RECENT ADVANCES IN NITROGEN-CONTAINING HETEROCYCLIC COMPOUNDS AND THEIR BIOLOGICAL SIGNIFICANCE

Abstract

Most scientific disciplines, including medicinal chemistry and biochemistry, involve the use of heterocyclic compounds. Heterocyclic compounds bridge the interface between chemistry and biology, where so much new scientific understanding, discovery, and application are occurring, and more than 90% of innovative drugs contain heterocycles. They owe their significance to the distinctiveness of the Skelton components that make up their structural makeup. They are naturally present in things like vitamins, antibiotics, hormones, and nucleic acids. compounds made from heterocyclic rings used in the domains of pharmacy, medicine, agriculture, plastic, and polymers. One notable class of heterocyclic compounds that has made a substantial contribution to medicinal chemistry is those that contain nitrogen. The quantity and positioning of nitrogen atoms determine the sorts of molecules.

In medicinal chemistry, the analogues of nitrogen-based heterocycles hold a unique place as a valuable source of therapeutic medicines. Drugs that have been FDA-approved and are currently on the market more than 75% of the time contain heterocyclic nitrogen molecules.

A significantly higher proportion of new medications with nitrogen as an ingredient is projected in the upcoming decade. We have compiled the most recent findings on new nitrogen-containing heterocycles and their various biological functions during the last year in this review. The utilization of nitrogen-based moieties in drug design and the creation of several

Authors

Popat Mohite
Aldel Education Trusts
St. John Institute of Pharmacy and Research, Palghar, Maharashtra, India
mohitepb@gmail.com

Chetan Kedari
Mula Education Society's College of Pharmacy, Sonai Tal-Newasa Ahmednagar, Newasa, Maharashtra, India
chetnsk@gmail.com

Ramdas Pandhare
Mula Education Society's College of Pharmacy, Sonai Tal-Newasa Ahmednagar, Newasa, Maharashtra, India
ramdaspandhare@gmail.com

Sagar Pardeshi
Aldel Education Trusts
St. John Institute of Pharmacy and Research, Palghar, Maharashtra, India
sagarpardeshi201@gmail.com

Nitin Bhoge
Mula Education Society's
Shri Dnyaneshwar Mahavidyalaya
Newasa, Ahmednagar, Maharashtra, India
nitinbhoge4550@gmail.com

competent and potent candidates against diverse diseases are themes that are highlighted in this review.

Keywords: Heterocycles, Nitrogen containing compounds biological activity, Triazole, Pyrazole etc.

I. INTRODUCTION

The creation of novel compounds and composites is a major focus of research in nitrogen-based heterocyclic chemistry, which is a significant and distinctive class among the applied areas of organic chemistry. Over the past two decades, these compounds have attracted more and more interest. They helped create many different organic synthesis procedures and were widely used in the chemical sciences. A cyclic compound with components of its ring or rings that are at least two different types of fundamental atoms is known as a heterocyclic compound or ring structure (1). The area of organic chemistry known as "heterocyclic chemistry" is concerned with the production, characteristics, and uses of these heterocycles (2). Examples of heterocyclic compounds include all of the nucleic acids, the vast majority of pharmaceuticals, the majority of biomass (cellulose and associated components), and other chemicals. Heterocycles account for more than half of all known chemicals. (3). Nitrogen heterocycles are included in 59% of medications approved by the US FDA (4)

II. CLASSIFICATIONS OF HETEROCYCLIC COMPOUNDS

The investigation of heterocyclic science centers particularly around unsaturated subordinates, and the lion's share of work and applications includes 5- and 6-membered rings represent the majority of applications and research in heterocyclic science, which is focused primarily on unsaturated subordinates. Pyridine, thiophene, pyrrole, and furan are among them. The reference to those entangled with benzene rings refers to yet another huge family of heterocycles. For instance, quinoline, benzothiophene, indole, and benzofuran are the individual combined benzene subordinates of pyridine, thiophene, pyrrole, and furan. Two benzene rings together create a third sizable group of compounds.

For this third group of mixes, acridine, dibenzothiophene, carbazole, and dibenzofuran, individually, are analogues of the recently mentioned heterocycles. The chemical structure of heterocyclic compounds can be used to organise them in a useful way. Heterocycles that have been soaked in solvent behave like noncyclic subsidiaries. Tetrahydrofuran and piperidine are thus normal amines and ethers with modified steric profiles. As a result, unsaturated rings are the focus of heterocyclic science research.

III. RATIONAL AND SIGNIFICANCE OF STUDY

1. Drug revelation and advancement is a cycle intends to plan protected and powerful meds to work on life's quality and to diminish enduring to least. Nonetheless, the interaction is exceptionally mind boggling, tedious, and asset concentrated, requiring multi-disciplinary skill and inventive methodologies (5).

2. Technology in medication and medical care has quickly changed throughout the last many years. Biomedical Engineering improvement has a fundamental rule in tackling clinical issues

3. Compared to traditional approaches of medication revelation, rational medication planning tactics save the time and money needed in the drug planning process. Studies on QSAR and QSPR can be used to develop new inhibitors and identify them, as well as to

advance the ingestion, appropriation, digestion, discharge, and hazard profile of known particles from various sources. The use of in silico strategies in the planning system has been facilitated by advancements in computational methods and hardware. Structure based drug design (SBDD) and ligand based drug design (LBDD) are two groups into which drug configuration can be divided (12). SBDD is a mechanism that uses the main medication information to support the drug's inhibitor. While LBDD relies on particles tied to the organic aim and is used without any evidence of the receptors 3D data. (6-11).

