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PHARMACOKINETICS AND TOXICITY PROFILING OF NOVEL NITROGEN HETEROCYCLIC SMALL MOLECULES USING DEEP-PK IN SILICO TOOLS

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1. ABSTRACT

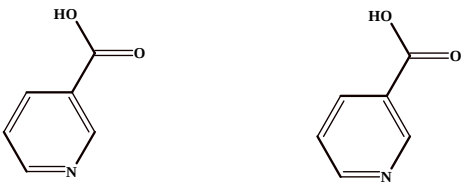
Nitrogen-containing heterocyclic compounds, especially pyridine derivatives, represent a pivotal class of molecules with extensive pharmacological and therapeutic potential. Pyridine, a planar aromatic heterocycle analogous to benzene but substituted with a nitrogen atom, serves as a fundamental scaffold in drug design due to its versatile chemical properties. This report highlights the synthesis, pharmacokinetic evaluation, and antimicrobial efficacy of novel small molecules that incorporate hybrid structures of pyridine, piperidine, benzimidazole, and pyrazole moieties. These hybrids exhibit diverse biological activities including antibacterial, anti-inflammatory, anticancer, and antiviral effects, making them promising candidates for pharmaceutical development. Through computational in silico approaches, the pharmacokinetics and toxicity profiles of these molecules were predicted, focusing on absorption, distribution, metabolism, excretion, and toxicity (ADMET) parameters. The selected compounds demonstrate favorable drug-like properties consistent with Lipinski's rule of five, including optimal molecular weight, lipophilicity, and hydrogen bonding capacity, predicting good oral bioavailability and membrane permeability. Metabolic pathway predictions indicate probable interactions with key enzymes like CYP isoforms and drug transporters, suggesting paths for further optimization. Toxicity assessments reveal safety in genetic and environmental endpoints but indicate potential risks for liver injury and respiratory effects, highlighting the need for in vivo validation. This study underscores the importance of integrating synthetic chemistry with computational pharmacokinetics to streamline the discovery of bioactive heterocycles. The novel hybrids presented provide a foundation for developing safe, effective therapeutic agents targeting infectious diseases, cancer, and inflammatory disorders.

KEYWORDS: Heterocyclic compounds, Insilico, Overview of nitrogen containing compounds, deep pk, Physiiochemical properties.

1. INTRODUCTION

Pyridine is a basic heterocyclic organic matter with the chemical formula C_5H_5N. In many respects, it is similar to the popular and simple aromatic chemical benzene, which has a nitrogen atom in place of one C-H group. Pyridine contains a conjugated system of six π-electrons that are delocalized over the heterocyclic ring, similar to how benzene has. The molecule matches the Huckel guidelines for aromaticity and is planar in nature.[5]

The Greek term "pyridine" is a mixture of the words "pyr," which shows fire, and "idine," which means aromatic bases. The first pyridine base, picoline (Compound 1), was identified by Anderson in 1846.Its organization was ultimately set up independently by Wilhelm Korner in 1869 and James Dewar in 1871. It is suggested that pyridine's structure might resemble that of naphthalene and quinoline. It has been shown that pyridine is formed from benzene and that substituting a nitrogen atom for a CH moiety can produce its structure. **Niacin and picoline** is a derivative from pyridine, as shown in **Figure 1, Compound 1, 2.**[5]



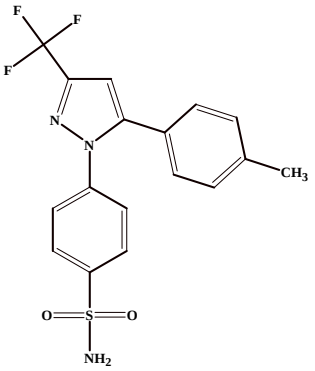
pyridine-3-carboxylic acid
1

pyridine-3-carboxylic acid
2

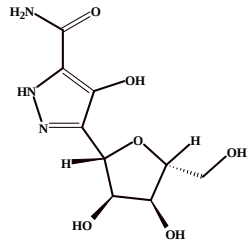
Figure 1: Niacin and picoline pyridine derivatives.

Given their synthetic and useful biological significance, 1,2,4-triazole-pyridine hybrids and their fused heterocyclic derivatives have drawn significant attention among a broad range of heterocyclic compounds being investigated for the expansion of fresh compounds for healthcare chemistry.[1] Our previous investigations show the **antibacterial, anti-inflammatory, and anticancer effects** of multiple substituted pyridine and Schiff base derivatives.[2]

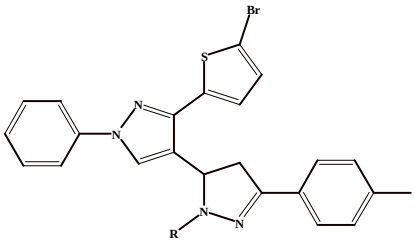
We recently demonstrated the value of 2,6-di substituted pyridine derivatives as congeners with biological properties.[3] Considering these results and as a continuation of our previous work in peptido-heterocyclic chemistry, we developed a few new substances with hetero-organic and amino acid moieties and investigated their potential biological consequences.[4] Some of our recently substituted heterocyclic compounds displayed **antiparkinsonian, cancer prevention. antimicrobial, and anti-inflammatory** effects in a prior study. Many different compounds in the interesting class of pyrazoles have wide pharmacological effects, including antipyretic, **antirheumatic, and analgesic properties.**[6] To evaluate their **antimicrobial efficacy**, we have synthesized several novel derivatives putting a heterocyclic ring fused with a substituted benzosuberone structure in light of these reports and in continuation of our earlier work in heterocyclic chemistry.[7] It was developed to produce a new series of pyrazole derivatives, structure 5 and 6, that would have a high safety margin and function as **dual antimicrobial, non-acidic, anti-inflammatory drugs** with little adverse reactions in the gut. To correspond with the diaryl heterocycle template of drugs known to work selectively as inhibiting **COX-2**, such celecoxib and pyrazofurin the substitution pattern of the pyridine ring was rationalized.[8]



Celecoxib
2



Pyrazofurin
3



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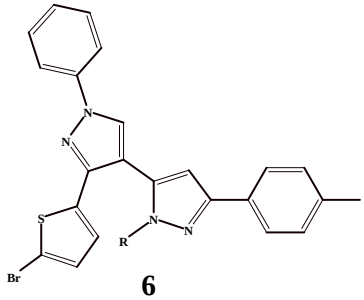


6

***Figure* 2: Compounds of pyrazofurin, celecoxib, and the recently.**

Introduced pyrazole 5 and 6 series[8]

