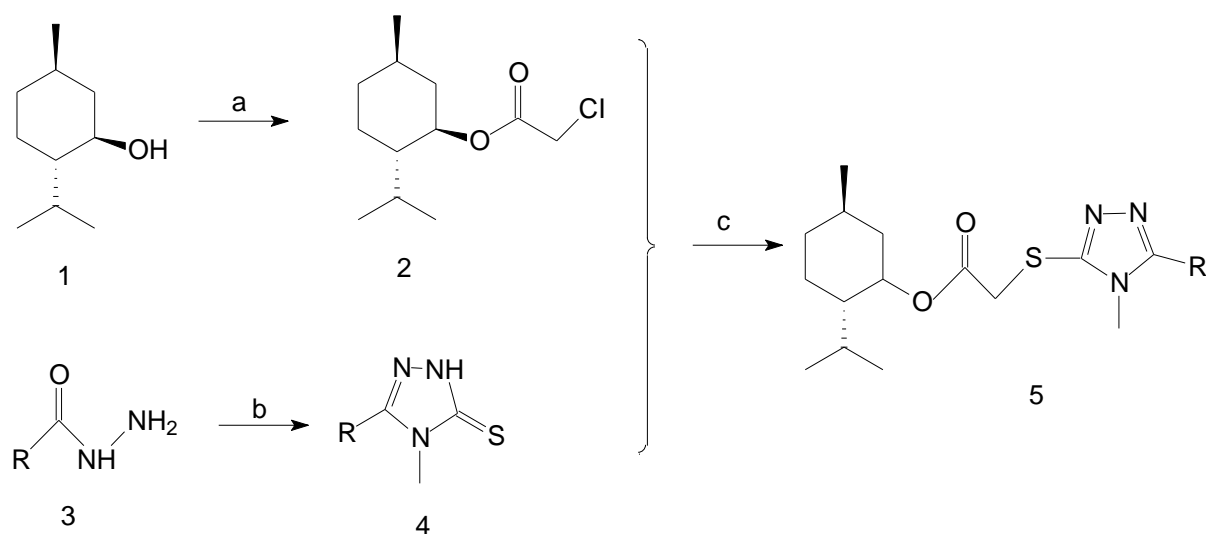

5a: R=Ph; 5b:R=o-CH$_3$ Ph; 5c: R=p-CH$_3$ Ph; 5d: R=o-OCH$_3$ Ph; 5e:R= p-OCH$_3$ Ph; 5f: R= o-F Ph; 5g: R= m-F Ph; 5h: R= p-F Ph; 5i: R=o-CI Ph; 5j: R= m-CI Ph; 5k: R= p-CI PH; 5l: p-Br Ph; 5m: R= o-l Ph; 5n: R= p-l Ph; 5o: R=o-CF$_3$ Ph; 5p: R= m-CF$_3$ Ph; 5q: R= p-OH Ph; 5r: p-OH Ph; 5s: R= o-NH$_2$ Ph; 5t: R= p-NH$_2$ Ph; 5u: R=p-C(CH$_3$)$_3$ Ph; 5v: R= m, p-OCH$_3$ Ph; 5w: R= m, m-OCH$_3$ Ph; 5x: R= α-furyl; 5y: R= α-thienly; 5z: R=β-pyridl

Figure 10. Synthesis of 5 type 1,2,4-triazole-thioether derivaties

Dahmani et al., studied to develop the a-glucosidase inhibition activity of triazol derivatives using QSAR method. The researcers built a computational model to develop a new QSAR model using different physio-chemical descriptors such as electronic descriptors (LUMO