4. Additionally, QSAR models are currently seen as a theoretically sound tool for predicting and classifying the organic activities of untested combinations, drug obstruction, harmfulness anticipation, and physicochemical characteristics expectation in the fields of drug discovery and natural toxicology.

The basis of the QSAR system is the hypothesis that differences in a series of mixes' organic actions can quantitatively correlate to variances in their sub-atomic structure. As a result, all natural processes and atoms have explicit sub-atomic descriptors that connect to them, and explicit relapse methodologies may be used to evaluate the general functions of those descriptors contributing to the organic consequence. (13)

IV. NOVEL HETEROCYCLIC COMPOUNDS AND THEIR BIOLOGICAL IMPORTANCE

1. **1, 2, 4-TRIAZOLE:** Popat B. Mohite et al in 2014; reported announced Microwave Assisted Synthesis of 1-[5-(Substituted Aryl)- 1H-Pyrazol-3-yl]-3,5-Diphenyl-1H-1,2,4-Triazole as Antimicrobial and pain relieving specialist. The blend of 1 - [5-(subbed aryl)-1 H-pyrazol-3-yl]-3,5-diphenyl-1H-1,2,4-triazolederivatives(S1-S10) portrayed in Figure 1. The recently blended chalcones were cyclized with hydrazine hydrate in acidic medium to get different pyrazoles clubbed with 1,2,4-triazole (14).

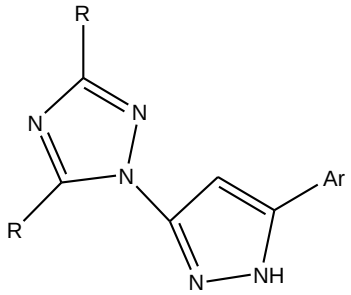


Figure 1: The substitute Aryl Shows A) Antimicrobial Properties B) Analgesic Activity

Rakesh Kumar et al, in 2014; new 1,2,4-triazole subordinates have been combined, shown, and organically evaluated as potent antibacterial .Novel 1,2,4-triazole subordinates are combined, shown, and organically evaluated as potent antibacterial and anti-inflammatory compounds. Biphenyl4-carboxylic corrosive was converted into another family of 1,2,4-triazoles by combining 3-(biphenyl-4-yl)-4-phenyl-1H-1,2,4-triazole-5(4H)-thione subsidiaries with other synthetic chemicals.

The integrated mixes were described using mass spectrometry, 1H-NMR, and FT-IR. The mice paw edoema restraint technique was inspired by the test not established by

Carrgeenan's anti-inflammatory effect. The integrated mixes' antibacterial activity was assessed, and it was compared to the delegate board of gram-positive Bacillus subtilis and Staphylococcus aureus. Gram-negative bacteria Pseudomonas aeroginosa and Escherichia coli (15)

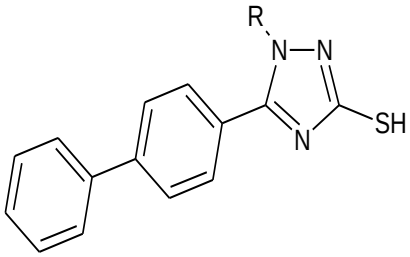


Figure 2: Triazole Derivatives Shows A) Antibacterial Activity B) Anti-Inflammatory Properties

Narayana Rao et al., in 2014 a novel 1,2,4-triazole subordinates that they have described. Additionally, the natural movement has been evaluated 4[(3-(4- substituted phenoxymethyl)-5-benzylsulfonyl)-1,2,4-triazol-4-yl]] -morpholine and all the chemicals listed in the title demonstrated excellent antibacterial and antifungal properties. (16).

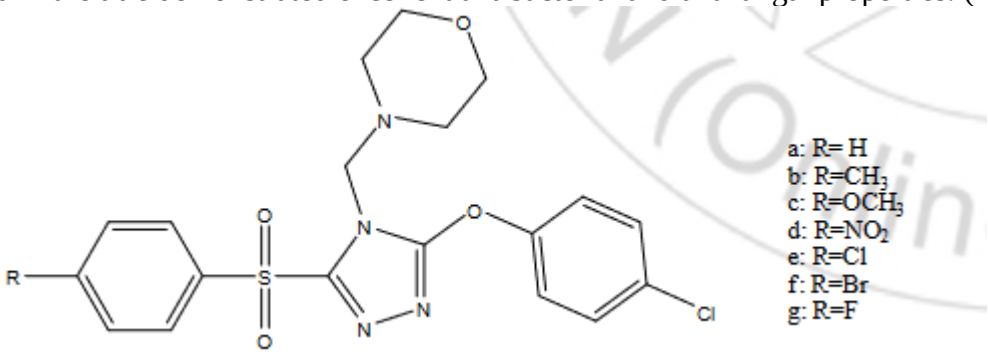


Figure 2 a: Triazole Derivatives Antibacterial and Antifungal Activity

Subbarao et al. in 2014 have reported and evaluated series of 1,2,4-triazolo [3,4-b] [1,3,4] thiadiazoles for good anti- inflammatory activities (17).