Here, we report the synthesis and antimicrobial analysis of a few new structural hybrids that combine the ring systems of **piperidine, pyridine, and benzimidazole**. In a bid to give the target molecules some synergistic biological significance, this combination was offered for studying the effect of such hybridization and structure variation on predicted biological activities and Benzimidazole and pyridine ring substitution sequences have been carefully selected to give the molecules different electrical power environs.[9] Important pharmacologically active chemical molecules present in medicinally beneficial compounds are the pyrazole moieties. Many pharmaceutical benefits, including **anti-cancer, anti-viral, anti-oxidant, anti-microbial, anti-pyretic, anti-diabetic, anti-inflammatory, anti-convulsant, anti-psychotic, anti-obesity,** an H2-receptor agonist, anti-depressant, or analgesic properties, have gained widespread attention for it.[10] Additionally, heterocyclic compounds containing nitrogen, such **quinoline, indoles, pyrroles, and pyrrolidines** (as likewise as their alkylated homologues), have become highly desirable in the manufacturing industry for use as intermediates in the production of **medicines, dyes, fungicides, herbicides,** as well as other compounds.[12] due to the broad spectrum of possible biological functions, pyrazole derivatives are the focus of many research efforts. Bernardino et al. developed and

evaluated different kinds of pyrazolonaphthyridine that might possess **anti-HSV-1** effects.[14] In medicinal chemistry, nitrogen-containing heterocyclic substances like pyrimidines, quinoline, pyrrole, indole, triazole, imidazole, pyrazole, and pyrazine play an essential part. Because of their pharmacological and biological properties, pyrazole, indole, and triazole are seen as the most important hetero moieties among them.[15] Since it directly contributes to high mortality and morbidity, antimicrobial resistance in bacterial pathogens is an important obstacle of the 21st century. Commercial antibiotics made readily available encourage bacteria to acquire resistance. In an effort to remedy this deficiency, there is a severe lack of effective interventions and preventative measures. This led several research teams worldwide to create novel medications and substitute antibacterial agents. We concentrated on the growth of molecules by combining various active pharmacophores, such as pyrazole, pyrazoline, and pyridine, into a single common structure in order to find the structure with exceptional biological activity. Numerous biological actions are shown by these tiny particles. Pyrazole substances have interesting biological activities, including **antiviral, antitubercular, antimicrobial, anti-consultant, even anticancer activities.** Drugs that contain pyrazoline and pyridine are crucial to pharmaceutical chemistry and have a number of therapeutic benefits. As seen in Fig. (3), Perampanel, Epirizole, and Edaravone showed distinct biological activities.[16]

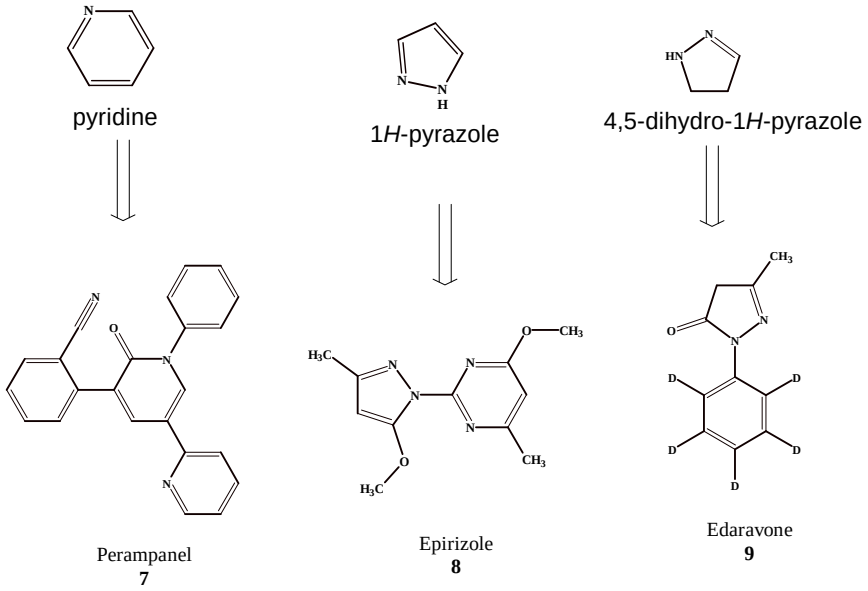
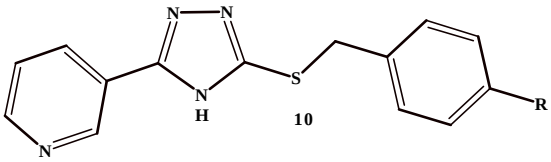


***Figure* 3: Marketed available drugs of Parampanel, Epirizole and Edaravone.[16]**

2. REVIEW OF LITERATURE

- Ahirwar J., *et al.* (2018). reported by Synthesis, Characterization, Molecular Modeling, and Biological Evaluation of 1,2,4-Triazole-pyridine Hybrids as Potential Antimicrobial Agents. Journal of Heterocyclic Chemistry.[1]

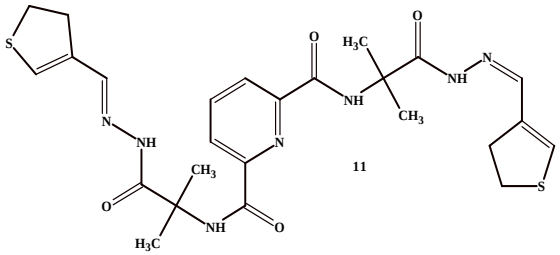


As methotrexate and fluconazole are used as reference drugs, the cup plate is used. In addition, **compounds 3g** and **3h** shown potent antibacterial properties over Acinebactoer baumanni and Staphylococcus aureus, whereas **compounds 3h** and **3i** demonstrated good antibacterial activity against E. coli and gram-negative bacteria. Out of all the compounds produced in this work utilizing a procedure with adjusting reagents, compounds **3c** exhibited a good binding affinity (-11.83) with bond lengths of 2.825 and 2.467, according to docking in the Argus lab investigation.

