In Silico Investigation of 5-Substituted 1H-Tetrazole Derivatives: Molecular Docking, PASS Analysis, and Toxicity Prediction

Mr. Jagdish Navnath Ghotekar[1], Dr. Yogeshwar Rajaram Baste[2], Mayur Bhaskar kute[3]
Balasaheb Pandharinath Pagar[4]
[1,2]Department of Chemistry, Research Centre, MVP Samaj's KSKW Arts, Science and Commerce College CIDCO, Nashik-422009, Maharashtra, India. Affiliated to S. P. Pune University Pune
[3]Department of Chemistry, Research Centre, MVP Samaj's KTHM College Nashik-422002, Maharashtra, India. Affiliated to S. P. Pune University Pune
[4]Department of Chemistry, MVP Samaj's SVKT Arts, Commerce and Science College, Deolali Camp, Nashik-422401, Maharashtra, India. Affiliated to S. P. Pune University Pune

Abstract—**As considering importance of 5-substituted 1H-tetrazole derivatives which is class of nitrogen rich heterocyclic compounds for their biological and pharmaceutical applications. In the present study we focused to investigate the in silico biological activities of selected 5-substituted 1H-tetrazole derivatives obtained using hydrothermally synthesized Cu- doped indium Oxide as an efficient heterogeneous catalyst. The catalyst was synthesized using hydrothermal method and characterized using various tools and found excellent morphology with orthorhombic having particle size 16.31 nm (matches with JCPDS card No. - 73-1592), while the BET analysis proves the surface area 183720 $cm^2 g^{-1}$. The main objective of this work is to evaluate the interaction of synthesized derivatives with selected biological targets and to predict their pharmacological activities through computational approach. Molecular docking studies were performed by the use of CB Dock-2 to find the binding affinity and interaction of ligand with targeted proteins of antioxidant enzyme, anti-inflammatory enzyme, and anti-cancer protein. In addition to this prediction of activity spectra for substances (PASS) was studied to find possible biological activities and toxicity of synthesized derivatives which is based on their structural features. The combined molecular docking and PASS analysis supports their candidacy for further in vitro and in vivo biological evaluation, Prediction of Toxicity, LD_{50} calculation which highlighting the significance of Cu-doped indium oxide–assisted synthesis in developing biologically relevant heterocyclic compounds.**

Index Terms—**Hydrothermal Synthesis; Heterogeneous catalysis; Tetrazole; Molecular Docking; PASS, Toxicity Prediction, LD_{50}.**

I. INTRODUCTION

Tetrazoles constitute an important class of nitrogen-rich heterocyclic compounds that have attracted considerable attention in organic synthesis, medicinal chemistry, and materials science. Structurally, tetrazoles are five-membered rings containing four nitrogen atoms and one carbon atom, which impart unique electronic characteristics, high thermal stability, and strong hydrogen-bonding ability. Among the various tetrazole isomers, 1H-tetrazoles, particularly 5-substituted 1H-tetrazoles, are of significant interest due to their wide range of biological activities and their role as bio isosteres of carboxylic acids. Replacement of carboxylic acid functionalities with tetrazole moieties often leads to enhanced metabolic stability, improved lipophilicity, and stronger receptor binding affinity, making them valuable scaffolds in drug design and development [1,2]. 5-Substituted 1H-tetrazoles are well known for their diverse pharmacological properties, including antimicrobial, antifungal, anti-inflammatory, antiviral, antitubercular, and anticancer activities. Several clinically important drugs, such as angiotensin II receptor blockers (e.g., losartan), incorporate tetrazole

rings as key structural motifs. The biological relevance of tetrazoles is largely attributed to their ability to participate in multiple non-covalent interactions, including hydrogen bonding, π–π stacking, and electrostatic interactions with biological macromolecules [3,4]. Consequently, the development of efficient synthetic strategies and systematic biological evaluation of novel tetrazole derivatives continues to be an active area of research.

Conventionally, 5-substituted 1H-tetrazoles are synthesized via [3+2] cycloaddition reactions between nitriles and azide sources under acidic or metal-catalyzed conditions. Although effective, many of these traditional methods suffer from drawbacks such as harsh reaction conditions, long reaction times, use of toxic solvents, and difficulties in catalyst recovery. In response to growing environmental and sustainability concerns, recent research has focused on the development of green, cost-effective, and recyclable catalytic systems that align with the principles of green chemistry [5–7].

