Current Trends in Biotechnology and Pharmacy
Vol. 20(2) 3021-3028 July 2026, ISSN 0973-8916 (Print), 2230-7303 (Online)
DOI: 10.5530/ctbp.2026.3.25

Design, Synthesis, In Silico ADMET Profiling, and Molecular Docking of a Novel Bis-dimethylamino Hydrazone as a Potent Dual Inhibitor of Monoamine Oxidases

Akram Al-Busaidi[1], Athra Al Habsi[1], Aflah Al Jamoudi[1], Taqwa Al Moqbali[1], Abir Al Rumhi[1], Dr. Mahammad Ishaq Beludari[1], Dr. Gopala Krishna Devisetty[2]*

[1]Department of Pharmacy, College of Applied Sciences and Pharmacy, University of Technology and Applied Sciences, Muscat, Oman.
[2]Department of Chemistry, College of Applied Sciences and Pharmacy, University of Technology and Applied sciences, Muscat, Oman.

***Corresponding author**: doctorgk2627@gmail.com

Abstract:

Monoamine oxidases (MAO-A and MAO-B) play a key role in the metabolism of neurotransmitters, and their dysregulation is linked to neurological disorders. Hydrazone scaffolds are known for their versatile biological activities, including MAO inhibition. In this work, a new hydrazone derivative, *4-(Dimethylamino) benzaldehyde (4-dimethylamino) benzylidene hydrazone* (DMBH-1), was synthesized through the condensation of hydrazine hydrate with para-dimethylamino benzaldehyde. The reaction produced a yellow crystalline solid with a 65% yield after recrystallization using chloroform. The molecular formula of the compound is $C_{18}H_{22}N_4$, with a molecular weight of 294.39 g/mol. Structural confirmation was achieved through UV–Visible spectroscopy, FT-IR, 1H and 13C NMR, and mass spectrometry. Molecular target prediction using SwissTargetPredict indicated affinity towards human monoamine oxidases MAO-A and MAO-B. Docking studies were performed using AutoDock against MAO-A PDB structures 2Z5X and 2BXR, and MAO-B structures 1GOS, 2V5Z, and 6FW0. DMBH-1 showed strong binding energies across all targets, with scores of –8.55 kcal/mol (2Z5X) and –8.35 kcal/mol (2BXR) for MAO-A. For MAO-B, the compound showed binding energies of –8.47 (1GOS), –8.74 (2V5Z), and –9.22 kcal/mol (6FW0). These values were superior to standard MAO-B inhibitors including safinamide (–7.18 to –8.72), rasagiline (–6.88 to –7.11), and selegiline (–6.23 to –6.94). DMBH-1 also showed stronger affinity than MAO-A inhibitors harmine (-7.13 to -7.67), moclobemide (-7.05 to -7.28), and clorgyline (6.35 to 6.60). SwissADME analysis showed favourable properties: molecular weight 294.39 g/mol, TPSA 31.20 Å², consensus LogP 3.25, high GI absorption, BBB permeability, and no PAINS alerts. The bioavailability score was 0.55 with a synthetic accessibility of 2.38. Overall, DMBH-1 exhibits strong predicted MAO inhibitory activity and promising drug-likeness, indicating good potential as a lead molecule for CNS-related drug discovery.

Key words: Monoamine oxidases, neurotransmitters, Hydrazone, NMR, mass spectrometry.

Introduction:

Monoamine oxidases, MAO-A and MAO-B, are key enzymes responsible for the oxidative breakdown of neurotransmitters such as dopamine, serotonin and norepinephrine. (1-2) Their abnormal activity is associated with depression, Parkinson's disease and other neurodegenerative disorders. (3) Although several

Figure 1 shows the synthesis of 4,4′-Bis(dimethylamino) benzaldazine (DMBH-1).