(ELUMO) and HOMO (EHOMO) energies, partial atomic charges (q)) and topological descriptors (polarizability (Pol), molar refractivity (MR), partition coefficient octanol/water (log P), molar volume (MV), surface area grid (SAG), molar weight (MW)), geometric descriptors (solvent accessible hardness and potential). Looking at the results of study, good correlation were seemed between experimental data and predicted pIC50 values. Actually, ıt can be said that, this model can be use succesfully to predict the a-glucosidase inhibitory activity of similar triazole derivatives (Dahmani et al., 2021).
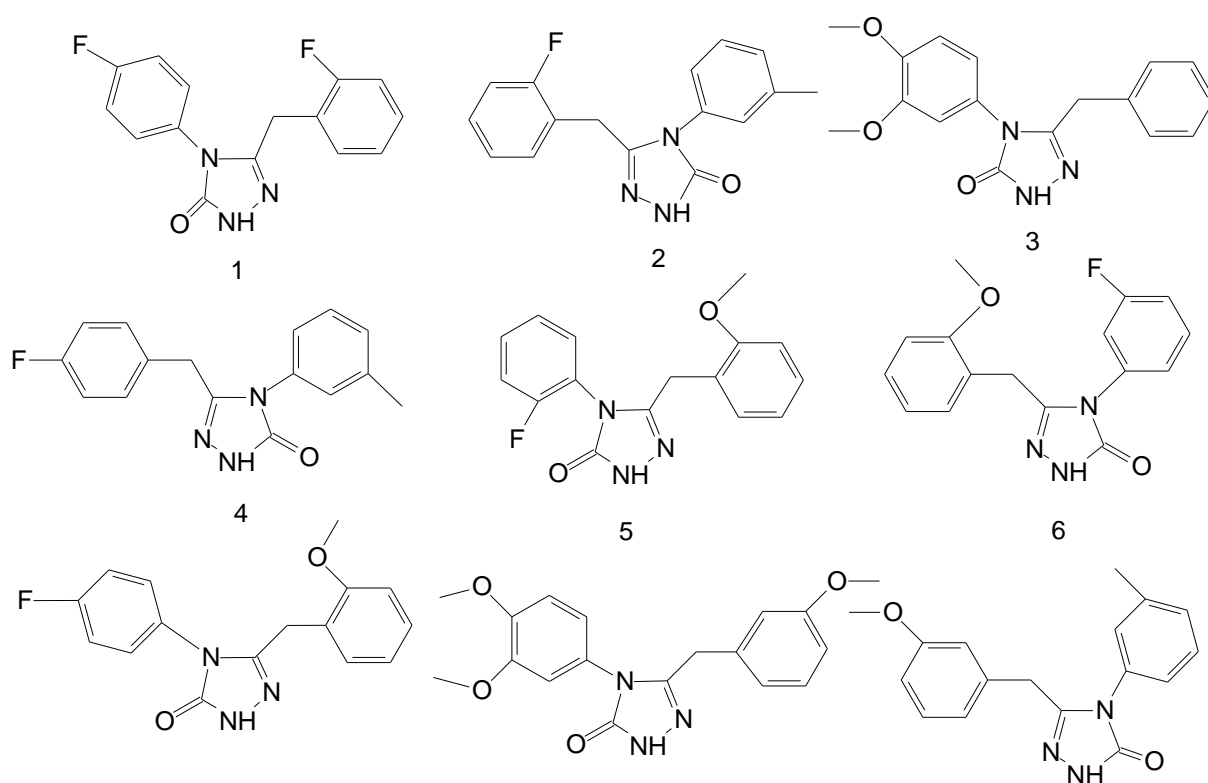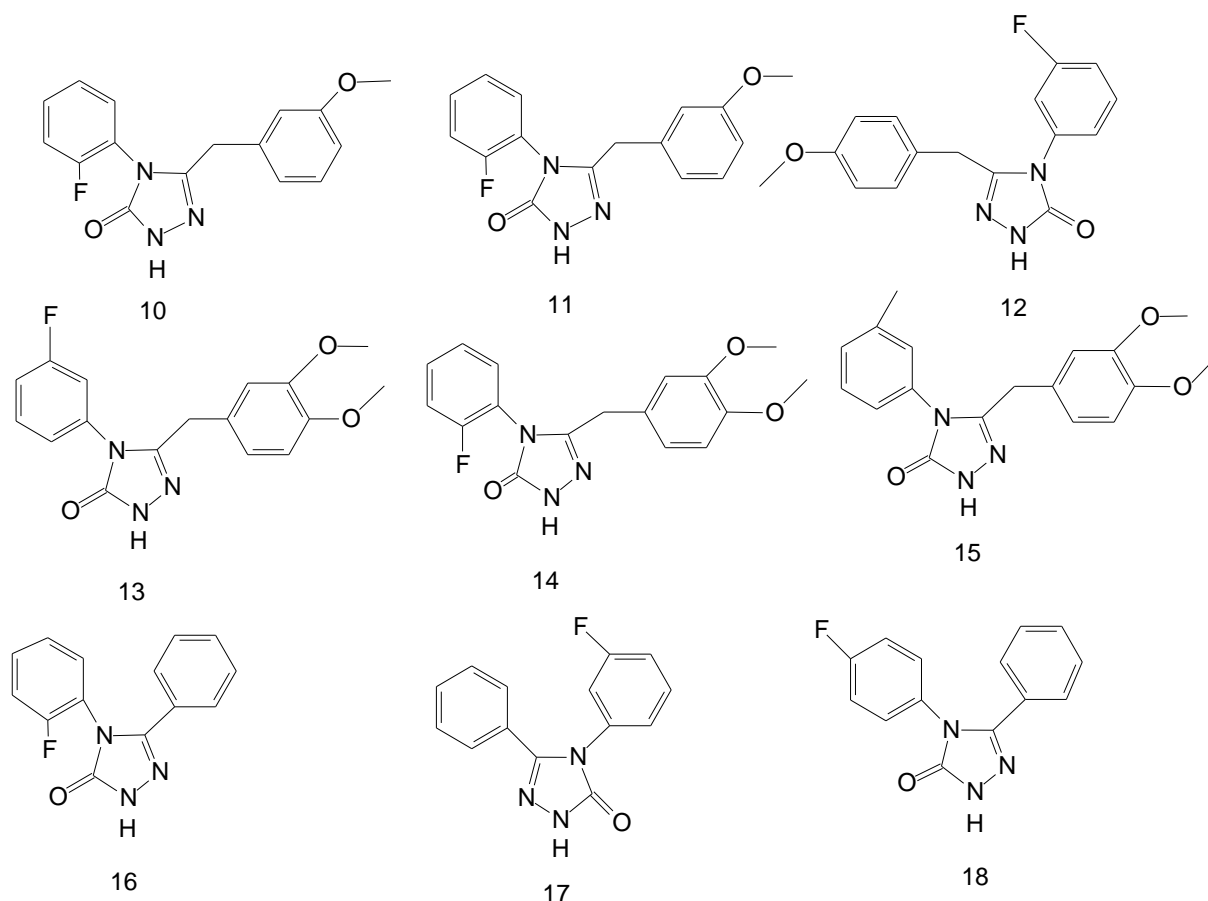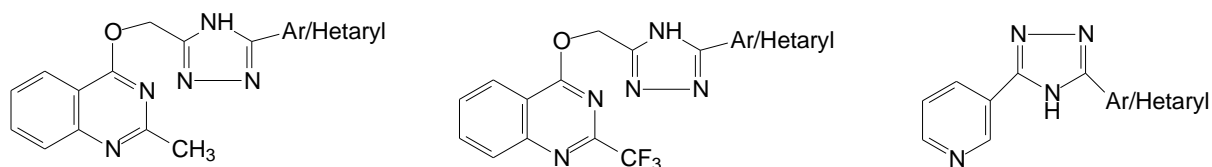
Figure 11. Structure of the investigated **18** 1,2,4-triazol-5(4H)-one derivatives.