In this context, nanostructured metal oxide catalysts have emerged as promising alternatives due to their high surface-to-volume ratio, electronic properties, and enhanced catalytic efficiency. Among them, indium oxide (In_2O_3) has gained attention as a versatile semiconductor material with applications in catalysis, gas sensing, and optoelectronics. Doping indium oxide with transition metals such as copper can significantly modify its structural, electronic, and surface properties, leading to improved catalytic activity and selectivity [8,9]. Cu-doped indium oxide nanoparticles offer synergistic effects arising from the Lewis acidity of In_2O_3 and the redox behavior of Cu^{2+}/Cu^{+} species, making them effective heterogeneous catalysts for multicomponent organic transformations. Recent studies have demonstrated the successful application of Cu-doped indium oxide as a recyclable nano-catalyst for the one-pot synthesis of 5-substituted 1H-tetrazole derivatives under mild reaction conditions. The catalytic system enables high product yields, short reaction times, and minimal by-product formation, while allowing easy separation and reuse of the catalyst. Such methodologies represent an environmentally benign and economically viable approach to heterocyclic synthesis [10–12]. Beyond synthesis, the evaluation of biological potential is a crucial step in identifying promising lead compounds. However, experimental biological screening is often time-consuming, costly, and resource-intensive. To overcome these limitations, in silico techniques have become indispensable tools in modern drug discovery. Computational approaches such as molecular docking, PASS, and activity spectrum analysis allow rapid assessment of molecular interactions and biological relevance prior to experimental validation [13].

II. EXPERIMENTAL

2.1. Synthesis of Cu-doped indium oxide and One Pot synthesis of 5-substituted 1H-tetrazole derivatives

High purity and with excellence morphological characteristics Cu-doped indium oxide was synthesized using hydrothermal method and were investigated by various analytical techniques to confirm the composition, particle size, surface area and surface morphology. The detailed procedure involving material, methods, catalytic synthesis of tetrazole derivatives and characterization is discussed in our article previously published article [7] "Synthesis of 5-substituted 1H-tetrazoles using Cu-doped indium oxide- molecular docking, ADME/pharmacokinetics, biological study © July 2025| IJIRT | Volume 12 Issue 2 | ISSN: 2349-6002".

2.2. Molecular docking

Molecular Docking is a widely used computational method that predicts the binding orientation and affinity of small molecules within the active site of a target protein. Docking studies provide insights into ligand–protein interactions, including hydrogen bonding, hydrophobic contacts, and electrostatic interactions, which are critical for understanding structure–activity relationships. In the case of tetrazole derivatives, docking studies have been effectively employed to explore their binding potential against enzymes and receptors involved in microbial infections, inflammation, and oxidative stress pathways [14–16].

2.3. PASS Analysis

Complementing molecular docking, PASS (Prediction of Activity Spectra for Substances) analysis is a powerful cheminformatics tool that predicts the probable biological activities of a compound based on its chemical structure. PASS estimates the probability of activity (Pa) and inactivity (Pi) across a wide range

of pharmacological effects using structure–activity relationship models derived from large datasets of known bioactive molecules. This approach enables early identification of potential biological profiles and helps prioritize compounds for further experimental testing [17,18].

2.4. Toxicity Prediction and LD_{50} calculation of 1-H Tetrazole Derivatives

The acute oral toxicity of the synthesized tetrazole derivatives was predicted using the ProTox-II web server. The chemical structures were drawn and converted into SMILES format before being submitted to the online prediction platform. The server estimated the LD_{50} (mg kg^{-1}) values, toxicity class, average structural similarity, and prediction accuracy based on machine learning algorithms and validated toxicological datasets. The predicted toxicity profiles were subsequently analyzed to assess the preliminary safety and drug-likeness of the synthesized compounds prior to experimental biological evaluation.

III. RESULTS AND DISCUSSION

3.1. Hydrothermal synthesis Cu-doped indium oxide and One Pot synthesis of 5-substituted 1H-tetrazole derivatives

The Cu-doped indium oxide was synthesized using hydrothermal method and was catalyzed by FTIR, UV-visible spectroscopy, XRD, SEM-EDS and BET-surface area; while synthesized 5-substituted 1H-tetrazole were synthesized by one pot method using aryl aldehyde (1 mmol), sodium azide (1 mmol), hydroxylamine hydrochloride (1 mmol) and characterized by FTIR, ^{1}H-NMR, ^{13}C-NMR and HRMS. Detail discussion is available in our previously published article [7] "Synthesis of 5-substituted 1H-tetrazoles using Cu-doped indium oxide- molecular docking, ADME/pharmacokinetics, biological study © July 2025| IJIRT | Volume 12 Issue 2 | ISSN: 2349-6002".