- Al-Omar MA., *et al.* (2010). reported by Synthesis of some new pyridine-2,6-carboxamide-derived schiff bases as potential antimicrobial agents. Molecules.[2]

Starting from 2,6-pyridinedicarbonyl dichloride (1) and L-alanine or 2-methylalanine methyl ester, a series of pyridine-bridged 2,6-bis-carboxamide Schiff's bases was constructed. The newly discovered compounds' structural assignments have been confirmed by spectroscopic and chemical data. The bactericidal and fungicidal effects of the newly synthesized compounds 2–5 have been assessed, and the Schiff's bases **4b–f** and **5b–f** exhibit notable antimicrobial properties in relation to streptomycin and fusidic acid, which were used as reference drugs for antifungal and antibacterial

properties, respectively. Two thienyl-derivatives, 4-chloro-4d, **5d**, 3-4,5-trimethoxy-**4c**, **5c**, 2-chloro-6-flouro-**4e**, **5e**, and substituted 4-methoxy-**4b**, **5b** When compared with **4a,5a,** which contain an unsubstituted phenyl group, 4f,5f have stronger antimicrobial effects.

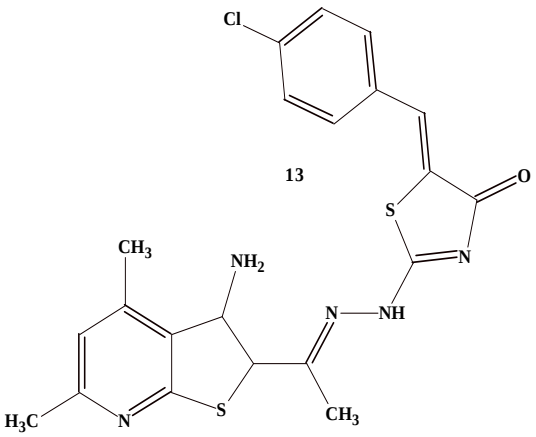


11

- Al-Salahi RA., *et al.* (2010) reported by Synthesis of chiral macrocyclic or linear pyridine carboxamides from pyridine-2,6-dicarbonyl dichloride as antimicrobial agents. Molecules.[3] We may conclude that pyridine and amide moieties are crucial based on the presented comprehensive synthesis, spectroscopic data, and antimicrobial screening for the obtained compounds for antibacterial benefits. We may infer from present findings that the antibacterial activity results from: The existence of heterocyclic rings of nitrogen. In general, the activity is increased by the presence of the amide linkage groups. The stated substances in the molecule's used reagents are the cause of any differences in activity between the compounds. The antibacterial capabilities of compounds 5, 6, 7, 9, 10, and 11 are higher compared to that of the other produced compounds.

- Alenazi NA., *et al.*(2023). reported by New thieno[2,3-b]pyridine-based compounds: Synthesis, molecular modelling, antibacterial and antifungal activities. Arabian Journal of Chemistry.[4]

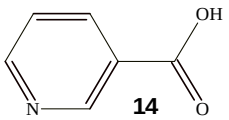
Strong antibacterial activity was demonstrated by compounds 8–10 against Gram-positive S. aureus, Gram-negative E. coli bacteria, and C. albicans (antifungal).



13

- Ali Altaf A., *et al.* (2015). reported by Review on the Medicinal Importance of Pyridine Derivatives. Journal of Drug Design and Medicinal Chemistry [Internet].[5]

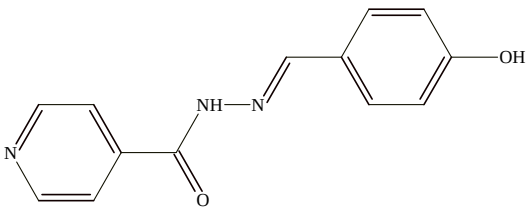
Many substances have clinical use, and pyridine derivatives have been shown to exhibit a range of biological functions. Additionally, pyridine derivatives become more and more significant in current medical applications.



14

- Amr AGE., *et al.* (2006). reported by Anticancer activities of some newly synthesized pyridine, pyrane, and pyrimidine derivatives. Bioorganic and Medicinal Chemistry.[6]

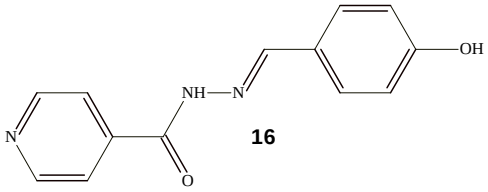
59 different human tumor cell lines—representing leukemia, melanoma, lung, colon, brain, ovary, breast, prostate, and the kidney—were used to evaluate the therapeutic properties of the synthesized compounds. Especially 2, 3, 4c, 6, 7, 9b, 10a, and 11, some of the compounds that were looked at had better in in vitro anticancer effects at low doses.



15

- Bekhit A., *et al.* (2012). reported by 70 A.[7]

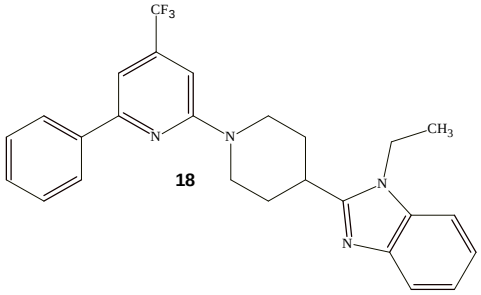
Compounds 2a, 2g, and 2h showed 90, 91, and 80% prevention of the parasite growth at the therapy level of 50 µmol/kg, respectively. likewise, compounds 2a, 2g, and 2h showed promising effects with an IC50 of 0.0402 µM were evaluated in vitro against strains of Plasmodium falciparum RKL9 which were resistant with CQ. At 300 and 100 mg/kg, respectively, the compounds were non-toxic were administered orally and via ingestion. Docking the most active chemicals (2a, 2g, and 2h) in the active region of the dihydrofolate reductase enzyme revealed a number of hydrogen and hydrophobic bonds that support the observed anti-malarial activities.



16

- Bekhit AA., *et al.* (2004). reported by Design, synthesis and biological evaluation of some pyrazole derivatives as anti-inflammatory-antimicrobial agents. Bioorganic and Medicinal Chemistry.[8]

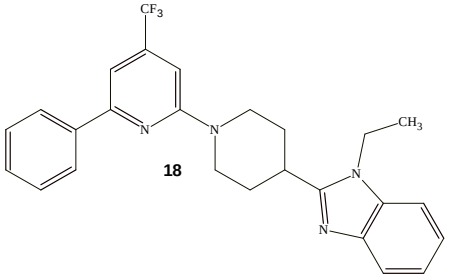
Because of their strong antibacterial properties similar to ampicillin against Gram-positive bacteria and their remarkable anti-inflammatory efficacy both in vivo and in vitro, compounds 4 and 12a are the most remarkable derivatives identified in the present study. Yet, compound 12a exhibited strong selective inhibition of the COX-2 enzyme. Therefore, the substance could act as a beneficial matrix for the creation of anti-inflammatory and antimicrobial candidates.