Current Trends in Biotechnology and Pharmacy
Vol. 20(2) 3021-3028 July 2026, ISSN 0973-8916 (Print), 2230-7303 (Online)
DOI: 10.5530/ctbp.2026.3.25

MAO inhibitors like safinamide, rasagiline and selegiline are available, the search for new scaffolds with improved binding and better CNS-related properties continues. (4) Hydrazone derivatives are known for their wide biological activity and have shown potential as MAO inhibitors because of their conjugated structure and ability to interact effectively within enzyme active sites. (5) A review of the existing literature indicates that dimethylamino-substituted hydrazones have not been extensively explored for MAO targeting, leaving space for new analogues with promising activity.

With this background, the aim of the present study is to synthesize a new hydrazone derivative from hydrazine hydrate and para-dimethylamino benzaldehyde, confirm its structure through spectroscopic characterization and evaluate its potential as an MAO-A and MAO-B inhibitor. The work also aims to predict molecular targets, perform docking studies using AutoDock and assess physicochemical and pharmacokinetic properties using SwissADME to understand its suitability as a potential CNS-active lead compound.

Materials and methods

Materials

Hydrazine hydrate and para-dimethylamino benzaldehyde were purchased from commercially available analytical-grade from Merck, USA. Chloroform was used for recrystallization. All solvents and reagents were used without further purification. UV–Visible, FT-IR, 1H NMR, 13C NMR and mass spectrometry instruments available in the department were used for analytical characterization. Protein structures for MAO-A (PDB IDs: 2Z5X, 2BXR) and MAO-B (PDB IDs: 1GOS, 2V5Z, 6FW0) were retrieved from the Protein Data Bank.

Synthesis of the hydrazone derivative

The compound was synthesized by condensing for 4hours using 2.5 mL 0.05 M hydrazine hydrate with 7.5 g 0.05M para-dimethylamino benzaldehyde in 50 mL ethanol as solvent system. The reaction mixture was stirred until completion, monitored through thin-layer chromatography. The resulting product was filtered, washed and recrystallized using chloroform to obtain pure crystals. The final yield was calculated based on the weight of the dried product. Figure 1 shows the the synthesis of *4-(Dimethylamino) benzaldehyde (4-dimethylamino) benzylidene hydrazone* (DMBH-1).

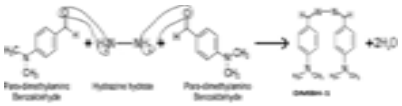


Figure 1 shows the synthesis of 4,4′-Bis(dimethylamino)benzaldazine (DMBH-1).

Analytical characterization

The synthesized molecule was confirmed using:

UV–Visible spectroscopy for electronic transitions

FT-IR spectroscopy to identify functional groups

1H NMR and 13C NMR for structural elucidation

Mass spectrometry for molecular ion confirmation

Target prediction

SwissTargetPredict was used to identify potential biological targets. The SMILES string of the compound was submitted to the server, and predicted targets with high probability scores were selected for further analysis. MAO-A and MAO-B were identified as primary targets.

Molecular Docking

Docking studies were performed using AutoDock. Protein structures were prepared by removing water molecules, adding polar hydrogens and assigning Kollman charges. The ligand was energy-minimized and converted to PDBQT format. Grid boxes were set around the active site pocket of each protein. Binding energies were recorded after running Lamarckian Genetic Algorithm simulations. (6)

Pharmacokinetic and drug-likeness analysis

SwissADME was used to evaluate physicochemical parameters, lipophilicity, wa-

ter solubility, pharmacokinetics, drug-likeness filters and medicinal chemistry properties. The SMILES structure was used as the input. (7)