3.2. Molecular Docking

Molecular docking is done with different antioxidant enzymes and different microbes with synthesized Schiff bases. Many software's can be used for the docking purpose like Auto Dock Vina, CB Dock 2 etc. Here we used commonly available platform such as CB-Dock 2 to estimate the binding affinity of ligand with the antioxidant enzyme (PDB ID: 1DGF), anti-inflammatory enzyme (Cyclooxygenase (COX-2) with PDB ID: 6COX), and anti-cancer protein (Epidermal Growth Factor Receptor with PDB ID: 1MI7) used for molecular docking study. Visualization of protein –ligand interaction was carried out using Chimera software. Molecular docking analysis helps to understand the target binding sites for docking. The software predicts the intermolecular Vander Waals interaction between the proteins and ligand. Following Table No. 1 represent different modes and affinity in kcal/mol for compounds I and II. As shown in Table 1; while docking cavities are shown in Fig. 1 and rainbow spectrum is shown in Fig. 2.

Table No. 1: Interaction of Ligand 4A-4B with selected proteins.

Sr No.	Protein	Ligand	Hydrophilic Interactions	Hydrophobic Contacts	No. of H-Bond
1	Antioxidant Enzyme (PDB ID: 1DGF)	4A	-	Arg 203(A), Gly 204 (A), Thr 150 (A), Ser 201 (A), Leu 199 (A), Asn 149 (A).	1 2.89 A^0
2	Antioxidant Enzyme (PDB ID: 1DGF)	4B	-	Thr 150 (A), Phe 446 (A), Leu 199 (A), Asn 149 (A), Arg 203 (A), Ser 201 (A), Gly 204 (A).	1 2.93 A^0

3	Anti-inflammatory Enzyme (PDB ID: 6COX)	4A	-	Gly 526 (A), Ser 530 (A), Val 349 (A), Val 523 (A), Leu 352 (A), Phe 518 (A).	1 2.86 A^0
4	Anti-inflammatory Enzyme (PDB ID: 6COX)	4B	-	Ser 530 (A), Phe 518 (A), Val 523 (A), Ser 353 (A), Leu 352 (A), Val 349 (A).	2 3.26 A^0 2.98 A^0
5	Anti-cancer Protein Epidermal Growth Factor Receptor (PDB ID: 1MI7)	4A	-	Leu 834 (A), Phe 832 (A), Ala 835 (A), Val 741 (A), Glu 738 (A), Asp 737 (A).	2 3.01 A^0 3.31 A^0
6	Anti-cancer Protein Epidermal Growth Factor Receptor (PDB ID: 1MI7)	4B	-	Leu 834 (A), Phe 832 (A), Ala 835 (A), Val 741 (A), Glu 738 (A), Asp 737 (A).	1 2.87 A^0

Docking Cavities

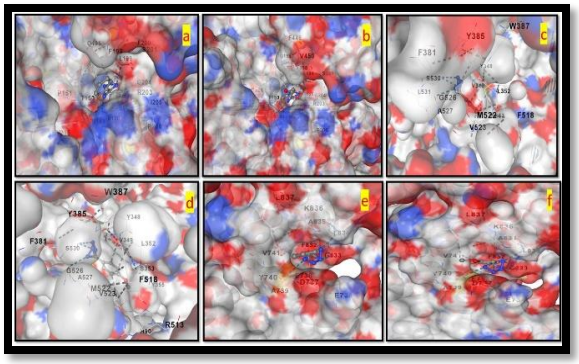

Fig. 1. Docking Cavities of 1a) Ligand 4A with 1DGF, 1b) Ligand 4B with 1DGF Antioxidant Enzyme, 1c) Ligand 4A with 6COX, 1d) Ligand 4B with 6COX Anti-inflammatory enzyme, 1e) Ligand 4A with 1M17, and 1f) Ligand 4B with 1M17 Anti-cancer protein.