In the "Synthesis and QSAR studies of some novel disubstituted 1,2,4-triazole as antimicrobialagents" study of Pande & Jain, they synthesized disubstituted 1,2,4-triazole derivatives and established reliable quantitative structure activity relationship (QSAR) model to understand the relationship between chemical structure properties and the bioactivity properties of synthesized compounds. In this study, statistical parameters for antibacterial activity and anti-fungal activity of compounds were calculated and evaluated comparing experimental data of compounds. Acording to results obtained from QSAR study molecule-bound halogen, methoxy group and heterocyclic structures are very important for bioactivty of molecule (Pande & Jain, 2014).

1a-k   2a-k   3a-k

Compounds	Ar	Compounds	Ar	Compounds	Ar
1a	$-C_6H_5$	2a	$-C_6H_5$	3a	$-C_6H_5$
1b	$4-FC_6H_4$	2b	$4-FC_6H_4$	3b	$4-FC_6H_4$
1c	$4-ClC_6H_4$	2c	$4-ClC_6H_4$	3c	$4-ClC_6H_4$
1d	$4-BrC_6H_4$	2d	$4-BrC_6H_4$	3d	$4-BrC_6H_4$
1e	$4-OHC_6H_4$	2e	$4-OHC_6H_4$	3e	$4-OHC_6H_4$
1f	$4-CH_3C_6H_4$	2f	$4-CH_3C_6H_4$	3f	$4-CH_3C_6H_4$
1g	$4-OCH_3C_6H_4$	2g	$4-OCH_3C_6H_4$	3g	$4-OCH_3C_6H_4$
1h	$3,4-(OCH_3)_2C_6H_3$	2h	$3,4-(OCH_3)_2C_6H_3$	3h	$3,4-(OCH_3)_2C_6H_3$
1i	$3,4,5-(OCH_3)_3C_6H_2$	2i	$3,4,5-(OCH_3)_3C_6H_2$	3i	$3,4,5-(OCH_3)_3C_6H_2$
1j	2-Furanyl	2j	2-Furanyl	3j	2-Furanyl
1k	2-Thiophenyl	2k	2-Thiophenyl	3k	2-Thiophenyl

Figure 12. Structures of disubstituted 1,2,4-triazole derivatives (Pande & Jain, 2014)

REFERENCES

Adegoke, R. O., Oyebamiji, A. K., & Semire, B. (2020). Dataset on the DFT-QSAR, and docking approaches for anticancer activities of 1, 2, 3-triazole-pyrimidine derivatives against human esophageal carcinoma (EC-109). *Data in brief*, *31*, 105963.

Al-Radadi, N. S., Zayed, E. M., Mohamed, G. G., & Abd El Salam, H. A. (2020). Synthesis, spectroscopic characterization, molecular docking, and evaluation of antibacterial potential of transition metal complexes obtained using triazole chelating ligand. *Journal of Chemistry*, *2020*, 1-12

Chai, X., Zhang, J., Cao, Y., Zou, Y., Wu, Q., Zhang, D. & Sun, Q. (2011). Design, synthesis and molecular docking studies of novel triazole as antifungal agent. *European journal of medicinal chemistry*, *46* (7), 3167-3176.

Cherkasov, A., Muratov, E. N., Fourches, D., Varnek, A., Baskin, I. I., Cronin, M. & Tropsha, A. (2014). QSAR modeling: where have you been? Where are you going to?. *Journal of medicinal chemistry*, *57* (12), 4977-5010.

Ciftci, E., Beytur, M., Calapoglu, M., Gursoy-Kol, O., Alkan, M., Togay, V. A. & Yuksek, H. (2018). Synthesis, Characterization, Antioxidant and Antimicrobial Activities and DNA Damage of Some Novel 2-[3-alkyl (aryl)-4, 5-dihydro-1H-1, 2, 4-triazol-5-one-4-yl]-phenoxyacetic acids in Human Lymphocytes. *Research Journal of Pharmaceutıcal Bıologıcal And Chemıcal Scıences*, *9* (5), 1760-1771.

Dahmani, R., Manachou, M., Belaidi, S., Chtita, S., & Boughdiri, S. (2021). Structural characterization and QSAR modeling of 1, 2, 4-triazole derivatives as α-glucosidase inhibitors. *New Journal of Chemistry*, *45* (3), 1253-1261.