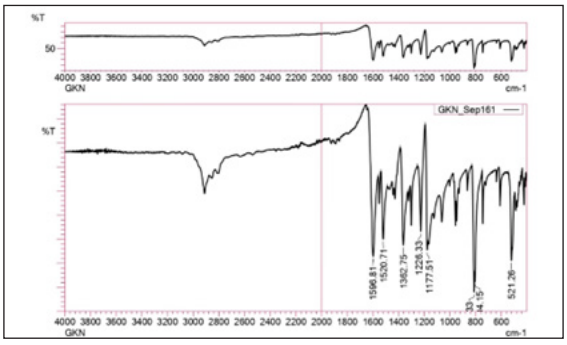
Results and discussion

Synthesis and Analytical Characterization

The reaction between hydrazine hydrate and para-dimethylamino benzaldehyde yielded the target hydrazone ($C_{18}H_{22}N_4$; MW 294.39 g/mol). The product was obtained as an orange crystalline solid after recrystallization with chloroform. The percentage yield was **65%**. The structure was confirmed using UV-Visible, IR, ^{1}H NMR, ^{13}C NMR, and mass spectrometry, showing characteristic peaks consistent with hydrazone formation. The melting point of DMBH-1 was found to be 271°C.

The synthesized molecule was confirmed using:**IR (KBr, cm^{-1}):** The spectrum shows a strong band at 1600–1635 cm^{-1} corresponding to the C=N stretching vibration of the hydrazone linkage. Aromatic C=C stretches appear at 1500–1580 cm^{-1}, while aliphatic C–H stretching bands from the N–CH_3 groups are observed around 2850–2950 cm^{-1}. Weak aromatic C–H stretches occur near 3020–3050 cm^{-1}. The absence of a carbonyl band at ~1700 cm^{-1} confirms complete conversion of the aldehyde to the hydrazone. Figure 2 shows the IR spectra DMBH-1.

Figure 2: IR spectra of DMBH-1



^{1}H NMR (600 MHz, $CDCl_3$): δ 3.00–3.10 (s, 12H, $N(CH_3)_2$ protons from two dimethylamino groups), 6.60–7.80 (m, 8H, aromatic protons from two para-disubstituted benzene rings showing AA′BB′ patterns), 8.30–8.70 (s, 1H, azomethine CH═N proton). No aldehydic proton at 9–10 ppm is observed, supporting hydrazone formation. An exchangeable NH proton, if present, appears weak or broadened due to solvent exchange. Figure 3-4 shows the ^{1}H NMR of DMBH-1

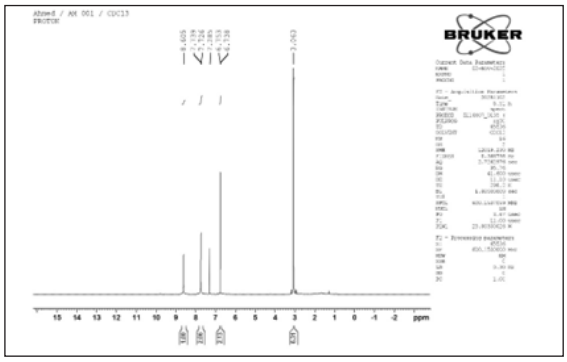


Figure 3: ^{1}H NMR of DMBH-1

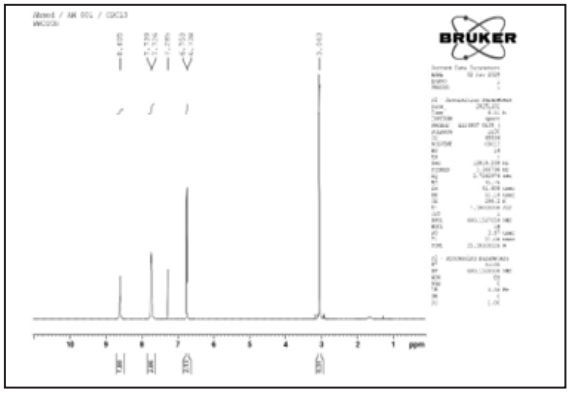


Figure 4: ^{1}H NMR of DMBH-1

^{13}C NMR (150 MHz, $CDCl_3$): Signals appear at δ ~40–45 (N-CH_3 carbons), 115–135 (aromatic CH carbons), and 150–160 ppm corresponding to the C=N carbon and ipso aromatic carbons bonded to nitrogen atoms. The chemical shift of the imine carbon in the 150+ ppm region confirms formation of the hydrazone functionality. Figure 5 and 6 shows ^{13}C NMR spectra of DMBH-1