Rainbow Spectrum

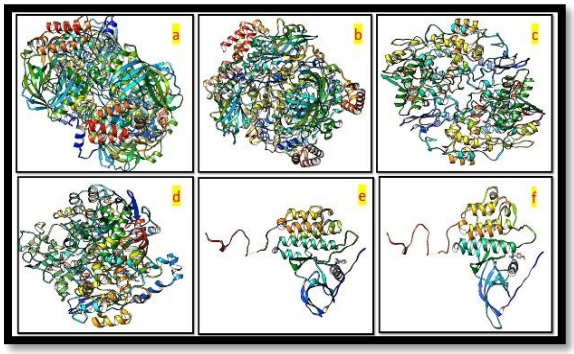

Fig. 2. Rainbow spectrum of 2a) Ligand 4A with 1DGF, 2b) Ligand 4B with 1DGF Antioxidant Enzyme, 2c) Ligand 4A with 6COX, 2d) Ligand 4B with 6COX Anti-inflammatory enzyme, 2e) Ligand 4A with 1M17, and 2f) Ligand 4B with 1M17 Anti-cancer protein.

The molecular docking of synthesized tetrazole derivatives with selected targeted proteins show highest docking score -7.7 Kcal/mol. The antioxidant enzyme (1DGF), the ligand 4B shows docking score -7.7 Kcal/mol, while 4B shows docking score -7.3 Kcal/mol with anti-inflammatory enzyme (6COX), and 4A and 4B ligand show equal affinity with anticancer protein (1M17) with docking score -6.3 Kcal/mol.

3.3. PASS

The PASS analysis for 5-substituted 1H-tetrazoles often indicates a spectrum of pharmacological properties, including: Antihypertensive activity, antimicrobial effects, Anti-inflammatory and

Analgesic properties, Anticancer/Antitumor potential, Antidiabetic effects, other activities.

The theoretical prediction for biological activities is done using PASS software and the results are interpreted in following Table No. 2.

Table No. 2: PASS analysis.

Sr. No	Pa	Pi	Activity
4A) 5-phenyl-1H-tetrazole			
1	0,967	0,001	Angiotensin AT1 receptor antagonist
2	0,964	0,001	Angiotensin antagonist
3	0,963	0,001	Angiotensin II receptor antagonist
4	0,950	0,004	Membrane integrity agonist
5	0,919	0,002	5 Hydroxytryptamine release inhibitor
6	0,848	0,003	Pterin deaminase inhibitor
7	0,834	0,004	Antihypertensive
8	0,831	0,003	Histamine release inhibitor
9	0,816	0,003	Antianorexic
10	0,768	0,002	Chloride channel blocker
11	0,764	0,003	Mediator release inhibitor
12	0,789	0,037	Aspulvinone dimethylallyltransferase inhibitor
13	0,751	0,001	G-protein-coupled receptor 120 agonist
14	0,759	0,011	Complement factor D inhibitor
15	0,722	0,019	5-O-(4-coumaroyl)-D-quinate 3'-monooxygenase inhibitor
16	0,703	0,004	GABA aminotransferase inhibitor
17	0,682	0,005	CYP2C8 inhibitor
18	0,676	0,008	Cytoprotectant
19	0,699	0,035	Nicotinic alpha6beta3beta4alpha5 receptor antagonist
20	0,725	0,065	Phobic disorders treatment
21	0,687	0,030	Glutamyl endopeptidase II inhibitor
22	0,702	0,054	Testosterone 17beta-dehydrogenase (NADP+) inhibitor
23	0,657	0,010	Aminobutyraldehyde dehydrogenase inhibitor
24	0,685	0,040	Glycosylphosphatidylinositol phospholipase D inhibitor
25	0,653	0,010	Gastrin inhibitor
26	0,669	0,039	Taurine dehydrogenase inhibitor
27	0,633	0,003	Growth hormone agonist
28	0,657	0,029	Glucose oxidase inhibitor
29	0,636	0,012	Gamma-guanidinobutyraldehyde dehydrogenase inhibitor
30	0,653	0,031	Omptin inhibitor
31	0,634	0,013	Corticosteroid side-chain-isomerase inhibitor
32	0,636	0,016	Nucleoside oxidase (H2O2-forming) inhibitor
33	0,647	0,030	Dehydro-L-gulonate decarboxylase inhibitor
34	0,643	0,026	Phthalate 4,5-dioxygenase inhibitor
35	0,644	0,027	Acute neurologic disorders treatment
36	0,635	0,022	Limulus clotting factor B inhibitor
37	0,666	0,054	Acrocylindropepsin inhibitor
38	0,666	0,054	Saccharopepsin inhibitor
39	0,666	0,054	Chymosin inhibitor