18

- Beulah K., *et al.* (2023). reported by Design, Synthesis and Biological Evaluation of Benzimidazole-pyridine-Piperidine Hybrids as a New Class of Potent Antimicrobial Agents.[9]

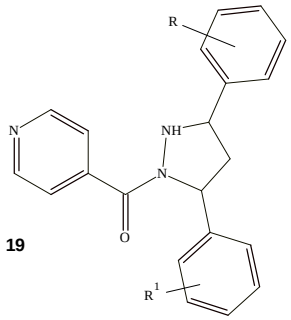
Compounds 4a-h and 5a-c were evaluated for their in vitro antibacterial activity against gram-positive (Bacillus subtilis, Staphylococcus aureus, and Staphylococcus epidermidis) and gram-negative (Escherichia coli, Pseudomonas aeruginosa, and Klebsiella pneumonia) organisms and fungal (Candida albicans, Saccharomyces cervisiae of yeasts, Aspergillus flavus, and Aspergillus niger) strains were evaluated according to with the CLSI Standard Protocol. Compound 5a was favorable advantages against all tested bacteria, with the exception of Bacillus subtilis, as opposed with currently available medications.



18

- Bhirud JD., *et al.* (2020). reported by Sulfamic acid catalyzed synthesis of new 3,5-[(sub)phenyl]-1H-pyrazole bearing N1-isonicotinoyl: And their pharmacological activity evaluation. Bioorganic and Medicinal Chemistry Letters.[10]

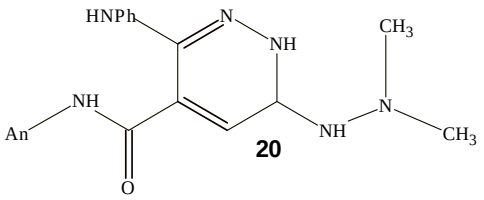
While antibacterial screening of compounds bringing 3e, 3k, and 3j found major inhibition (27 mm) against Staphylococcus aureus, in vitro anti-mycobacterial activity of compounds bearing 3e and 3k showed total inactivation (99%) at the MIC of 31 and 34 µM, respectively.



19

- Bondock S., *et al.* (2008). reported by Synthesis and antimicrobial activity of some new heterocycles incorporating antipyrine moiety. European Journal of Medicinal Chemistry.[11]

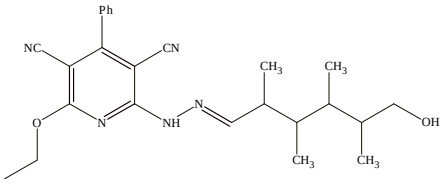
According to the antibacterial activity results, compounds 2, 13, and 14 showed beneficial effects. However, most of the produced compounds 2, 10, and 14 displayed oddly potent antifungal activity in contrast to the reference chemotherapeutics.



20

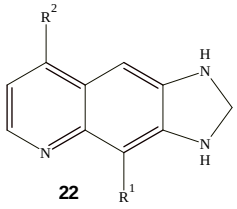
- Campanati M., *et al.* (2000). reported by Environment-friendly synthesis of nitrogen-containing heterocyclic compounds.[12]

The vapour phase synthesis of quinolines or alkylquinolines can be performed using solid acid catalysts such as acid-treated clays or zeolites. The hypothesized chemical route uses solid acid catalysts to create 2-methyl-8-ethylquinoline (MEQUI).



- Carta A., *et al.* reported by Quinoline tricyclic derivatives. Design, synthesis and evaluation of the antiviral activity of three new classes of RNA-dependent RNA polymerase inhibitors. Bioorganic and Medicinal Chemistry.[13]

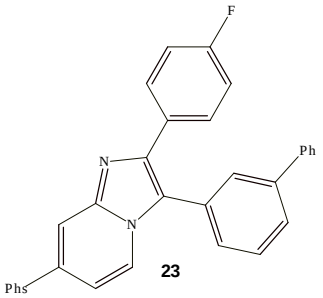
In the present study, the quinoline nucleus fused with 1,2,3-triazole with imidazole generated three novel families of linear N-tricyclic molecule. The cytotoxicity and antiviral activity of title compounds have been tested in cell-based assays against RNA viruses that are representative of the three genera of the Flaviviridae family: BVDV (pest virus), YFV (flavivirus), and HCV (hepacivirus). The imidazoquinolines 2e and 2h, the pyridoquinoxalines 4h, 4j, and 5n (EC50 range 1–5 lM), and the bis-triazoloquinoline 1m were among the most efficient. Compound 2h was the first derivative to exhibit anti-HCV activity in a replicon assay (EC50 = 3.1 lM). In enzyme tests, the BVDV RNA-dependent RNA polymerase (RdRp) were severely inhibited by 1m, 2h, 5m, and 5n, while only 2h also inhibited the recombinant HCV enzyme.



22

- De A., *et al.* (2021). reported by Recent advances on heterocyclic compounds with antiviral properties. Chemistry of Heterocyclic Compounds.[14]

Because of the wide variety of physiological effects, heterocyclic compounds are becoming more and more crucial in medicinal chemistry. Derivatives of indole, imidazole, thiazole, pyridine, and quinaxoline are the most promising among heterocycles of N and S. The antiviral effects of these heterocyclic compounds are noted in this review.

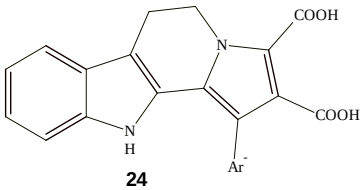


23

- Depa N., *et al.* (2022). reported by Synthesis and biological active compounds of nitrogen-containing heterocyclic compounds: a review. Rasayan Journal of Chemistry.[15]

Many heterocyclic substances containing nitrogen as a heteroatom have significant biological properties and significant applications in medicine.

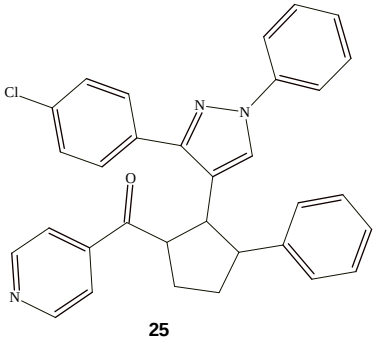
This review article focuses on novel moieties of indole, pyrazole, and triazole compounds and their medical value. Nitrogen-containing heterocyclic compounds are regarded as an important category given their wide range of therapeutic applications, like antibacterial, antimalarial, anticancer, antifungal, anti-HIV, and anti-inflammatory properties.