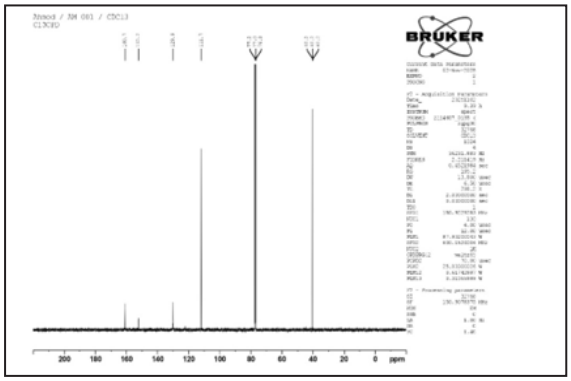


Figure 5: ^{13}C NMR spectra of DMBH-1

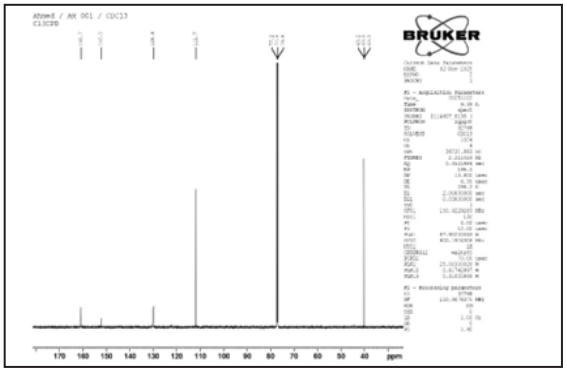
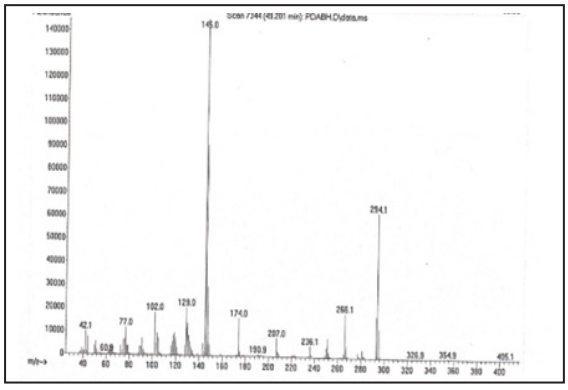


Figure 6: ^{13}C NMR spectra of DMBH-1

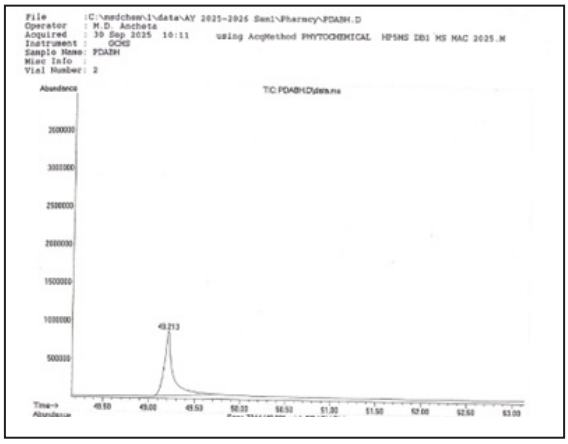
Mass spectrometry (ESI-MS): m/z 294 [M^+], consistent with the calculated molecular weight 294.39 g/mol for $C_{18}H_{22}N_4$. Fragmentation peaks corresponding to losses of N-methyl groups and aromatic fragments further support the proposed structure. Figure 7 shows the



Mass spectra of DMBH-1

Figure 7: The Mass spectra of DMBH-1

GC analysis: The chromatogram shows a single major peak with dominant area

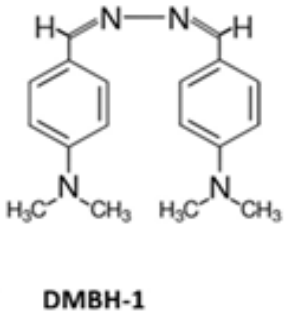


percentage, indicating good purity of the synthesized compound. Figure 8 shows the GC chromatogram of DMBH-1.