40	0,633	0,026	Venombin AB inhibitor
41	0,649	0,044	Sugar-phosphatase inhibitor
42	0,609	0,005	Taurine-2-oxoglutarate transaminase inhibitor
43	0,614	0,013	S-alkylcysteine lyase inhibitor
44	0,621	0,024	Thioredoxin inhibitor
45	0,613	0,023	Chloride peroxidase inhibitor
46	0,617	0,027	Phospholipid-translocating ATPase inhibitor
Sr. No	Pa	Pi	Activity
4B) 5-(4-methoxyphenyl)-1H-tetrazole			
1	0,949	0,004	Membrane integrity agonist
2	0,912	0,002	5 Hydroxytryptamine release inhibitor
3	0,861	0,017	Aspulvinone dimethylallyltransferase inhibitor
4	0,808	0,003	Histamine release inhibitor
5	0,780	0,003	Mediator release inhibitor
6	0,768	0,003	Antianorexic
7	0,730	0,005	Antihypertensive
8	0,701	0,003	Chloride channel blocker
9	0,686	0,006	Cytoprotectant
10	0,679	0,005	GABA aminotransferase inhibitor
11	0,686	0,014	Pterin deaminase inhibitor
12	0,713	0,041	Saccharopepsin inhibitor
13	0,713	0,041	Acrocylindropepsin inhibitor
14	0,713	0,041	Chymosin inhibitor
15	0,665	0,007	CYP2C8 inhibitor
16	0,665	0,024	Complement factor D inhibitor
17	0,691	0,061	Gluconate 2-dehydrogenase (acceptor) inhibitor
18	0,639	0,013	Gastrin inhibitor
19	0,670	0,046	Chlordecone reductase inhibitor
20	0,607	0,002	Angiotensin antagonist
21	0,606	0,002	Angiotensin AT1 receptor antagonist
22	0,606	0,002	Angiotensin II receptor antagonist
23	0,610	0,015	Antiallergic
24	0,587	0,034	JAK2 expression inhibitor
25	0,615	0,064	Fibrinolytic
26	0,604	0,055	Taurine dehydrogenase inhibitor
27	0,566	0,032	Preneoplastic conditions treatment
28	0,525	0,004	Growth hormone agonist
29	0,559	0,041	Calcium channel (voltage-sensitive) activator
30	0,544	0,031	CYP2C9 substrate
31	0,604	0,106	Ubiquinol-cytochrome-c reductase inhibitor
32	0,553	0,055	Acute neurologic disorders treatment
33	0,525	0,030	Antipruritic, allergic
34	0,513	0,022	Plastoquinol-plastocyanin reductase inhibitor
35	0,505	0,024	Cardiovascular analeptic
36	0,495	0,015	UGT1A6 substrate
37	0,483	0,004	Uric acid excretion stimulant
38	0,503	0,027	Antiasthmatic

39	0,541	0,067	5-O-(4-coumaroyl)-D-quinate 3'-monooxygenase inhibitor

The exploration of biological activities through pass analysis is shown in above Table No. 2. Compounds are considered to be more potent if the compound possess high Pa values (probability to be active) than Pi (probability to be inactive). In our study, high drug activity can be correlated with Pa >0.8, moderate therapeutic potential for 0.5 > Pa < 0.8 while poor pharmaceutical activity in Pa < 0.5. As per PASS predictions the compound showed pharmaceutical activity. Ligand 4A shows highest activity Pa=0.967 with Angiotensin AT1 receptor antagonist. While 4B shows Pa=0.949 with Membrane integrity agonist.

3.4. Toxicity Prediction of 1-H Tetrazole derivatives

The in-silico toxicity assessment of the synthesised tetrazole derivatives was carried out using the Pro Tox-II platform, and the predicted acute oral toxicity parameters are summarised in Table X. Both compounds were classified under toxicity class 4, indicating a comparatively low level of acute toxicity and suggesting a favourable preliminary safety profile. Among the evaluated derivatives, 5-(4-methoxyphenyl)-1H-tetrazole exhibited a higher predicted LD_{50} value of 1190 mg kg^{-1} compared with 5-phenyl-1H-tetrazole (890 mg kg^{-1}). Since a higher LD_{50} value corresponds to lower acute toxicity, the methoxy-substituted derivative is predicted to be less toxic than the unsubstituted analogue. This observation implies that the introduction of an electron-donating methoxy group on the aromatic ring may contribute to reducing the compound's acute toxic potential while preserving the tetrazole framework (Fig. 3 and 4).

