DESIGN, SYNTHESIS, AND CHARACTERIZATION OF NOVEL HETEROCYCLIC SCAFFOLDS FOR DUAL BIOLOGICAL AND MATERIAL APPLICATIONS

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ABSTRACT

Heterocyclic scaffolds of natural as well as synthetic origin provide almost all categories of drugs exhibiting a wide range of pharmacological activities, such as antibiotics, antidiabetic and anticancer agents, and so on. Under normal homeostasis, aldose reductase 2 (ALR2) regulates vital metabolic functions; however, in pathological conditions like diabetes, ALR2 is unable to function and leads to secondary diabetic complications. ALR2 inhibitors are a novel target for the treatment of retinopathy (cataract) influenced by diabetes. Epalrestat (stat), an ALR2 inhibitor, is the only drug candidate that was approved in the last four decades; the other drugs from the stat class were retracted after clinical trial studies due to untoward iatrogenic effects. The present study summarizes the recent development of this pharmacologically active ALR2 heterocyclic scaffold and illustrates the rationale behind the design, structure–activity relationships, and biological studies performed on these molecules. Heterocyclic nucleus plays a fundamental role in the medicinal chemistry and serves as a key template for the development of various therapeutic agents including broad spectrum antibacterial drugs. In an effort to develop new antibacterial agents, a bicyclic twelve-membered heterocyclic nucleus derived from coumarin was prepared by an uncomplicated method. The rate of ring closure for this nucleus, which was given the name coumacine, in addition to two of its derivatives was monitored spectroscopic ally and this rate followed zero order kinetics.

Keywords: *novel heterocyclic scaffolds, drugs exhibiting, biological studies, pharmacological activities*

INTRODUCTION

Among other biological uses, azo dyes are used as thermoplastics, anti-inflammatory, anti-diabetic, and cleaning agents in chemotherapy settings. These compounds' strong colour and notable electrical, optical, and environmental resilience make them suitable for usage as dyes and pigments. Hetero cyclic compounds especially those with numerous ring members have become more and more attractive in pharmaceutical and industrial uses. Ox diastole, for example, are hetero cyclic chemicals used in the production of pigments, plastics, and medications. Because of their wide range of possible biological functions, compounds including pyramidal, pyrimidine, and trampoline, as well as their derivatives, have been the focus of much investigation. Reviews of the literature indicate that these compounds are adaptable chemicals with a broad range of biological features and uses due to their large diversity of pharmacological activity. For instance, it has been shown that pyramidal and some of its derivatives are UV stabilizers or emitters. In recent years, many techniques for forming the epinephrine ring have been documented. However, since epinephrine rings are important medicinal medications and active ingredients in biological systems, the straightforward and effective method of making them is still recommended. Hetero-cyclic compounds are increasingly being produced via bio-catalysis, a green chemical process that uses

natural catalysts like enzymes. Complex compounds with high intended selectivity and few side reactions may be synthesized thanks to the remarkable specificity and selectivity of enzymes at moderate reaction conditions. In the manufacturing of medicines, where the end product's purity and stereo-chemistry are essential to biological function, this approach is very helpful. Additionally, the synthesis of hetero-cyclic molecules has showed a lot of promise using flow chemistry, which performs reactions in a continuous flow system as opposed to batch processes. Flow chemistry may make the shift from laboratory to industrial scale safer and more effective since it provides exact control over reaction parameters like temperature and pressure. By integrating several reaction steps into a single continuous process, this technique also shortens the total reaction time and boosts synthesis efficiency. The use of these cutting-edge synthetic techniques not only boosts the sustainability and productivity of hetero-cyclic compound manufacturing, but it also creates new opportunities for the discovery of novel compounds with special and advantageous biological characteristics. One instance of how optimized synthetic methods may be used to create therapeutically useful molecules is the synthesis of novel aquiline derivatives with strong antibacterial and anti-fungal activity. Furthermore, it is now possible to forecast the results of synthetic routes and determine the most effective strategies by integrating computational chemistry and molecular modelling in the design and optimization of synthetic processes for hetero-cyclic molecules. By simulating chemical pathways and providing information on the stability and reactivity of intermediates, these technologies may help choose the best reaction conditions and lessen the need for lengthy experimental trial and error. To sum up, creating and refining innovative and effective synthetic processes to create unique hetero-cyclic molecules requires a multi-pronged strategy that combines cutting-edge analytical methods, computer programs, and green chemistry concepts.