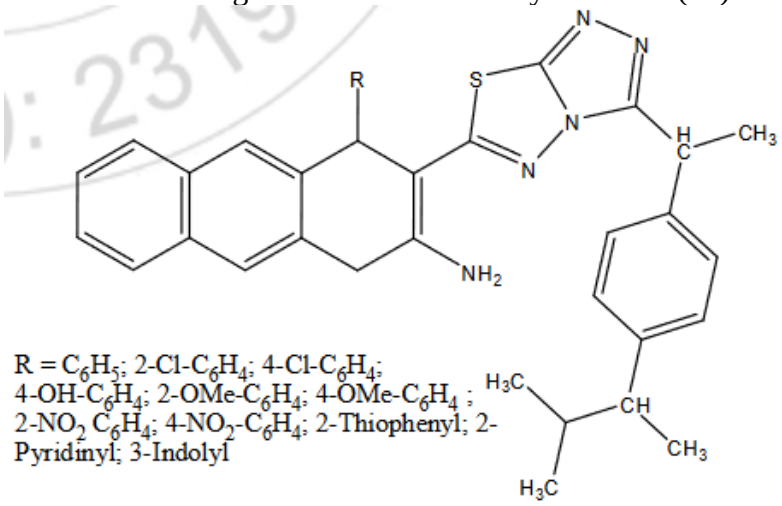


Figure 2 b: 1, 2, 4-Triazole Derivatives Anti-Inflammatory Activity

2. **IMIDAZOLE:** Fatemah Elahian et al, in 2014; reported use of 2, 4, 5, and triaryl imidazole derivatives in combination therapy against cancer.The combination of four 2, 4, and 5-triarylimidazole derivatives and their anticancer activities are depicted in this work. The reaction of benzaldehyde and benzoin derivatives in the presence of ammonium acetic acid derivation and ammonium vanadate produced the objective mixes. Using the MTT assay, the anticancer activities of each of the blended combinations were evaluated against the T47D and MDA-MB231 cell lines. However, our obtained data showed a striking difference between the cytotoxicity of colchicine and its homologs on treated MDA-MB231 and T47D cells; one compound (4a) shown a crucial IC50 on MDA-MB231 cells in cell culture evaluation. (18).

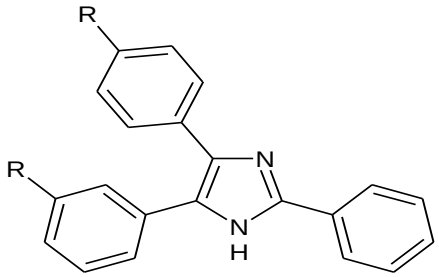


Figure 3: Imidazole derivatives show A) Anticancer activity

Zala SP et al , in 2012 have revealed a combination of a progression of 2,4,5-triphenyl-1H-imidazole-1-yl derivatives and tried for their calming action in vitro involving Phenylbutazone as a kind of perspective medication and antimicrobial movement utilizing clotrimazole and ciprofloxacin as a standard medication. Every one of the incorporated mixtures were evaluated for their enemy of contagious movement against Candida albicans and for antimicrobial action against B. subtilis and E. coli. Compound 8 was viewed as the most intense subsidiary of the series (19).

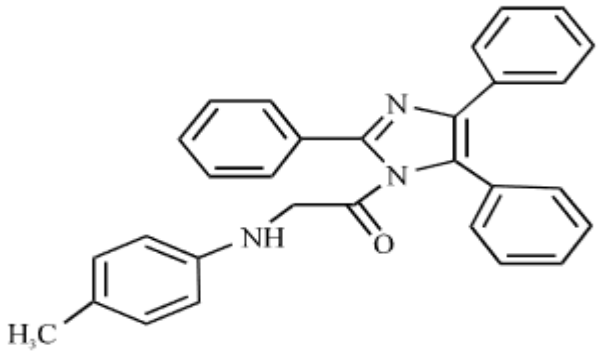


Figure 3 b: Imidazole Derivatives Show Anti-Inflammatory Activity

3. **TETRAZOLE:** Leila Zamani and Bi Fatemeh Mirjalili et al, 2015; have reported some 5-subbed 1-H Tetrazoles in presence of Nano-TiCl4.SiO2 having Anti-parasitic movement. They explored the blend of 5-subbed 1H-tetrazole within the sight of nano-TiCl4.SiO2 (20).

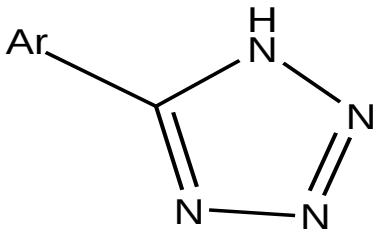


Figure 4: Tetrazoles Derivatives Shows A) Antifungal Activity

Phoebe F. Lamie et al, 2017; revealed some novel tetrazole and cyanamide subsidiaries as inhibitors of cyclooxygenase-2enzyme having calming action. The manufactured courses of the objective mixtures are summed up in 1-[4-(1 H-Tetrazol-1-yl)phenyl]ethanone2 was gotten utilizing 4-aminoacetophenone as the beginning material as per the writing. Chalcone derivatives 3a and b were orchestrated in exceptional returns (79-86%) by a base catalyzed Claisen-Schmidt buildup of acetophenone subsidiary 2 and subbed aryl aldehydes specifically: 3,4-dimethoxybenzaldehyde and 3,4,5-trimethoxybenzaldehyde, individually (21).

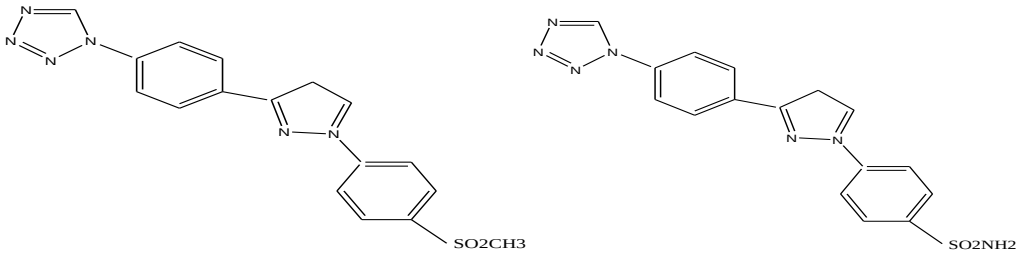


Figure 5: Tetrazoles and Cynamides shows A) Anti-inflammatory activities

Safaa I. Elewa et al, 2020 detailed some tetrazoles and their imminent, N-(1H-tetrazol-5-yl)- 1-(aryl) methanimine and 1-(4-alkoxyphenyl)- N-(1H-tetrazol-5-yl)methanimine having antibacterial and antimicrobial action. Natural examines Activity file screening the antibacterial movement of the orchestrated tetrazoles, utilizing dissemination procedures uncovered that they evidently showed antibacterial exercises as per their primary subbed assembles with the principal skeleton action (22)