Furthermore, both molecules achieved 100% average structural similarity and 100% prediction accuracy, indicating a high level of confidence in the computational predictions generated by the ProTox-II model. Although these results provide valuable preliminary insight into the toxicological behaviour of the synthesised compounds, experimental toxicological investigations remain necessary for definitive safety evaluation. Overall, the predicted toxicity profile suggests that both tetrazole derivatives possess acceptable safety characteristics, with 5-(4-methoxyphenyl)-1H-tetrazole emerging as the more promising candidate for subsequent biological and pharmacological investigations due to its lower predicted acute toxicity (Table No. 3).

Fig. 3: Toxicity Study of 5-phenyl-1H-tetrazole a) Oral Toxicity Prediction, b) Comparison of input compound with dataset compounds, c) Radar Chart, d) Network Chart, and e) Toxicity Model Report.

Fig. 4: Toxicity Study of 5-(4-methoxyphenyl)-1H-tetrazole a) Oral Toxicity Prediction, b) Comparison of input compound with dataset compounds, c) Radar Chart, d) Network Chart, and e) Toxicity Model Report.

Table No. 3: Toxicity Prediction.

Sr. No.	Name of Compound	LD_{50} (mg/Kg)	Predicted Toxicity Class	Average similarity (%)	Prediction accuracy (%)
1	5-phenyl-1H-tetrazole	890	4	100	100
2	5-(4-methoxyphenyl)-1H-tetrazole	1190	4	100	100

IV. CONCLUSION

The Cu-doped indium oxide was successfully implied for the one pot synthesis of 5-substituted 1H-

tetrazoles. The synthesized derivatives of tetrazole show high docking score also PASS proves the theoretical prediction of biological activities of synthesized tetrazole derivatives. The toxicity prediction shows that the 5-phenyl-1H-tetrazole has LD_{50} 890 mg/Kg, while 5-(4-methoxyphenyl)-1H-tetrazole has 1190 mg/Kg. This all proves that synthesized tetrazole derivatives show active biological activities.

SUPPLEMENTARY DATA

The required supplementary data will be available on demand. Also, the essential data is available in our previously published article [7] "Synthesis of 5-substituted 1H-tetrazoles using Cu-doped indium oxide- molecular docking, ADME/pharmacokinetics, biological study © July 2025| IJIRT | Volume 12 Issue 2 | ISSN: 2349-6002".

AUTHOR CONTRIBUTIONS

JNG, YRB authors designed the research; JNG author performed the experiments; YRB and BPP authors analyzed the data; JNG, MBK author wrote the manuscript draft; YRB and BPP authors revised the manuscript.

All authors approved the final version of the manuscript.

CONFLICT OF INTEREST

Authors declared no conflict of interest.

ACKNOWLEDGMENT

I would like to express my sincere gratitude to Maratha Vidya Prasarak Samaj's Nashik for providing opportunity for the research. I would like to express sincere gratitude to Prof. Dr. Suresh Jadhav, Principal, MVP Samaj's KSKW Arts, Science and Commerce College, CIDCO, Nashik, for his valuable guidance and constant support throughout this work. Authors are very thankful to CIF S P Pune University Pune, DST FIST Jaysingpur College, Rapture Biotech Bengluru for support and co-operation.

Finally, I am grateful to my family and friends for their encouragement and patience during the course of this research.

REFERENCES

[1] Butler, Richard N., and Anthony G. Coyne. "Water: Nature's Reaction Enforcer Comparative Effects for Organic Synthesis "In-Water" and "On-Water"." Chemical reviews 110, no. 10 (2010): 6302-6337.

[2] Demko, Zachary P., and K. Barry Sharpless. "A Click Chemistry Approach to Tetrazoles by Huisgen 1, 3-Dipolar Cycloaddition: Synthesis of 5-Acyltetrazoles from Azides and Acyl Cyanides." Angewandte Chemie 114, no. 12 (2002): 2217-2220.

[3] Jadhav, Popat M., A. B. Kanagare, Anand B. Dhirbassi, Atam B. Tekale, R. M. Borade, S. U. Tekale, Keshav Lalit Ameta, and R. P. Pawar. "Recent advances in nanocatalyzed synthesis of triazoles and tetrazoles and their biological studies." Nanocatalysis (2022): 177-200.

[4] Gao, Feng, and D. Wayne Goodman. "Model catalysts: simulating the complexities of heterogeneous catalysts." Annual review of physical chemistry 63, no. 1 (2012): 265-286.

[5] Anastas, Paul T., and John C. Warner. Green chemistry: theory and practice. Oxford university press, 2000.