LITERATURE REVIEW

Ali H. Alsadoon (2024) Hetero-cyclic compounds with a -triangle moiety have attracted a lot of scientific and medical interest due to their unique structure and many applications in chemical biology, organic synthesis, and medication development. Although triangle derivatives are not found in nature, they are crucial in many domains. However, little is known about their potential for anti-fungal and antibacterial therapies. The goal of this research is to modify the antibiotic triangle in order to produce novel triangle derivatives and evaluate its structural and biological properties. For characterisation, FTIR, H-NMR, and melting point studies were used. Staphylococcus aureus, Bacillus species, Candida albicans, Escherichia coli, and Pseudonymous oleaginous were tested for anti-fungal and antibacterial properties at 250–500 mg/mL. The results of a delayed hypersensitivity skin test confirmed that they were not allergic. The findings demonstrated robust antibacterial activity, highlighting 1,2,4-triazoles' potential for the development of novel pharmaceuticals.

Sebastián Montalvo-Vázquez (2023) Breast cancer is now the most common illness, with the American Cancer Society projecting that 287,850 new cases will be discovered in 2022. It is essential to find a treatment that works for this sickness. Chalcones are α,β-unsaturated systems that exist naturally. Because of their wide spectrum of biological effects, these

compounds are often used as synthetic targets. Since chalkiness are composed of two aromatic substituent connected by an enone bridge, they have a large number of derivatives. Due to the compounds' biological importance, novel chalkiness derived from conference-hetero cycles were synthesized and described using a hybrid drug design approach. These hetero-cyclic substances had theosophic, pyrimidine, thiazolyl, and indole groups. Fourteen novel hetero-cyclic ferrymen chalcones were synthesized and characterized by us. Compared to their system 1 counterparts, system 3 ferrocenyl chalcones exhibited better anticancer properties.

Monir Uzzaman (2022) Hetero-cyclic compounds have garnered a lot of attention because of their several significant biological and therapeutic uses. Researchers are very interested in hetero-cyclic compounds because of their many synthetic investigations and real-world applications. They act as a bridge between chemistry and biology, where most scientific research and application occurs, and are found in over 90% of novel drugs. Additionally, hetero-cycles are used in many fields, such as medicinal chemistry and biology. The main applications for hetero-cyclic compounds are in veterinary medicine, agrochemical, and pharmaceuticals. Our review covers most of the recently synthesized bio-active hetero cycles and also looks at a new phase of potential anti-fungal, anti-inflammatory, antibacterial, antiviral, antioxidant, anticonvulsant, antipathetic, antipathetic antipyretic s, anti-allergic, antihistamine, herbicidal, anticancer, anti-hypertensive, and anti-leprosy therapeutics.

Jitendra N. Borase, (2021) In addition to having interesting coordination chemistry, hetero-cyclic Schiff base metal complexes have recently attracted more attention in biological applications. This work explores the formation of novel hetero-cyclic methyl-substituted pyridine Schiff base transition metal complexes of Fe(III), Co(III), Cu(II), and Ni(II) by reacting metal acetate or metal salts (FeCl3, CoOAc, CuOAc, and NiOAc) with a substituted hetero-cyclic ligand. After being characterized by spectroscopic data, each newly created metal complex was investigated for elemental analysis, FT-IR, ESR, magnetic susceptibility, and TGA. According to their electronic spectra and magnetic susceptibility tests, these complexes have octahedron and square planer geometry, which further suggests a structure in which the (N, O) group acts as a bidentate ligand. The thermodynamic properties, rate of breakdown, and thermal stability of the synthesized metal complexes were assessed using the Freeman Carroll technique.

Hetero-cyclic Compounds' Significance in Biology

Hetero-cyclic compounds are common in nature, vital to life, and involved in the metabolism of all living organisms. Hetero-cyclic compounds are highly prized commercial products that are often employed as medical treatments due to their high degree of structural diversity. The primary structural component of bio-molecules, including DNA, RNA, vitamins, chlorophyll, haemoglobin, and physiologically active substances with insecticidal, fungicidal, and herbicidal properties, is the hetero-cyclic ring. They are often used as a crucial structural element in agricultural chemicals and synthetic medications. They serve as catalysts, facilitating the creation of other organic compounds. Many natural

substances, including alkaloids like morphine, inelastic, and reserpine, as well as antibiotics like cephalopod and penicillin's, include a hetero-cyclic moiety. Hetero-cyclic compounds come in a wide variety and are necessary for biological function.