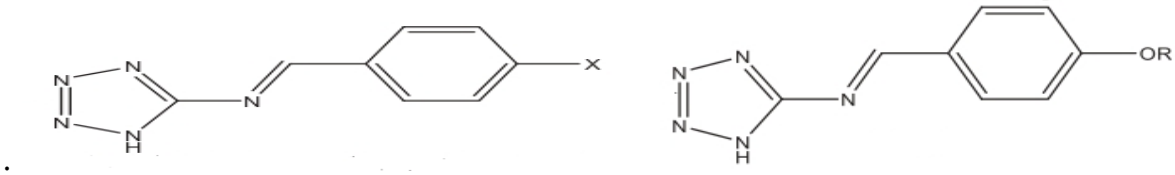


Figure 6: A Novel Tetrazole Shows A) Antibacterial Activity

Girdhar Pal Singh et al, 2021 described amalgamation of novel tetrazole Tetrahydrobenzo[b] Thiophene through Ugi-MCR as new antileishmanial model. The system of amalgamation of tetrazole development has been displayed in Scheme 2. The

initial step is the imine arrangement 9 by the response of amine and aldehydes. Imine 9 believers into imine 10, which gave nucleophilic expansion with isocyanide to structure transitional 11. After azide inclusion middle of the road 11 give tetrazole. Absolute 11 mixtures have orchestrated through highway (23).

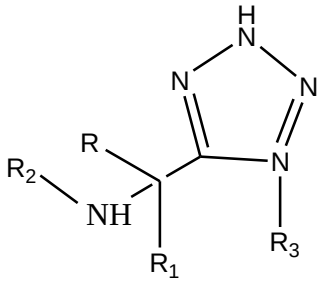


Figure 7: A Novel Tetrazole Shows A) Antileishmanial Activity

Valery N. Kizhnyaev et al, 2022 have reported tetrazole-containing polyelectrolytes in light of chitosan, starch, and arabinogalactan (TEC, TES, TEAG) showing polyampholytic properties. Although the macromolecules of chitosan, starch, and arabinoga lactan polysaccharides used in this study all contain the same fundamental pyranose components, their functions and fanning patterns differ.. In each pyranose cycle, a direct chitosan macromolecule bears, alongside hydroxyl gatherings, the amino or remaining acylamino func tions, which doesn't take part in the concentrated on change responses. Starch and arabinogalactan have just a single kind of responsive practical gathering (hydroxyl). However, these polysaccharides' macromolecules have a distributed design.

Tetrazole rings can thus be introduced into the primary and side polymer chains as a result of these polysaccharides. It should be noted that our goal in this instance was to achieve the most radical change of practical (24)

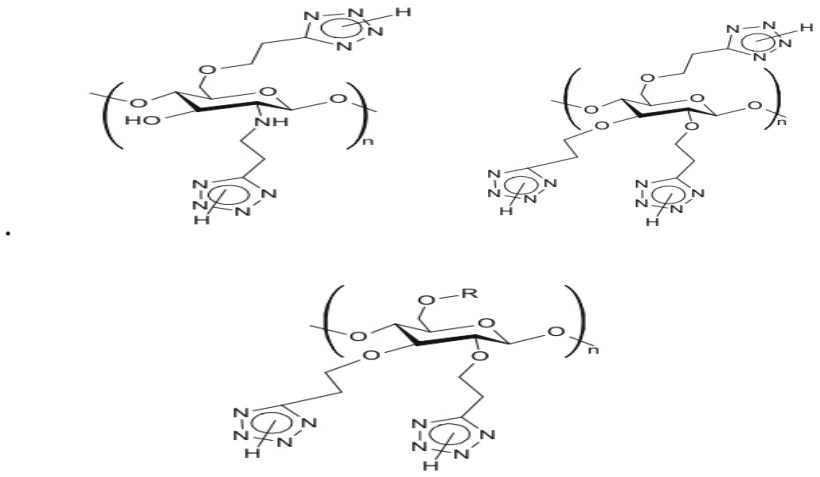


Figure 8: A tetrazole shows A) polyampholytic properties

4. **1-3-4 OXADIAZOLE:** Neeraj K et al, in 2016; revealed combination, portrayal and antimicrobial assessment of 2-phenyl propionic corrosive determined another oxadiazoles. The 2-Phenyl propanoic corrosive and oxadiazoles are known to have antimicrobial action Phenyl propane hydrazide a subsidiary of methyl 2-phenyl propionate on crystallization with fragrant acids offered new 2-aryl-5-(1-phenylethyl) 1-3-4 oxadiazole subordinate (25).