[6] Morris, Garrett M., Ruth Huey, William Lindstrom, Michel F. Sanner, Richard K. Belew, David S. Goodsell, and Arthur J. Olson. "AutoDock4 and AutoDockTools4: Automated docking with selective receptor flexibility." Journal of computational chemistry 30, no. 16 (2009): 2785-2791.

[7] Yogeshwar Rajaram Baste, Jagdish Navnath Ghotekar (2025). Synthesis of 5-substituted 1H-tetrazoles using Cu-doped indium oxide-molecular docking, ADME/pharmacokinetics, biological study. International Journal of Innovative Research In Technology (IJIRT), 12(2), 2506-2517.

[8] Ahmadiasl, R., Moussavi, G., Shekoohiyan, S., & Razavian, F. (2022). Synthesis of Cu-doped TiO2 nanocatalyst for the enhanced photocatalytic degradation and mineralization of gabapentin under UVA/LED irradiation: characterization and photocatalytic activity. Catalysts, 12(11), 1310.

[9] Kitchen, Douglas B., Hélène Decornez, John R. Furr, and Jürgen Bajorath. "Docking and scoring in virtual screening for drug discovery: methods

and applications." Nature reviews Drug discovery 3, no. 11 (2004): 935-949.

[10] Ferreira, L. G., Dos Santos, R. N., Oliva, G., & Andricopulo, A. D. (2015). Molecular docking and structure-based drug design strategies. Molecules, 20(7), 13384-13421.

[11] Verma, Abhishek Kumar, and Sandeep Kumar Srivastava. "In silico and structural investigation of sulfonamides targeting VraSR two component system in methicillin-resistant Staphylococcus aureus." Journal of Biomolecular Structure and Dynamics 43, no. 11 (2025): 5606-5626.

[12] Lionta, Evanthia, George Spyrou, Demetrios K Vassilatis, and Zoe Cournia. "Structure-based virtual screening for drug discovery: principles, applications and recent advances." Current topics in medicinal chemistry 14, no. 16 (2014): 1923-1938.

[13] Filimonov, D. A., A. A. Lagunin, T. A. Gloriozova, A. V. Rudik, D. S. Druzhilovskii, P. V. Pogodin, and V. V. Poroikov. "Prediction of the biological activity spectra of organic compounds using the PASS online web resource." Chemistry of Heterocyclic Compounds 50, no. 3 (2014): 444-457.

[14] Al-Agel, Faisal A., Esam Al-Arfaj, Ahmed A. Al-Ghamdi, Yaroslav Losovyj, Lyudmila M. Bronstein, and Waleed E. Mahmoud. "A novel recipe to improve the magnetic properties of Mn doped CeO2 as a room temperature ferromagnetic diluted metal oxide." Journal of magnetism and magnetic materials 360 (2014): 73-79.

[15] Siddiqui, Hafsa, M. S. Qureshi, and Fozia Z. Haque. "One-step, template-free hydrothermal synthesis of CuO tetrapods." Optik 125, no. 17 (2014): 4663-4667.

[16] Mr. Jagdish Navnath Ghotekar, Dr. Yogeshwar Rajaram Baste "Photocatalytic, Antimicrobial, Swiss-ADME Studies and Characterization of Hydrothermally Synthesized Pure and Ni-Doped Indium Oxide" International Journal of Scientific Research in Science and Technology (IJSRST), Online ISSN: 2395-602X, Print ISSN: 2395-6011, Volume 12, Issue 11, pp.16-25, March-April-2025.

[17] Afsarian, Mohammad Hosein, Mojtaba Farjam, Elham Zarenezhad, Somayeh Behrouz, and Mohammad Navid Soltani Rad. "Synthesis, antifungal evaluation and molecular docking studies of some tetrazole derivatives." Acta Chimica Slovenica 66, no. 4 (2019): 874-887.

[18] Alasadi, Yuosra Khalaf, Fawzi Hameed Jumaa, Adil Hussein Dalaf, Safa Mahmood Shawkat, and Mohammed Ghanam Mukhlif. "Synthesis, Characterization, and Molecular Docking of New Tetrazole Derivatives as Promising Anticancer Agents." Journal of Pharmaceutical Negative Results 13, no. 3 (2022): 513-522.

[19] Afsarian, Mohammad Hosein, Mojtaba Farjam, Elham Zarenezhad, Somayeh Behrouz, and Mohammad Navid Soltani Rad. "Synthesis, antifungal evaluation and molecular docking studies of some tetrazole derivatives." Acta Chimica Slovenica 66, no. 4 (2019): 874-887.