24

- Desai NC., *et al.* (2019). reported by Synthesis, Biological Evaluation and Molecular Docking Study of Pyrazole, Pyrazoline Clubbed Pyridine as Potential Antimicrobial Agents. Anti-Infective Agents.[16]

We report the synthesis of several pyrazole, pyrazoline, and pyridine-based novel bioactive heterocycles (3a-t) as a part of our ongoing look for new antimicrobials. A review of newly synthesized compounds' antibacterial properties was conducted. The antibacterial effect of pounds 3c, 3h, 3i, 3k, 3n, and 3q was noteworthy.



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- Ebenezer O., *et al.* (2022). reported by An Overview of the Biological Evaluation of Selected Nitrogen-Containing Heterocycle Medicinal Chemistry Compounds. Vol. 23, International Journal of Molecular Sciences.[17]

Since heterocyclic compounds are a class of chemicals that occur naturally with useful properties, they provide significant advantages for health. They also have major medical importance. This review discusses recent new research on the biological study of nitrogen-containing compounds, including pyrimidines, quinolines, imidazole/benzimidazoles, triazoles, and tetrazoles. It focuses at papers published from April 2020 to February 2022 and will be useful to researchers in medicinal chemistry and pharmacology. The structure of the current work is determined by the size of the heterocyclic ring.

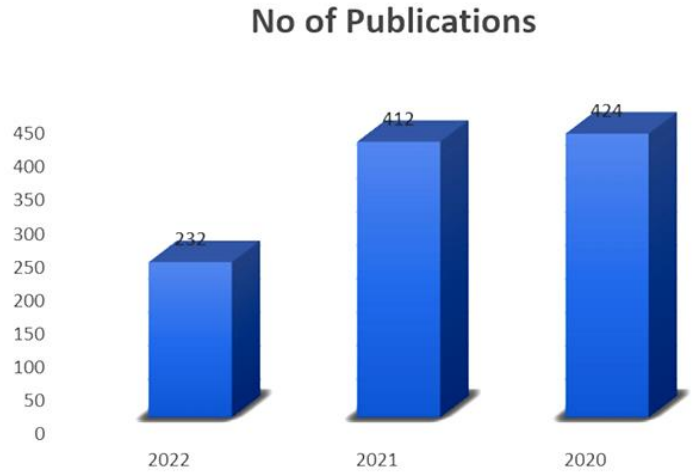
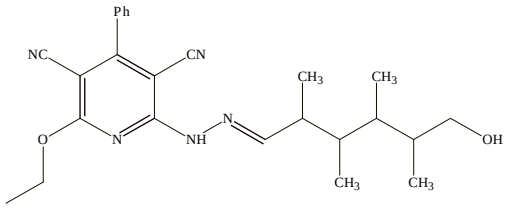


Fig.1: **The number of publications with the term"nitrogen-containing compounds" in the titles is based on the calendar year of publishing (July 1068 articles).**

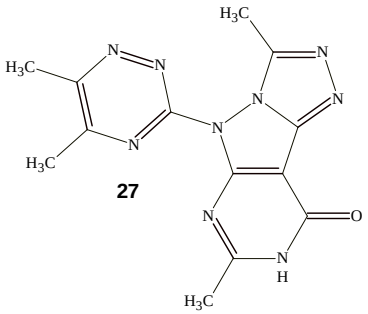
- El-Sayed HA., *et al.* (2017). reported by A series of pyridines and pyridine based sulfa-drugs as antimicrobial agents: Design, synthesis and antimicrobial activity. Russian Journal of General Chemistry.[18]

The antibacterial abilities of a variety of pyridines and their sulfa drug derivatives are discussed here. High activity was demonstrated by compounds 8–11 and 17–19 in the antimicrobial testing of the freshly produced compounds.



- El-Sayed Ali T., *et al.* (2009). reported by Synthesis of some novel pyrazolo[3,4-b]pyridine and pyrazolo[3,4-d]pyrimidine derivatives bearing 5,6-diphenyl-1,2,4-triazine moiety as potential antimicrobial agents. European Journal of Medicinal Chemistry.[19]

Each substance has undergone evaluation for antifungal and antibacterial properties. The highest activity of compounds 9, 10, 13, 19, and 21 were equal to that of the standard drugs, with compounds 9 and 10 showing lower toxicity.



27

- Elsayed MA., *et al.* (2024). reported by Novel biologically active pyridine derivatives: Synthesis, structure characterization, in vitro antimicrobial evaluation and structure-activity relationship. Medicinal Chemistry Research.[20]

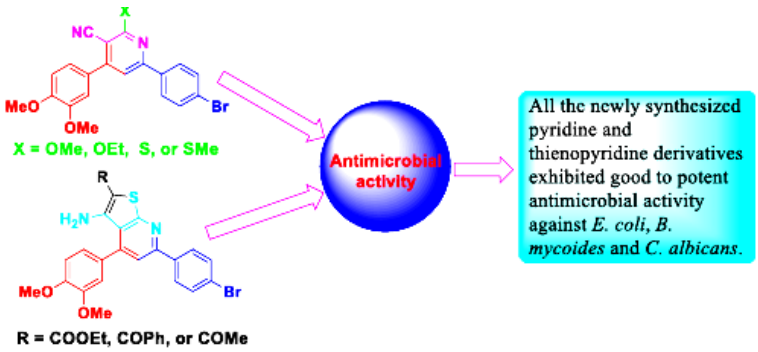


Fig. 2: Nitrogen containing derivatives compounds with potential antimiocrobial activity.