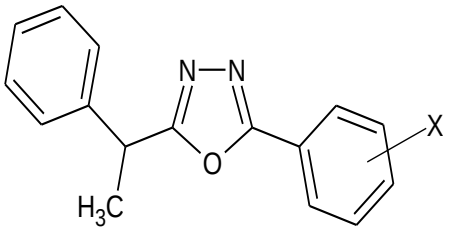


Figure 9: A New Oxadiazoles Shows A) Antimicrobial Properties

Bakshi Anjali et al, 2019; reported some oxadiazole moiety substituted oxadiazole Mannich bases showing antibacterial and anti-fungal activity. Compounds were synthesized as shown in figure 10. Compounds were characterized by infra-red spectroscopy and1H NMR spectra. The details of synthesized compounds (K1, K2 and K3) like molecular structure, nature of compound, yield, molecular formula and molecular weight. All the synthesized compounds of oxadiazoles in the present study showed significant activity against bacteria employed at the concentration of 100µg/ml when compared with that of ampicillin as standard. All the synthesized compounds of oxadiazole in the present study showed significant activity against the fungi employed at the concentrations of 100µg/ml when compared with that of ketoconazole as standard (26).

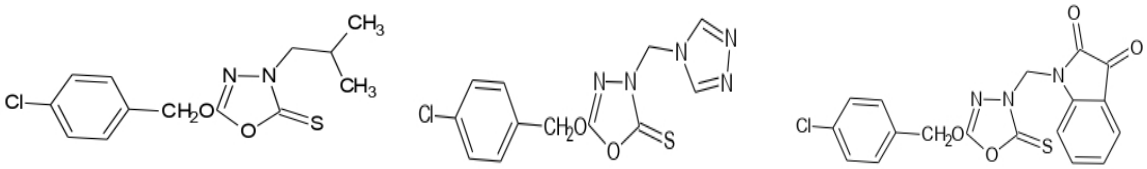


Figure 10: Oxadiazole Moiety Shows A) Antibacterial Activity B) Antifungal Activity

Ahmed Mutanabbi Abdula et al; in 2016, described synthesis, antimicrobial and docking investigation of three novel 2, 4, 5-triarylimidazole subordinates. 5-(4-Substituted phenyl)furan-2-carboxaldehyde were acquired by the response of the diazonium salts RPhN2+ Cl and furan-2-carboxaldehyde within the sight of cuprous chloride (Meerwein technique). Novel 2-[5-(4-subbed phenyl)furan-2-yl]-4,5-diphenyl-1H-imidazole subsidiaries (2a-c) were blended in brilliant yield by the refluxing of aldehyde compounds, benzil and ammonium acetic acid derivation combination in the presence of chilly acidic corrosive (27).

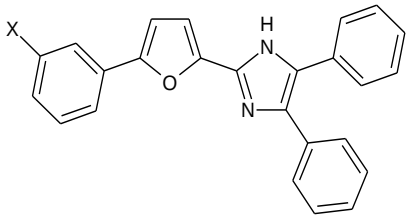


Figure 11: Triaryl Imidazole Shows A) Antimicrobial Activities

5. **ISOXAZOLE:** M. E. Ibrahim et al, in 2016; have described Synthesis and Biological Evaluation of Some Novel Isoxazole Derivatives. The Mannich reaction behavior of 5-amino-3-methylisoxazole (1). It works as an enamine when combined with formalin with dibasic optional amines such as 1,3-di(piperidin-4-yl)propane (2) or piperazine in a molar ratio (2:2:1) to manage 4,4′-(propane-1,3-diyl)bis(piperidine-4,1-diyl)) bis (methylene) bis(3-methylisoxazol amine) (3) and 4,4′ In addition, the cost of 5-amino-3-methyl-4-(piperidin-1-ylmethyl)isoxazole(5) and 5-amino-4-[(dimethylamino) methyl]-3-methylisoxazole(6) was managed separately by the Mannich response of 1 with a combination of formalin and monobasic optional amines, such as piperidine or dimethylamine in a molar proportion (1:1:1). Additionally, we present in this article another straightforward and quick engineered passage to combine unsubstituted isoxazolo[5,4-b]pyridine ring frameworks by using Mannich bases at position 4. (28).

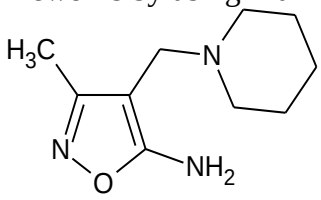


Figure 12: Isoxazoles Derivatives Shows A) Anticancer Agents B) In Biomedical Studies

Vijayakumar K et al, 2017; reported some 4-(1-Methyl-1H-benzo[d]imidazol-2-yl)aniline, N-(4-(1-methyl-1H-benzo[d]imidazol-2-yl)phenyl) benzamide, 4-Chloro-N-(4-(1-methyl-1H-benzo[d]imidazol-2-yl)phenyl) benzamide, N-(4-(1-methyl-1H-benzo[d]imidazol-2-yl)phenyl)-4-nitrobenzamide, 2-(4-(5-(4-Fluorophenyl)-1H-tetrazol-1-yl)phenyl)-1-methyl-1H-benzo[d] imidazole, 2-(4-(5-(4-Chlorophenyl)-1H-tetrazol-1-yl)phenyl)-1-methyl-1H-benzo[d] imidazole, 4-(1-(4-(1-Methyl-1H-benzo[d]imidazol-2-yl)phenyl)-1H-tetrazol-5-yl)benzonitrile, 1-Methyl-2-(4-(5-(4-nitrophenyl)-1H-tetrazol-1-yl)phenyl)-1H-benzo[d]imidazole having Anti-cancer activity (29).