Hetero-cyclic Compounds' Biological Activity

Hetero-cycles are present in many bio-molecules, including enzymes, vitamins, natural products, physiologically active chemicals, and enzyme inhibitors, and they also have insecticidal, anti-diabetic, and anti-HIV properties. They also make up an essential structural element of pharmacological chemistry. The IC50 value was used to quantify the biological activity in vitro in order to identify correlations that enable the improvement of new scheme. Despite this, N-tetracycline compounds are significant in medicinal chemistry. Thus, the mixture of natural and synthetic drugs is a significant factor from the standpoint of medicinal chemistry. Since hetero-cyclic chemicals are likely to interact with pockets that bind enzymes, they are an excellent starting point for creating drugs that disrupt targets and biological processes linked to the development of cancer. The study and creation of novel pharmacological compounds that are highly targeted to cancerous cells is a crucial area for modern science and medicine as it would reduce the burden of side effects.

New hetero-cyclic compound synthesis

Hetero-cyclic compounds may be synthesized using a variety of methods, including metal-catalyzed processes, conventional organic synthesis, and more recent methods including microwave-assisted synthesis and green chemistry approaches. The production of hetero-cyclic compounds has relied heavily on traditional organic synthesis techniques including condensation and inclinations. A common technique for creating pyrimidine derivatives with possible anticancer properties is the Hantzsch synthesis. Metal-catalyzed methods have changed the synthesis of hetero-cyclic molecules, such as palladium-catalyzed cross-coupling processes. These reactions allow for the precise and effective construction of complex structures. For instance, hetero-cyclic molecules with possible anticancer characteristics may be produced via the Suzuki-Miyaura coupling. A contemporary method for speeding up chemical processes, decreasing reaction times, and increasing yields is microwave-assisted synthesis

Creating novel medications using bio-active hetero-cycles

Bio-active hetero-cycles have garnered significant interest from the agricultural and pharmaceutical industries due to their strong biological effects and easily accessible nature. These hetero-cyclic structures are found in many natural chemicals, including vitamins, alkaloids, and antibiotics. These substances are very beneficial for drug development and crop protection due to their strong pharmacological or pesticide qualities. Hetero-cyclic motifs are significant in medicinal chemistry, as shown by the fact that they are present in over 90% of recently developed medications. These compounds are great resources for researching biological processes and developing new treatments because of their many biological potentials, including their anti-fungal and anti-inflammatory qualities. Amino acids like proline, tidiness, and tryptophan are examples of bio-active hetero-cyclic molecules used in pharmaceuticals. Through their interactions with biological

targets that regulate their activity, these chemicals have a significant influence on our understanding of biology and the creation of therapeutic therapies.

The importance of hetero-cyclic molecules in chemistry

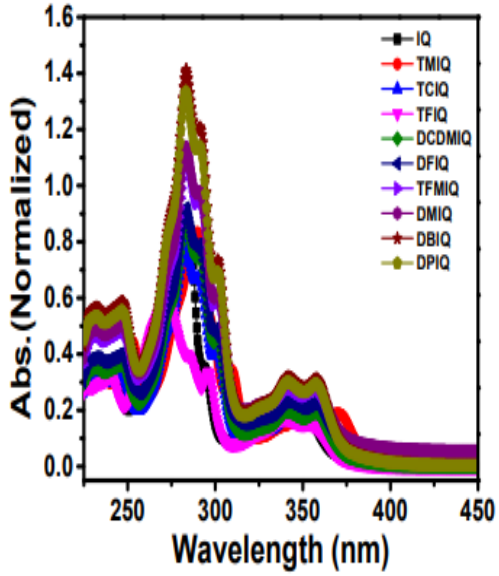
Applied chemistry has several applications in various scientific fields, and hetero-cyclic molecules are recognized as an important category in organic chemistry. Applied chemistry has several applications in various scientific fields, and hetero-cyclic molecules are recognized as an important category in organic chemistry. According to reports, hetero-cyclic compounds make up almost half of all therapeutic drugs created and sold to date. Chemists appear to have concentrated on biologically active molecules with hetero-atoms like nitrogen, sulphur, and oxygen due to the challenges of synthesizing these compounds and the potential for their use as therapeutic drugs and tool compounds in medicine and the pharmaceutical sciences. Therefore, it is highly wanted to identify new and effective methods for producing hetero-cyclic molecules.