3. SYNTHETIC SCHEME

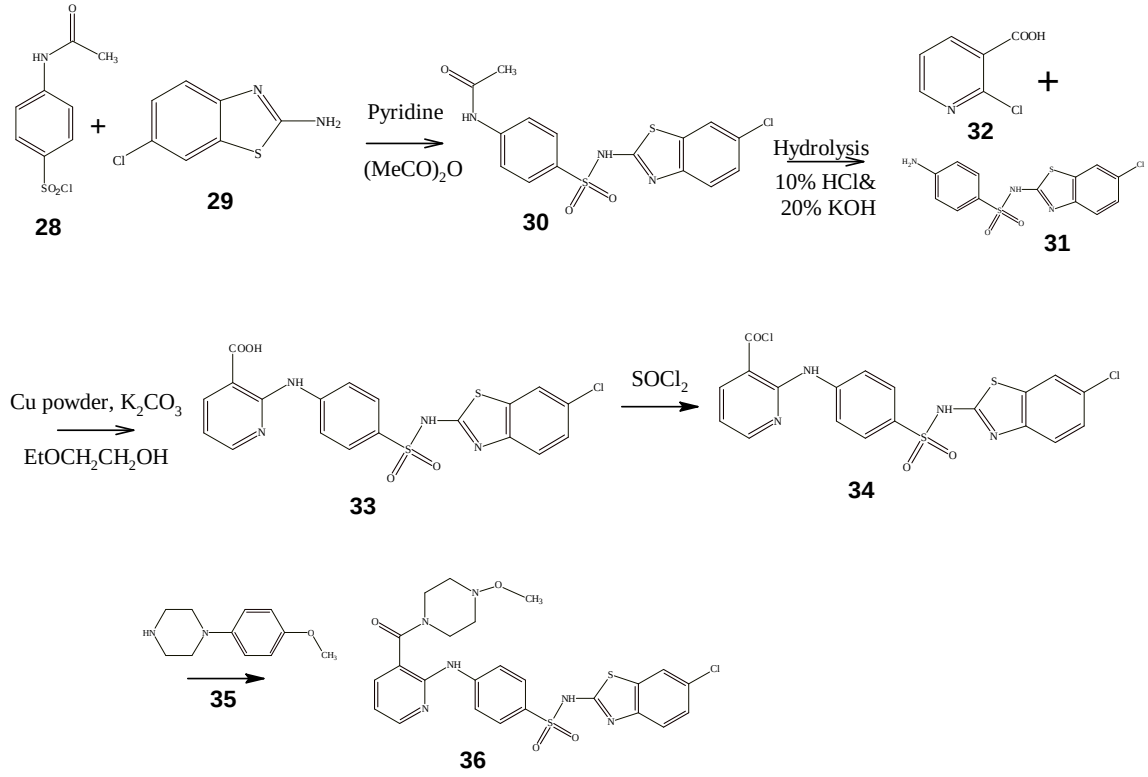


Fig. 3: **Synthetic scheme of pyridine nitrogen containing heterocyclic derivativesPhysiochemical properties of compounds 28, 30, 31, 32, 33, 34, 35 and 36.**

Table No. 1: Physiochemical properties of compounds 28,29,30 and 31.

Sl.No	Parameter	Compounds			
		28	**29**	**30**	**31**
1.	Molecular Formula	**C8H8ClNO3S**	**C7H5ClN2S**	**C15H12ClN3O3S2**	**C13H10ClN3O2S2**
2.	Molecular Weight	233.67202	184.646	381.85708	339.8204
3.	Composition (Elemental Percentage)	C(41.12%) H(3.45%) Cl(15.17%) N(5.99%) O(20.54%) S(13.72%)	C(45.53%) H(2.73%) Cl(19.20%) N(15.17%) S(17.37%)	C(47.18%) H(3.17%) Cl(9.28%) N(11.00%) O(12.57%) S(16.79%)	C(45.95%) H(2.97%) Cl(10.43%) N(12.37%) O(9.42%) S(18.87%)
4.	Molar Refractivity	53.42 ± 0.4 cm3	49.70 ± 0.3 cm3	95.27 ± 0.4 cm3	85.87 ± 0.4 cm3
5.	Molar Mass	159.1 ± 3.0 cm3	120.4 ± 3.0 cm3	240.4 ± 3.0 cm3	209.6 ± 3.0 cm3
6.	Surface Tension	55.2 ± 3.0 dyne/cm	71.3 ± 3.0 dyne/cm	80.2 ± 3.0 dyne/cm	84.6 ± 3.0 dyne/cm
7.	Density	1.468 ± 0.06 g/cm3	1.532 ± 0.06 g/cm3	1.588 ± 0.06 g/cm3	1.621 ± 0.06 g/cm3
8.	Average Mass	233.672 Da	184.646 Da	381.8571 Da	339.8204 Da
9.	M+:	232.990792 Da	183.985647 Da	381.00031 Da	338.989746 Da
10.	M-:	232.991889 Da	183.986744 Da	381.001408 Da	338.990843 Da

Table No. 2 Physiochemical properties of compounds 32,33,34,35 & 36.

Sl.No	Parameter	Compounds				
		32	33	34	35	36
1.	Molecular Formula	C6H4ClNO2	C19H13ClN4O4S2	C19H12Cl2N4O3S2	C11H16N2O	C24H23ClN6O4S2
2.	Molecular Weight	157.55446	460.91392	479.35958	192.25754	559.06022
3.	Composition (Elemental Percentage)	C(45.74%) H(2.56%) Cl(22.50%) N(8.89%) O(20.31%)	C(49.51%) H(2.84%) Cl(7.69%) N(12.16%) O(13.88%) S(13.91%)	C(47.61%) H(2.52%) Cl(14.79%) N(11.69%) O(10.01%) S(13.38%)	C(68.72%) H(8.39%) N(14.57%) O(8.32%)	C(51.56%) H(4.15%) Cl(6.34%) N(15.03%) O(11.45%) S(11.47%)
4.	Molar Refractivity	36.16 ± 0.3 cm3	114.68 ± 0.4 cm3	117.98 ± 0.4 cm3	56.48 ± 0.3 cm3	143.77 ± 0.4 cm3
5.	Molar Mass	107.1 ± 3.0 cm3	279.1 ± 3.0 cm3	292.9 ± 3.0 cm3	181.7 ± 3.0 cm3	357.2 ± 5.0 cm3
6.	Surface Tension	61.0 ± 3.0 dyne/cm	91.8 ± 3.0 dyne/cm	83.6 ± 3.0 dyne/cm	36.7 ± 3.0 dyne/cm	86.9 ± 5.0 dyne/cm
7.	Density	1.470 ± 0.06 g/cm3	1.651 ± 0.06 g/cm3	1.636 ± 0.06 g/cm3	1.057 ± 0.06 g/cm3	1.56 ± 0.1 g/cm3
8.	Average Mass	157.5545 Da	460.9139 Da	479.3596 Da	192.2575 Da	559.0602 Da
9.	M+:	156.992507 Da	460.006124 Da	477.972237 Da	192.125715 Da	558.090522 Da
10.	M-:	156.993605 Da	460.007221 Da	477.973334 Da	192.126812 Da	558.09162 Da

Computational software tools are frequently employed in modern drug research to predict the pharmacokinetic (PK) properties and toxicity profiles of substances. These in imitation techniques greatly cut down on the expense and time involved in experimental assessments, allow for quick screening of chemical libraries, and contribute to identifying any ADMET-related problems.