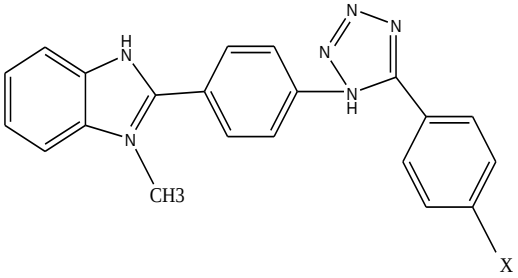


Figure 13: Amides and Imidazoles Shows A) Anticancer Properties

Mounir Cherfi et al, 2021; ethyl 1-(cyanomethyl)- 5-methyl-1H-pyrazole-3-carboxylate-2, ethyl 1-((2H-tetrazol-5-yl)methyl)- 5-methyl-1H-pyrazole-3-carboxylate-3, ethyl 1-((2-(3-bromopropyl)- 2H-tetrazol-5-yl)methyl)- 5-methyl-1H-pyrazole-3-car (30).

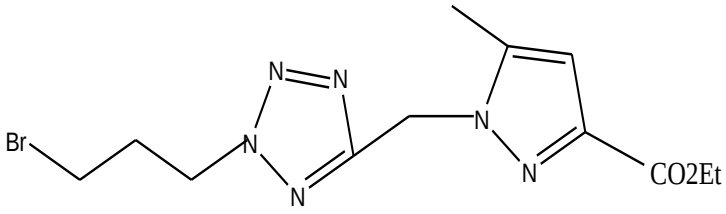


Figure 14: Pyrazole and Tetrazoles Shows A) Vasorelaxant Effects

Younas Aouine et al, 2021; revealed exploratory and computational examinations on N-tetrazole 1,5-and 2,5-AMTs subordinates was done through the N-alkylation response beginning from 5-AMT, which contains a free N-H bond.[28] The compound 5-AMT was gotten in high return . Notwithstanding, the control of its immaculateness by the Thin-Layer Chromatography (TLC) showed that there was just an exceptionally meager path, which demonstrated that the 5-AMT as an indistinguishable combination of two tautomeric structures 1H and 2H. To have a thought on the proportion of each subsequent regioisomers from its N-alkylation, we played out this response with benzyl bromide within the sight of K2CO3 as base (31).

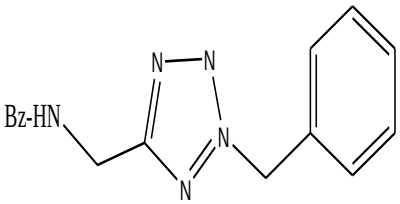


Figure 15: Tetrazoles Shows A) Antibacterial Properties B) Antimicrobial Properties

6. **THIAZOLE:** G. A. Kashid et al, 2018; have reported novel tetrazole, n-(subbed benzylidene) - 4-(4-subbed phenyl) thiazole-2-carbohydrazides) gs-5i having against oxidant movement. In view of the writing review, the current examination was planned and broad interest has been displayed in Oxadiazoles containing accumulates looking for possible medications. Oxadiazole subordinates are known to show a variety of organic exercises. Every one of the mixtures tried and compounds were showed moderate % hindrance and were viewed as critical among every one of the tried mixtures. Remaining mixtures showing gentle action (32).

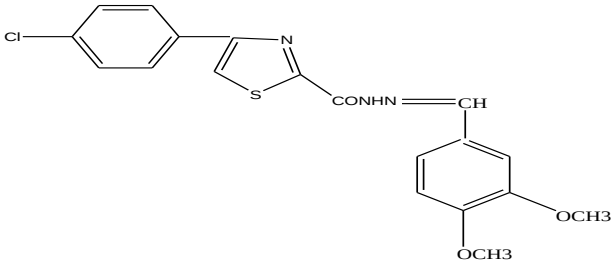


Figure 16: Tetrazoles and Thiazoles shows A) Antioxidant activity

7. **INDOLE:** Maged A. Aziz et al,2021; announced some newer 1 H-3-Indolyl derivativess like 3-(4-(thiophen-2-yl)- pyridin/pyran/pyrimidin/pyrazol-2-yl)- 1H-indole subordinates (2-12) having cancer prevention agent movement. Another series of 3-(4-(thiophen-2-yl)-pyridin/pyran/pyrimidin/pyrazol-2-yl)- 1Hindole subordinates were planned and incorporated as promising cell reinforcement up-and-comers in view of the presentation of identical diminishing heterocyclic rings similar to that of ascorbic corrosive. Applying a quantitative examination of the construction movement relationship (2D-QSAR) on up-and-comers showed a different scope of possibly encouraging cell reinforcement exercises. Concerning ascorbic corrosive cancer prevention agent action, these combined mixtures were classified into three highlighted gatherings of cell reinforcements in view of the aftereffects of their natural searching skills against the assessed extremists in vitro. Moreover, the instrument of activity for the new mixtures was proposed as cytochrome c peroxidase inhibitors by means of sub-atomic docking contrasted with ascorbic corrosive as a source of perspective norm (33)

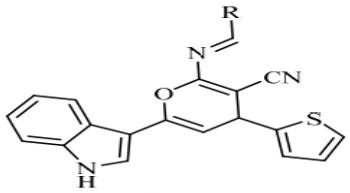
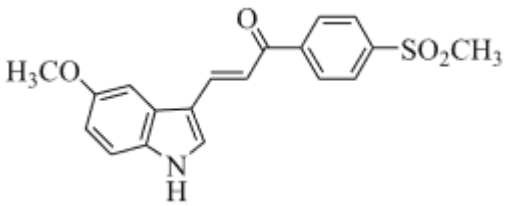
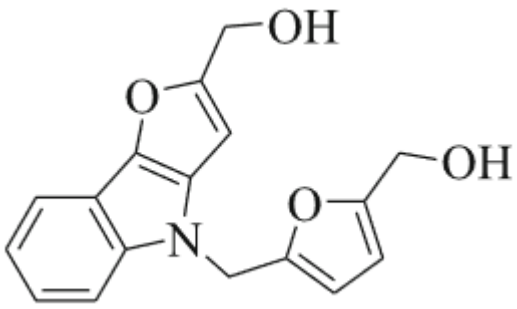


Figure 17: A new Indolyl Derivatives Shows A) Antioxidant Activity

Ozdemir A et al 2017 have reported COX-1 and COX-2 inhibitors based on indole Compounds 3- (5-bromo-1H-indol-3-yl)-1-(4-cyanophenyl)prop-2-en-1-one) and 3- (5-methoxy-1H-indol-3-yl)- It was observed that 1-(4-(methylsulfonyl)phenyl)prop-2-en-1-one exhibited a significant activity (34).