Figure 8: The GC chromatogram of DMBH-1

Overall interpretation

All spectral data (IR, ^{1}H NMR, ^{13}C NMR, MS) are fully consistent with the proposed structure of DMBH-1, containing two N,N-dimethylaminophenyl rings connected through a conjugated hydrazone (C═N–NH–) linkage. The disappearance of aldehydic signals, appearance of C=N resonance, presence of dimethylamino signatures, and correct molecular ion confirm successful synthesis. Figure 9 shows the molecular structure of DMBH-1.



DMBH-1

Figure 9: The molecular structure of DMBH-1

Current Trends in Biotechnology and Pharmacy
Vol. 20(2) 3021-3028 July 2026, ISSN 0973-8916 (Print), 2230-7303 (Online)
DOI: 10.5530/ctbp.2026.3.25

Molecular docking results

Docking studies were carried out against MAO-A (2Z5X, 2BXR) and MAO-B (1GOS, 2V5Z, 6FW0). The synthesized compound (coded as **DMBH**) showed strong binding with both enzyme isoforms. Table 1 shows the binding energies of DMBH and standard MAO inhibitors.

Table 1. Binding energies of DMBH and standard MAO inhibitors

Ligand	Binding energies				
	MAO-A Targets		MAO-B Targets		
	2Z5X	2BXR	1GOS	2V5Z	6FW0
DMBH-1	-8.55	-8.35	-8.47	-8.74	-9.22
Safinamide	-	-	-7.18	-7.96	-8.72
Rasagiline	-	-	-6.88	-6.88	-7.11
Selegiline	-	-	-6.23	-6.33	-6.94
Harmine	-7.13	-7.67	-	-	-
Moclobemide	-7.28	-7.05	-	-	-
Clorgyline	-6.35	-6.60	-	-	-

DMBH showed better binding affinity than several marketed MAO inhibitors, especially towards MAO-B (up to –9.22 kcal/mol). Figure 10 shows the Protein ligand interactions.

2Z5X (MAO-A)

DMBH fits well into the 2Z5X active site, mainly through several hydrophobic contacts with Ile19, Ala44, Ile273 and Leu277, which help stabilize the ligand in the pocket. The compound forms a strong hydrogen bond with Ala44, supporting its anchoring within the cavity. In addition, π-stacking with Tyr402 adds extra stabilization by aligning the aromatic ring of the ligand with the aromatic side chain of the residue. Together, these interactions explain the favorable binding energy observed for this target.

2BXR (MAO-A)

In 2BXR, the key interaction is a π-cation contact between DMBH and Lys379. The positively charged Lys residue interacts with the aromatic region of the ligand, creating a strong non-covalent attraction. This interaction likely plays a major role in the binding affinity seen with this MAO-A structure.

1GOS (MAO-B)

DMBH shows a dense network of hydrophobic interactions in 1GOS, especially with Phe168, Leu171, Ile199 and several Tyr residues that surround the ligand. These contacts help position the compound securely within the active site. A notable hydrogen bond with Cys172 strengthens the binding further by providing a directional interaction that complements the hydrophobic environment.

2V5Z (MAO-B)

The binding of DMBH to 2V5Z is driven mainly by hydrophobic interactions with residues such as Phe168, Leu171, Ile199, Tyr326 and Tyr398. These residues form a non-polar pocket that accommodates the ligand's aromatic and hydrophobic groups. The consistent contact pattern suggests a stable fit that supports the strong docking score for this structure.