Deswal, Y., Asija, S., Kumar, D., Jindal, D. K., Chandan, G., Panwar, V., & Kumar, N. (2022). Transition metal complexes of triazole-based bioactive ligands: synthesis, spectral characterization, antimicrobial, anticancer and molecular docking studies. *Research on Chemical Intermediates*, *48* (2), 703-729.

Dixit, D., Verma, P. K., & Marwaha, R. K. (2021). A review on 'triazoles': their chemistry, synthesis and pharmacological potentials. *Journal of the Iranian Chemical Society*, *18* (10), 2535-2565.

Elmchichi, L., Belhassan, A., Aouidate, A., Ghaleb, A., Lakhlifi, T., & Bouachrine, M. (2020). QSAR study of new compounds based on 1,2,4-triazole as potential anticancer agents. *Physical Chemistry Research*, *8* (1), 125-137.

El-Metwaly, N., Farghaly, T. A., & Elghalban, M. G. (2020). Synthesis, analytical and spectral characterization for new VO (II)-triazole complexes; conformational study beside MOE docking simulation features. *Applied Organometallic Chemistry*, *34* (4), e5505.

Glen, R. C., & Adams, S. E. (2006). Similarity metrics and descriptor spaces–which combinations to choose?. *QSAR & Combinatorial Science*, *25*(12), 1133-1142.

Golbraikh, A., Shen, M., Xiao, Z., Xiao, Y. D., Lee, K. H., & Tropsha, A. (2003). Rational selection of training and test sets for the development of validated QSAR models. *Journal of computer-aided molecular design*, *17*(2), 241-253.

Hawkins, D. M., Basak, S. C., & Shi, X. (2001). QSAR with few compounds and many features. *Journal of Chemical Information and Computer Sciences*, *41* (3), 663-670.

Huang, M., Duan, W. G., Lin, G. S., & Li, B. Y. (2021). Synthesis, antifungal activity, 3D-QSAR, and molecular docking study of novel menthol-derived 1, 2, 4-triazole-thioether compounds. *Molecules*, *26* (22), 6948.

Kardaş, F., Manap, S., Gursoy Kol, Ö., Beytur, M., & Yüksek, H. (2016). Synthesis and Antioxidant Properties of Some 3-Alkyl (Aryl)-4-[3-ethoxy-2-(4-toluenesulfonyloxy)-benzylidenamino]-4, 5-dihydro-1H-1, 2, 4-triazol-5-ones. *Der Pharma Chemica*, *8* (18), 274-281.

Lass-Flörl, C. (2011). Triazole antifungal agents in invasive fungal infections. *Drugs*, *71*(18), 2405-2419.

Manap, S., (2022). Synthesis and *in vitro* Antioxidant and Antimicrobial Activities of Novel 2-Methoxy-4-[(3-alkyl/aryl-4,5-dihydro-1*H*-1,2,4-triazol-5-on-4-yl)-azomethine]-phenyl Furan-2-carboxylates and their N-Acetyl, N-Mannich Base Derivatives. *Journal of the Iranian Chemical Society, 19*, 1347–1368.

Mehta, C. C., Patel, A., & Bhatt, H. G. (2020). New molecular insights into dual inhibitors of tankyrase as Wnt signaling antagonists: 3D-QSAR studies on 4H-1, 2, 4-triazole derivatives for the design of novel anticancer agents. *Structural Chemistry*, *31* (6), 2371-2389.

Muhammad, U., Uzairu, A., & Ebuka Arthur, D. (2018). Review on: quantitative structure activity relationship (QSAR) modeling. *Journal of Analytical & Pharmaceutical Research*, *7* (2), 240-242.

Odds, F. C., Cockayne, A., Hayward, J., & Abbott, A. B. (1985). Effects of imidazole-and triazole-derivative antifungal compounds on the growth and morphological development of Candida albicans hyphae. *Microbiology*, *131* (10), 2581-2589.