Zhuang et al. 2013 revealed an anticancer movement against the (human NCI-60) growing cell lines using 2, 4-disubstituted furo [3,2-b]indoles. Compound (5-((2-(hydroxy-methyl)- 4H-furo[3,2-b] indol-4-yl)methyl)furan-2-yl)methanol had the most anticancer action among the tested mixtures. According to the analysis of the results, NSC-754549 is the compound 48's comparative unique mark. (35).



V. CONCLUSION

Utilization of heterocyclic chemicals in biological processes is considerable. Therefore, in order to enhance the quality of human life, scientists are attempting to understand the chemistry of heterocycles The current review enumerates and concentrates on recent advancements in the synthesis, QSAR analysis, and pharmacological evaluation of novel nitrogen heterocycles as well as their adaptability as scaffolds in the synthesis of various classes of compounds from medicinal perspectives. It also describes studies on their structure-activity relationships. The various applications in photo sensing and optical switching devices are investigated through the examination of physical aspects like semiconductor, optical, and fluorescence properties. The structure and structural optimization offer hope for future medication research, design, and discovery. This review may be very helpful to the young researchers working in this field because we showed that novel heterocyclic compounds have anti-cancer, antimicrobial, antibacterial, anti-inflammatory, antioxidant, and antifungal actions based on the information provided in this overview.

VI. ACKNOWLEDGMENTS

The authors are grateful to Dr. Savita Tauro , Principal St. John Institute of Pharmacy and Research, Palghar and Dr. V. K. Deshmukh, Principal, Mula Education Society’s College of Pharmacy, Sonai for continuous guidance and support.

REFERENCES

[1] IUPAC Gold Book heterocyclic compounds
[2] Thomas L. Gilchrist "Heterocyclic Chemistry" 3rd ed. Addison Wesley: Essex, England, 1997. 414 pp. ISBN 0-582-27843-0.
[3] Rees, Charles W. (1992). "Polysulfur-Nitrogen Heterocyclic Chemistry". Journal of Heterocyclic Chemistry. 29 (3): 639–651. doi:10.1002/jhet.5570290306.
[4] Edon Vitaku, David T. Smith, Jon T. Njardarson (2014). "Analysis of the Structural Diversity, Substitution Patterns, and Frequency of Nitrogen Heterocycles among U.S. FDA Approved Pharmaceuticals". J. Med. Chem. 57 (24): 10257–10274.
[5] Kapetanovic IM. Drug Discovery and Development - Present and Future. InTech. 2016; DOI: 10.5772/1179.
[6] Badnjevic A, Beganovic E, Music O. Facts about solution based and cartridge based devices for blood gas analyses. IEEE 18th International Conference on System, Signals and Image Processing. 16-18 June 2011, 1-5,