Table No. 3: Computational properties of compounds 37.

Compounds 36		
Descriptor	**Value**	**Significance**
Molecular Weight (MW)	381.866 g/mol	Indicates the total mass of the molecule. According to Lipinski's Rule of Five, drug-like molecules typically have an MW < 500 g/mol. Your compound (381.866 g/mol) is within the optimal range, suggesting good oral bioavailability.
LogP	3.709	Represents the lipophilicity of the compound, i.e., how soluble it is in fats vs. water. An ideal range for drug-like compounds is 0–5. Here, a value of 3.709 suggests moderate lipophilicity, which is favorable for absorption and membrane permeability.
#Rotatable Bonds	5	Measures the molecule's flexibility. Fewer rotatable bonds (<10) generally enhance oral bioavailability and metabolic stability. A value of 5 is ideal.
#Acceptors	6	Number of hydrogen bond acceptor atoms (like oxygen, nitrogen). Lipinski recommends ≤10 for good permeability. Your compound has 6, which is well within the limit.
#Donors	2	Number of hydrogen bond donor atoms (typically –OH and –NH groups). Lipinski suggests ≤5; a value of 2 is optimal for drug-like behavior.
Surface Area	88.16 Å²	Refers to the topological polar surface area (TPSA), important for absorption and blood-brain barrier (BBB) penetration. Compounds with TPSA < 140 Å² usually have better oral bioavailability. With 88.16 Å², your compound is suitable for oral administration.

4. COMPUTATIONAL ANALYSIS OF ABSORPTION, DISTRIBUTION, METABOLISM AND TOXICITY OF DRUGS PARAMETER

4.1 Computational Analysis of Absorption Parameter

Table No. 4: Computational properties of compounds 37.

COMPOUNDS 36				
Parameter	**Prediction**	**Probability**	**Interpretation**	**Significance**
Caco-2 Permeability (logPaap)	-4.48	—	Value indicates low-to-moderate permeability	Caco-2 cell monolayer simulates intestinal absorption. A more positive value means higher absorption; here, absorption may be moderate.
Human Oral Bioavailability ≥ 20%	Bioavailable	0.816	Medium confidence	Indicates the compound has a good chance (>20%) to be absorbed and reach systemic circulation.
Human Oral Bioavailability ≥ 50%	Bioavailable	0.897	High confidence	Suggests excellent oral availability potential.
Human Intestinal Absorption (HIA)	Absorbed	0.975	High confidence	High absorption probability, indicating strong intestinal uptake.
Madin-Darby Canine Kidney (MDCK) Permeability	-4.57	—	Proper value > 2 × 10^{-6} cm/s	Suggests limited permeability in kidney cells; however, this is less critical for oral drug candidates compared to Caco-2 data.
P-glycoprotein (P-gp) Inhibitor	Non-inhibitor	0.001	High confidence	P-gp pumps drugs out of cells; non-inhibition is favorable since it avoids drug-drug interactions.
P-glycoprotein (P-gp) Substrate	Non-substrate	0.065	High confidence	Non-substrate status improves bioavailability since the compound is not effluxed.
Skin Permeability (logKP)	-3.19	—	Low permeability	Indicates poor transdermal absorption, meaning the compound is better suited for oral administration.

According to in silico absorption predictions, the molecule has favorable pharmacokinetic features. Effective absorption through the gastrointestinal tract is suggested by the oral bioavailability (>50%) and human intestinal absorption probability (0.975) with high confidence. Since the substance is neither a P-glycoprotein substrate nor an inhibitor, there is less chance of efflux-related problems with absorption and a lesser chance of drug-drug interactions. The overall oral bioavailability profile is still encouraging even though the Caco-2 permeability value (-4.48) indicates modest passive absorption. Moreover, the compound's limited skin permeability (logKP = -3.19) indicates that oral formulations are a better option than transdermal administration.

The molecule is a good candidate for preclinical testing and additional pharmacokinetic optimization because of these characteristics.

6.2 Computational Analysis of Metaboliosm Parameter

Target	**Prediction**	**Confidence / Probability**	**Risk**
BCRP (Breast Cancer Resistance Protein)	Inhibitor	High (0.977)	High
CYP1A2	Non-Inhibitor / Non-Substrate	High (0.037 / 0.15)	Low
CYP2C19	Inhibitor	High (0.973)	High
CYP2C19	Non-Substrate	Low (0.467)	Low
CYP2C9	Inhibitor	—	High
CYP3A4	Substrate	Medium	Medium
OATP1B1	Non-Inhibitor	Low (0.367)	Low
OATP1B3	Non-Inhibitor	High (0.128)	Low

There is a significant chance that the chemical will interact with CYP2C19, CYP2C9, and BCRP. As a CYP3A4 substrate, it carries a medium risk, suggesting potential interactions linked to metabolism. OATP1B1, CYP1A2, and OATP1B3 exhibit low risk, indicating little impact on these pathways. All things considered, the molecule may mainly result in drug-drug interactions via inhibiting CYP and blocking BCRP.

Table No. 5: Computational properties of compounds 37.

Target	Prediction	Probability / Confidence	Interpretation / Risk
Clearance	-0.03	None	Not applicable
Organic Cation Transporter 2 (OCT2)	Non-Inhibitor	0.045 (High)	Low
Half-Life of Drug	< 3 hours	0.285 (Medium)	Short half-life

There is little chance of transporter-related excretion problems because the compound is unlikely to block OCT2. Its brief half-life (less than three hours) suggests that it might be eliminated rapidly, which could have an impact on how frequently you take it. Overall, the excretion profile seems to be low risk of contact and safe.

6.3 Full Toxicity Prediction Table

Table No. 6: Computational properties of compounds 37.