6FW0 (MAO-B)

In 6FW0, DMBH is stabilized by several hydrophobic interactions with Phe168, Leu171, Ile199, Phe343 and Tyr435. The presence of two Phe343 interactions indicates tight packing in the binding pocket. A π-stacking interaction with Tyr398 further enhances binding by aligning the aromatic systems. This combination of contacts explains why 6FW0 shows one of the most favorable binding energies for the compound.

Current Trends in Biotechnology and Pharmacy
Vol. 20(2) 3021-3028 July 2026, ISSN 0973-8916 (Print), 2230-7303 (Online)
DOI: 10.5530/ctbp.2026.3.25

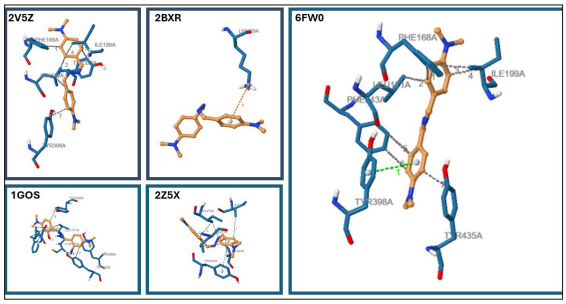


Figure 10: Protein ligand interactions

ADME Profiling

SwissADME predictions showed that the molecule complies with major drug-likeness filters (Lipinski, Ghose, Veber, Egan, Muegge). GI absorption was predicted to be high, and the molecule is BBB permeant, indicating CNS activity potential. It is non-substrate for P-gp and showed predicted inhibition of CYP1A2, CYP2C19, and CYP2D6. The bioavailability score was 0.55. Table 2 shows the key physicochemical and pharmacokinetic parameters.

Table 2. Key physicochemical and pharmacokinetic parameters

Parameter	Value
Molecular weight	294.39 g/mol
TPSA	31.20 Å²
H-bond donors	0
H-bond acceptors	2
Rotatable bonds	5
Consensus LogP	3.25
Water solubility (ESOL)	3.16 × 10^{-2} mg/mL
GI absorption	High
BBB permeation	Yes
Bioavailability score	0.55
PAINS	0 alerts
Synthetic accessibility	2.38

Discussion

The condensation of hydrazine hydrate with para-dimethylamino benzaldehyde successfully produced a hydrazone derivative with good yield and clean analytical confirmation. Hydrazones are widely known for their MAO inhibitory potential, and the docking results in this study support this activity. (8-9)

The synthesized compound (**DMBH-1**) exhibited strong binding affinity towards both MAO-A and MAO-B. Notably, the MAO-B binding energy of –9.22 kcal/mol was superior to standard drugs like safinamide (–8.72 kcal/mol), rasagiline (–7.11 kcal/mol), and selegiline (–6.94 kcal/mol). This suggests that the compound can fit efficiently into the hydrophobic active site of MAO-B.

The ADME profile further strengthens its potential as a CNS-active agent. Its low TPSA (31.20 Å²) and moderate lipophilicity (LogP ~3.25) support effective blood-brain barrier penetration. The absence of PAINS alerts and good synthetic accessibility score (2.38) indicate that the molecule is chemically clean and feasible for further optimization. (10)

Predicted inhibition of certain CYP enzymes (CYP1A2, CYP2C19, CYP2D6) points to metabolism considerations for future development but does not detract from its promise as a lead scaffold.

Conclusion

The hydrazone derivative synthesized from hydrazine hydrate and para-dimethylamino benzaldehyde was obtained in good yield and confirmed through multiple analytical techniques. Docking studies demonstrated strong affinity toward MAO-A and MAO-B, with MAO-B showing especially favorable interactions. The ADME predictions reveal good drug-likeness, high GI absorption, and BBB permeability, supporting its potential as a CNS therapeutic lead. Overall, the compound (DMBH) emerges as a promising scaffold for the development of new monoamine oxidase inhibitors.