[7] Badnjevic A, Gurbeta L, Boskovic D, Dzemic Z. Medical devices in legal metrology. IEEE 4th Mediterranean Conference on Embedded Computing (MECO). 14 – 18 June 2015, 365-367
[8] Badnjevic A, Gurbeta L, Boskovic D, Dzemic Z. Measurement in medicine – Past, present, future. Folia Medica Facultatis Medicinae Universitatis Saraeviensis Journal, 2015; 50(1): 43-46
[9] Boskovic D, Badnjevic A. Opportunities and Challenges in Biomedical Engineering Education for Growing Economies. IEEE 4th Mediterranean Conference on Embedded Computing (MECO), 14 – 18 June 2015, 407-410
[10] Badnjevic A, Gurbeta L. Development and Perspectives of Biomedical Engineering in South East European Countries. IEEE 39th International convention on information and communication technology, electronics and microelectronics (MIPRO), 30. May to 03. June 2016.
[11] Badnjevic A, Beganovic E, Gvozdenovic V, Sehic G. Automated Closed Loop Controller of Insipred Oxygen System for Improved Mechanical Ventilation in Newborns. IEEE 34th International convention on information and communication technology, electronics and microelectronics (MIPRO), 23.-27. May 2011. 145-149
[12] Aparoy P, Reddy K, Reddanna P. Structure and Ligand Based Drug Design Strategies in the Development of Novel 5-LOX Inhibitors, Current Medicinal Chemistry. 2012; 19(19)
[13] Kubinyi H. QSAR: Hansch Analysis and Related Approaches. In Methods and Principles in Medicinal Chemistry; Mannhold R, Kroogsgard-Larsen P, Timmerman H, Eds.; Wiley-VCH: Weinheim, Germany, 1993; 1, 240.
[14] Shantaraman G. Khanage, Popat B. Mohite, Ramadas B. Pandhare, Appala S. Raju, Microwave Assisted Synthesis of 1-[5-(Substituted Aryl)-1H-Pyrazol-3-yl]-3,5- Diphenyl-1H-1,2,4-Triazole as Antinociceptive and Antimicrobial Agent, Advanced Pharmaceutical Bulletin 2014;4(2):105-112.
[15] Elahian, Fatemeh. and Akbari, Morteza. and Ghasemi, Maryam. and Behtooee, Neda. and Taheri, Mohaddeseh. and Amini, Mohsen. Synthesis and anticancer activity of 2, 4, 5-triaryl imidazole derivatives. Letters in Drug Design & Discovery 2014; 11(7).
[16] DVN. Rao, ARG. Prasad, YN. Spoorthy, DR. Rao, & LK. Ravindranath, Synthesis, "Characterization and Pharmacological Studies of Sulphur Containing 1,2,4- Triazole Derivatives, J. Taibah Uni. Med. Sci., 9 (4), 293-300, 2014.
[17] J. Subbarao, S. Vidhyadhara, & N. Srinivasulu, "Antimicrobial and Anti-inflammatory Activities of Some Novel Triazolothiadiazoles, Int. J. Pharm., 4 (1), 304-308, 2014.
[18] Zala, S.P., R. Badmanaban, D.J. Sen and C.N. Patel, 2012. Synthesis and biological evaluation of 2,4,5- triphenyl-1H-imidazole-1-yl derivatives. J. Applied Pharm. Sci., 2: 202-208.
[19] Rakesh Kumar, M. Shahar Yar , Birendra Srivastava and A. K. Rai, Synthesis, characterization and biological evaluation of novel 1,2,4-triazole derivatives as potent antibacterial and anti-inflammatory agents, Der Pharma Chemica 2014;6(1):137-143.
[20] L. Zamani, B.B.F. Mirjalili, K. Zomorodian and S. Zomorodian, S. Afr. J. Chem 2015;68:133–137.
[21] Neeraj K.F, Shivkanya F, Kaveti B, Sundram K, Kathiresan S, Ajay J, Ugrappa S, Malipeddi H, Synthesis, characterization and antimicrobial evaluation of 2-phenyl propanoic acid derived new oxidiazoles, Indian journal of heterocyclic chemistry 2016;26:037-042.
[22] Tomi, I.H.R. et al., Synthesis, antimicrobial and docking study of three novels 2, 4, 5-triarylimidazole derivatives. Journal of Saudi Chemical Society. 2016;1-8.
[23] M. E. Ibrahim, W. S. Hamama, and H. H. Zoorob, Synthesis and Biological Evaluation of Some Novel Isoxazole Derivatives, Wiley Online Library J. Heterocyclic Chem. 2016.
[24] Phoebe F. Lamie, John N. Philoppes, Amany A. Azouz & Nesreen M. Safwat Novel tetrazole and cyanamide derivatives as inhibitors of cyclooxygenase-2 enzyme:design, synthesis, anti-inflammatory evaluation, ulcerogenic liability and docking study, Journal of Enzyme Inhibition and Medicinal Chemistry. 2017;32(1):805-820.

[25] Vijayakumar K, Sountharrajan S, Suganya E, Synthesis, Characterization, Evaluation of Cancer Prevention Activity of Novel Modifid Heterocyclic Compounds, Asian Pacific Journal of Cancer Prevention. 2017; 19:247-252.
[26] Kashid GA, Singh SK and Saravanan J: Synthesis and QSAR study of novel thiazole moieties having antioxidant activity. Int J Pharm Sci & Res 2018;9(12):5363-72.
[27] Bakshi A, Kammari S, Awasthi A, Bhutada S, Pola S and Mantripragada BR. Synthesis evaluation of some novel heterocyclic compounds containing an oxadiazole moiety. GSC Biological and Pharmaceutical Sciences 2019; 6(2):09-20.
[28] Safaa I. Elewa, Nesreen A. Fatthallah, Maher I. Nessim, Ahmed F. El-Farargy, Synthesis, characterization of some tetrazol and their prospective for aerobic micro-fouling mitigation, Arabian Journal of Chemistry 2020;13:8750-8757.
[29] Aziz M.A, Shehab, W.S, Al-Karmalawy, A.A. EL-Farargy, A.F. Abdellattif, M.H. Design, Synthesis, Biological Evaluation, 2D-QSAR Modeling, and Molecular Docking Studies of Novel 1-H-3-Indolyl Derivatives as Significant Antioxidants. Int.J.Mol.Sci 2021;22:1-23, 10396.
[30] Cherfi M, Dib I, Harit T, Ziyyat A, Malek F. Synthesis and characterization of new pyrazole–tetrazole derivatives as new vasorelaxant agents. Drug Dev Res 2021;1–8:
[31] Aouine.Y, Jmiai. A, Alami. A, El Asri. A, El Issami. S and Bakas. I. Experimental and Computational Studies on N-alkylation Reaction of N-Benzoyl5-(Aminomethyl) Tetrazole. Chemistry. 2021; 3:704–713.
[32] Girdhar P.S, Sultan P. Synthesis of novel tetrazole tetrahydrobenzo thiophene via Ugi-MCR: As new antileishmanial prototype, Journal of Saudi chemical society (Elsevier). 2021; 25:10295, 1-7.
[33] Valery N. K, Fedor A. P, Helen V. A, Synthesis and properties of tetrazole – containing polyelectrolytes based on chitosan, starch, and arabinogalactan, De Gruyter, e-Polymers 2022;22: 203–213.
[34] Ozdemir A, Altıntop MD, Zitouni GT, Çiftçi GA, Ertorun I, Alatas O, Kaplancıklı ZA (2015) Synthesis and evaluation of new indole-based chalcones as potential anti-inflammatory agents. Eur J Med Chem 89:304–309.
[35] Zhuang SH, Lin YC, Chou LC, Hsu MH, Lin HY, Huang CH, Lien JC, Kuo SC, Huang LJ (2013) Synthesis and anticancer activity of 2, 4-disubstituted furo[3,2-b]indole derivatives. Eur J Med Chem 66:466–479