Endpoint	Prediction	Probability	Interpretation
AMES Mutagenesis	Safe	0.0	Safe (High Confidence)[1]
Avian	Safe	0.067	Safe (High Confidence)[1]
Bee	Safe	0.218	Safe (Medium Confidence)[1]
Bioconcentration Factor	0.98	nan	Safe[1]
Biodegradation	Safe	0.0	Safe (High Confidence)[1]
Carcinogenesis	Safe	0.071	Safe (High Confidence)[1]
Crustacean	Safe	0.338	Safe (Low Confidence)[1]
Liver Injury I (DILI)	Toxic	0.733	Toxic (Medium Confidence)[1]
Eye Corrosion	Safe	0.0	Safe (High Confidence)[1]
Eye irritation	Safe	0.005	Safe (High Confidence)[1]
Maximum Tolerated Dose	Toxic	0.888	MTRD > 0.477: High[1]
Liver Injury II	Safe	0.022	Toxic (High Confidence)[1]
hERG Blockers	Safe	4.73	Safe (High Confidence)[1]
Micronucleos	Toxic	0.997	Toxic (High Confidence)[1]
NR-AhR	Safe	0.273	Safe (Medium Confidence)[1]
NR-AR	Safe	0.097	Safe (High Confidence)[1]
NR-AR-LBD	Safe	0.023	Safe (High Confidence)[1]
NR-Aromatase	Safe	0.0	Safe (High Confidence)[1]
NR-ER	Safe	0.072	Safe (High Confidence)[1]
NR-ER-LBD	Safe	0.0	Safe (High Confidence)[1]
NR-GR	Safe	0.136	Safe (High Confidence)[1]
NR-PPAR-gamma	Safe	0.038	Safe (High Confidence)[1]
NR-TR	Safe	0.004	Safe (High Confidence)[1]
T. Pyriformis	1.27	-	PIGC50% > -0.5 log ug/L: toxic[1]
Fathead Minnow	5.13	-	LC50% < 0.5mM: High Acute Toxicity[1]
Respiratory Disease	Toxic	0.987	Toxic (High Confidence)[1]
Skin Sensitisation	Safe	0.356	Safe (Low Confidence)[1]
SR-ARE	Toxic	0.696	Toxic (Medium Confidence)[1]
SR-ATAD5	Safe	0.0	Safe (High Confidence)[1]
SR-HSE	Safe	0.016	Safe (High Confidence)[1]
SR-MMP	Safe	0.398	Safe (Low Confidence)[1]
SR-p53	Safe	0.008	Safe (High Confidence)[1]

This compound is marked **safe** in many environmental and genetic endpoints (mutagenesis, hERG, NR-x nuclear receptors, avian/bee toxicity). However, there is a notable **toxic** classification for endpoints related to liver injury, micronucleus formation, respiratory disease, acute aquatic toxicity, and some stress response markers. These results strongly recommend further in vivo and clinical safety studies, particularly considering the adverse predictions in human-relevant organs and environmental toxicity endpoints

DISCUSSION

- Start by briefly summarizing key findings of the research.
- Interpret these findings by explaining their meaning and significance.
- Relate findings to existing literature to show how they fit or contrast with prior work.
- Discuss the practical or theoretical implications of the results.
- Acknowledge limitations of the study without undermining its value.

- Suggest specific avenues for future research based on findings and limitations.

CONCLUSION

- Provide a concise summary answering the main research question.
- Highlight the overall significance and contribution of the work.
- Include any overarching recommendations or final insights.
- Keep it brief and focused, distinct from the detailed discussion.

ACKNOWLEDGEMENT

- Thank those who provided intellectual, technical, or financial support.
- Mention advisors, collaborators, funding bodies, institutions, or anyone with a key role.
- Keep it formal, concise, and sincere.

REFERENCE

1. Ahirwar J, Ahirwar D, Lanjhiyana S, Jha AK, Dewangan D, Badwaik H. Journal of Heterocyclic Chemistry, Nov. 1, 2018; 55(11): 2598–609.
2. Al-Omar MA, Amr AEGE. Molecules, Jul. 2010; 15(7): 4711–21.
3. Al-Salahi RA, Al-Omar MA, Amr AEGE. Molecules, Sep. 2010; 15(9): 6588–97.
4. Alenazi NA, Alharbi H, Fawzi Qarah A, Alsoliemy A, Abualnaja MM, Karkashan A, Arabian Journal of Chemistry, Nov. 1, 2023; 16(11).
5. Ali Altaf A, Shahzad A, Gul Z, Rasool N, Badshah A, Lal B, Journal of Drug Design and Medicinal Chemistry [Internet]. 2015; 1(1): 1–11. Available from: http://www.sciencepublishinggroup.com/j/jddmc
6. Amr AGE, Mohamed AM, Mohamed SF, Abdel-Hafez NA, Hammam AEFG. Bioorganic and Medicinal Chemistry, Aug. 15, 2006; 14(16): 5481–8.
7. Bekhit A. 70 A., 2012.
8. Bekhit AA, Abdel-Aziem TBioorganic and Medicinal Chemistry, Apr.15, 2004; 12(8): 1935–45.
9. Beulah K, Kumar AR, Peda B, Lingaiah V, Rao S, Narsaiah B.
10. Bhirud JD, Patil RD, Narkhede HP Bioorganic and Medicinal Chemistry Letters, Dec. 1, 2020; 30(23).
11. Bondock S, Rabie R, Etman HA, Fadda AA. European Journal of Medicinal Chemistry, Oct. 2008; 43(10): 2122–9.
12. Campanati M, Vaccari A, Piccolo O. Environment-friendly synthesis of nitrogen-containing heterocyclic compounds. Vol. 60, Catalysis Today, 2000.
13. Carta A, Briguglio I, Piras S, Corona P, Boatto G, Nieddu M, Bioorganic and Medicinal Chemistry, Dec. 1, 2011; 19(23): 7070–84.
14. De A, Sarkar S, Majee A. Chemistry of Heterocyclic Compounds, Apr. 1, 2021; 57(4): 410–6.
15. Depa N, Erothu H. Rasayan Journal of Chemistry, Jul. 1, 2022; 15(3): 1709–17.
16. Desai NC, Vaja D v., Jadeja KA, Joshi SB, Khedkar VM., Jun. 27, 2019; 18(3): 306–14.
17. Ebenezer O, Jordaan MA, Carena G, Bono T, Shapi M, Tuszynski JA. Vol. 23, International Journal of Molecular Sciences. MDPI, 2022.
18. El-Sayed HA, Moustafa AH, El-Torky AE, Abd El-Salam EA. Russian Journal of General Chemistry, Oct. 1, 2017; 87(10): 2401–8.
19. El-Sayed Ali T. European Journal of Medicinal Chemistry, Nov. 2009; 44(11): 4385–92.
20. Elsayed MA, Elsayed AM, Sroor FM. Medicinal Chemistry Research, Mar. 1, 2024; 33(3): 476–91.
21. Patel NB, Agravat SN, Chemistry of Heterocyclic Compounds, 2009; 45.