[20] Alasadi, Yuosra Khalaf, Fawzi Hameed Jumaa, Adil Hussein Dalaf, Safa Mahmood Shawkat, and Mohammed Ghanam Mukhlif. "Synthesis, Characterization, and Molecular Docking of New Tetrazole Derivatives as Promising Anticancer Agents." Journal of Pharmaceutical Negative Results 13, no. 3 (2022): 513-522.

[21] Gorle, Sridevi, Suresh Maddila, Surya N Maddila, Kovashnee Naicker, Moganavelli Singh, Parvesh Singh, and Sreekantha B Jonnalagadda. "Synthesis, molecular docking study and in vitro anticancer activity of tetrazole linked benzochromene derivatives." Anti-Cancer Agents in Medicinal Chemistry (Formerly Current Medicinal Chemistry-Anti-Cancer Agents) 17, no. 3 (2017): 464-470.

[22] Mekheimer, Ramadan Ahmed, Gamal El-Din A. Abuo-Rahma, Mohamed Abd-Elmonem, Ramadan Yahia, Mohamed Hisham, Alaa M. Hayallah, Sara M. Mostafa, Fatma A. Abo-Elsoud, and Kamal Usef Sadek. "New s-Triazine/Tetrazole conjugates as potent antifungal and antibacterial agents: Design, molecular docking and mechanistic study." Journal of Molecular Structure 1267 (2022): 133615.

[23] Aziz, Hamid, Aamer Saeed, Farukh Jabeen, Noor ud Din, and Ulrich Flörke. "Synthesis, single crystal analysis, biological and docking evaluation of tetrazole derivatives." Heliyon 4, no. 9 (2018).

[24] Hameed, Anwar A., Ahmed SM Al-Janabi, Abdulrahman M. Saleh, Saad Shaaban, and Mustafa Alheety. "Spectroscopic, biological activity, molecular docking and hydrogen storage

studies of tetrazole-thione complexes." Journal of Molecular Structure 1312 (2024): 138672.

[25] Abd ElMonaem, Heidi S., Naglaa I. Abdel-Aziz, Mohammad A. Morsy, Farid A. Badria, Fardous ElSenduny, Mahmoud B. El-Ashmawy, and Mohamed A. Moustafa. "Synthesis, in vitro antiproliferative evaluation and molecular docking of new tetrazole-chalcone and tetrazole-pyrazoline hybrids." Journal of Applied Pharmaceutical Science 8, no. 5 (2018): 075-087.

[26] Abdul Wahed Abdul, Sattar Talluh, Saleh Mohammed Jwher, and Saleh Jamil Nadhem. "Preparation, Characterisation and Study of the Molecular Docking of Some Derivatives of the Tetrazole Ring and Evaluation of their Biological Activity." World of Medicine: Journal of Biomedical Sciences 1, no. 7 (2024): 15-23.

[27] Abdul Wahed Abdul, Sattar Talluh, Saleh Mohammed Jwher, and Saleh Jamil Nadhem. "Preparation, Characterisation and Study of the Molecular Docking of Some Derivatives of the Tetrazole Ring and Evaluation of their Biological Activity." World of Medicine: Journal of Biomedical Sciences 1, no. 7 (2024): 15-23.

[28] Al-Hourani, Baker Jawabrah, Musa I. El-Barghouthi, Robert Mcdonald, Wajdy Al-Awaida, and Frank Wuest. "Docking studies and the crystal structure of two tetrazole derivatives: 5-(4-chlorophenyl)-1-{4-(methylsulfonyl) phenyl}-1H-tetrazole and 4-{5-(4-methoxyphenyl)-1H-tetrazol-1-yl} benzenesulfonamide." Journal of Molecular Structure 1101 (2015): 21-27.

[29] Zala, Mayursinh, Jwalant J. Vora, and Vijay M. Khedkar. "Synthesis, characterization, antitubercular activity, and molecular docking studies of pyrazolylpyrazoline-clubbed triazole and tetrazole hybrids." ACS omega 8, no. 23 (2023): 20262-20271.

[30] Sadeghi, Zahra, Hoda Abolhasani, Zohreh Mirjafary, Gholamreza Najafi, and Fatameh Heidari. "Efficient synthesis, molecular docking and ADMET studies of new 5-substituted tetrazole derivatives." Journal of Molecular Structure 1277 (2023): 134867.