Panda, S. S., & Jain, S. C. (2014). Synthesis and QSAR studies of some novel disubstituted 1, 2, 4-triazoles as antimicrobial agents. *Medicinal Chemistry Research*, *23* (2), 848-861.

Pokuri, S., K Singla, R., G Bhat, V., & G Shenoy, G. (2014). Insights on the antioxidant potential of 1, 2, 4-triazoles: synthesis, screening & QSAR studies. *Current Drug Metabolism*, *15* (4), 389-397.

Puzyn, T., Gajewicz, A., Leszczynska, D., & Leszczynski, J. (2010). Nanomaterials–the next great challenge for QSAR modelers. *Recent advances in QSAR Studies,* 383-409. Springer, Dordrecht.

Rodriguez-Fernandez, E., Manzano, J. L., Benito, J. J., Hermosa, R., Monte, E., & Criado, J. J. (2005). Thiourea, triazole and thiadiazine compounds and their metal complexes as antifungal agents, *Journal of Inorganic Biochemistry*, 99 (8), 1558-1572.

Singh, A., Argal, A., Kumar, D., & Jain, S. K. (2020). Synthesis, Evaluation and QSAR Study of Substituted 1, 2, 4 Triazole Nucleus: A Review. *International Journal of Pharmacy & Life Sciences*, *11* (7).

Sumrra, S. H., Habiba, U., Zafar, W., Imran, M., & Chohan, Z. H. (2020). A review on the efficacy and medicinal applications of metal-based triazole derivatives. *Journal of Coordination Chemistry*, *73* (20-22), 2838-2877.

Tang, H. J., Yang, L., Li, J. H., & Chen, J. (2016). Molecular modelling studies of 3, 5-dipyridyl-1, 2, 4-triazole derivatives as xanthine oxidoreductase inhibitors using 3D-

QSAR, Topomer CoMFA, molecular docking and molecular dynamic simulations. *Journal of the Taiwan Institute of Chemical Engineers*, *68*, 64-73.

Tropsha, A. (2010). Best practices for QSAR model development, validation, and exploitation. *Molecular informatics*, *29* (6-7), 476-488.

Tüzün, B. (2008). Elektron konformasyonel-genetik algoritma 4D-QSAR metodu ile piridin karboksilik asit, oksadiazol, pirimidin ve oksazoltürevlerine ait farmakofor gruplarının belirlenmesi ve biyoaktivite hesabı. Cumhuriyet Üniversitesi, Fen Bilimleri Enstitüsü, Sivas.

Veerasamy, R., Rajak, H., Jain, A., Sivadasan, S., Varghese, C. P., & Agrawal, R. K. (2011). Validation of QSAR models-strategies and importance. *International Journal of Drug Design and Discovery*, *3*, 511-519.

Wu, J. W., Yin, L., Liu, Y. Q., Zhang, H., Xie, Y. F., Wang, R. L., & Zhao, G. L. (2019). Synthesis, biological evaluation and 3D-QSAR studies of 1, 2, 4-triazole-5-substituted carboxylic acid bioisosteres as uric acid transporter 1 (URAT1) inhibitors for the treatment of hyperuricemia associated with gout. *Bioorganic & medicinal chemistry letters*, *29* (3), 383-388.

Zhang, Y., Zhan, Y. Z., Ma, Y., Hua, X. W., Wei, W., Zhang, X., & Wang, B. L. (2018). Synthesis, crystal structure and 3D-QSAR studies of antifungal (bis-)-1,2,4-triazole Mannich bases containing furyl and substituted piperazine moieties. *Chinese Chemical Letters*, *29* (3), 441-446.

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To Cite This Chapter

Boy, S. & Manap, S. (2022). QSAR studies of 1,2,4-Triazoles. In H. Yüksek & M. Beytur (Eds.), *Chemistry of 1,2,4-Triazoles in Current Science,* (196-212). ISRES Publishing.