Future Work

Further studies will focus on validating the MAO-A and MAO-B inhibitory activity of DMBH-1 through in vitro enzyme assays to confirm the docking predictions. Structure–activity relationship (SAR) optimization will be carried out by synthesizing and evaluating analogues with different electron-donating or electron-with-

drawing substituents on the aromatic rings. Additional computational studies, including molecular dynamics simulations, will be employed to assess the stability of binding interactions within MAO active sites. Comprehensive in vitro ADME and cytotoxicity profiling will also be conducted to evaluate the compound's drug-likeness and safety. If promising, in vivo behavioral and pharmacological studies will be planned to explore its potential as a CNS-active lead compound.

Authorship contribution

Akram Al-Busaidi, Athra Al Habsi, Aflah Al Jamoudi, and Taqwa Al Moqbali carried out the experimental work including synthesis of the compound, purification, analytical characterization (UV–Vis, FT-IR, NMR, MS, GC), data collection, and preliminary interpretation of results. They also assisted in literature review and manuscript preparation.

Dr. Mahammad Ishaq Beludari and Abir Al Rumhi contributed to the study design, supervision of experimental and computational work, guidance in analytical characterization, interpretation of results, and drafting and critical revision of the manuscript.

Dr. Gopala Krishna Devisetty conceptualized the research, designed and supervised the project, guided the molecular docking and in silico ADMET studies, validated the scientific content, and served as the corresponding author responsible for final manuscript review and submission.

Conflict of interest

The authors declare that they have no conflict of interest.

Ethical approval:

Not applicable

Finding:

No funding source applicable.

References:

1. Ostadkarampour M, Putnins EE (2021). Monoamine oxidase inhibitors: a review of their anti-inflammatory therapeutic potential and mechanisms of action. *Frontiers in Pharmacology*, 12: 676239.
2. Uzbekov MG (2021). Monoamine oxidase as a potential biomarker of the efficacy of treatment of mental disorders. *Biochemistry (Moscow)*, 86(6): 773–783.
3. Özdemir Z, Alagöz MA, Bahçecioğlu ÖF, Gök S (2021). Monoamine oxidase-B (MAO-B) inhibitors in the treatment of Alzheimer's and Parkinson's disease. *Current Medicinal Chemistry*, 28(29): 6045–6065.
4. Naoi M, Maruyama W, Shamoto-Nagai M, Riederer P (2025). Type A monoamine oxidase: its unique role in mood, behavior and neurodegeneration. *Journal of Neural Transmission*, 132(3): 387–406.
5. Maliyakkal N, Oh JM, Kumar S, Gahori P, Tengli A, Beeran AA, Kim H, Mathew B (2024). Synthesis, biochemistry, and in silico investigations of isatin-based hydrazone derivatives as monoamine oxidase inhibitors. *Applied Biological Chemistry*, 67(1): 63.
6. Ali Kharl HA, Nadeem H, Khan AU, Mehreen A, Afzal A, Mehdi SM, Fozilova S (2025). Synthesis, molecular docking, and investigation of enzyme inhibition activities of benzimidazole-pyrazole hybrids. *Journal of Visualized Experiments*, 1.
7. Yusuf SE (2025). Pharmacokinetic evaluation of sulfadicramide through SwissADME: a computational insight into drug-likeness and bioavailability. *MAS Journal of Applied Sciences*, 10(2): 357–362.
8. Agwom FM, Afolabi EO, Bot KJ, Yakubu NS, Olaitan IJ, Kindala JT (2019). In silico studies, comparative synthesis and antibacterial activity of some imine derivatives of isonicotinic hydrazide. *Organic and Medicinal Chemistry International Journal*, 8(5): 106–113.
9. Yeye EO, AkintundeAdeniyi-Akee M, Ahmed SA, Aboaba SA (2023). In silico

studies and antimicrobial investigation of synthesised novel N-acylhydrazone derivatives of indole. *Scientific African*, 19: e01463.

10. Talevi A (2024). In silico prediction of CNS bioavailability. In: *CNS Drug Development and Delivery: Concepts and Applications*, pp. 93–112. Springer Nature, Cham.