METHODOLOGY

Similarly, because of their structural resemblance to indoles, 4-aza indole derivatives have been synthesized and have garnered a lot of attention in medicinal chemistry. These compounds have remarkable biological activity, including antimalarial, antithetic, intuitive, non-narcotic, anti-diabetic, antiviral, interscholastic, and anticancer properties. Because of its importance in biology and pharmacology, ind-ole-foxhole's synthesis, biological activity, and isolation have all been the subject of much research in recent decades. The alkaloid imprinter based on ind-ole, for instance, possesses strong anti-epileptic and mono amine oxidase (MAO) inhibitory qualities. Furthermore, foxholes are five-member hetero-cyclic scaffolds that have garnered attention throughout time and are crucial structural components for applications in medicinal chemistry. Examples of biological effects include receptor tyro-sine kines (RTK), insecticidal, herbicidal, anti-tubercular, anti-fungal, and A2A adenine receptor antagonists. The characterization data will be interpreted and possible structure will be assigned. The characterized compounds will be sent to collaborators for biological activity. After biological activity of synthesized compounds, the structure activity relation-ship will be predicted.

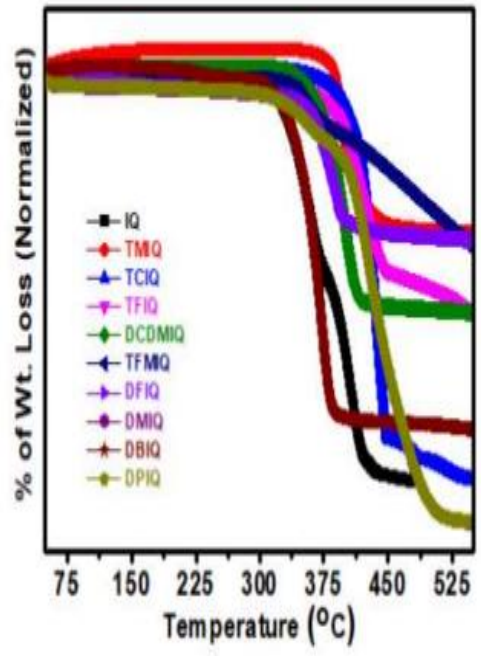
RESULTS AND DISCUSSIONS

Graph 1 show the UV-vis absorption spectra that were acquired in diluted hydrochloride. Only the distinctive BTBT absorption pattern, with absorption maxima in the 360–375 nm range, is visible in these versions. When the diluted IQ solutions were subjected to UV light for four hours, there was no discernible change in the function of UV-visible absorption over time These compounds, like pyrimidine and indole, are made up of two hetero-cyclic units joined to one another. Unlike reference materials like pentacle, the hetero-cyclic linear and fused structure hinders molecular photo-stability. This kind of photochemical stability has also been shown for BTBTs.



Graph 1: UV-vis spectra of IQ ordering as transcribed in hydrochloride.

The thermal gravimeter graphs for the IQ series are shown in Graph 2, and the decomposition temperatures for weight loss below 10% are found in Table 1. These IQ derivatives demonstrated high-thermal stability, degrading at temperatures over 300 oC.11. The molecule with the greatest Td in the IQ series is TCIQ, which has four chlorine atoms added.



Graph 2: Thermos grams of IQ series

Table 1. Photo-physical properties, HOMO–LUMO energies, and thermal data of IQ series

Compd.	[a]λ onset (nm)	[b]EHOMO (eV)	[c]ELUMO (eV)	[d]Eg (eV)	[e]Td (° C)
IQ	369	-5.431	-2.071	3.36	328
TMIQ	394	-5.413	-2.263	3.15	383
TCIQ	378	-5.426	-2.146	3.28	402
TFIQ	375	-5.435	-2.125	3.31	396
DCDMIQ	385	-5.466	-2.246	3.22	372
TFMIQ	380	-5.456	-2.196	3.26	348
DFIQ	389	-5.405	-2.245	3.19	351
DMIQ	381	-5.416	-2.166	3.25	346
DBIQ	405	-5.408	-2.348	3.06	337
DPIQ	396	-5.411	-2.281	3.13	342

a maximum of absorption. ELUMO = EHOMO − Eg. D. B EHOMO as determined by CV The absorption and emission spectra intersection yielded the optical band gap, or Eg. E At 5% weight loss, the thermal decomposition temperature was observed.

CONCLUSION

A unique family of hetero-cyclic compounds is successfully designed, synthesized, and described in this work, with an emphasis on the possible pharmacological and physical uses of these molecules. Because of their extensive use in agrochemical, medications, natural goods, and advancements in materials science, hetero-cyclic scaffolds continue to be one

of the most important and adaptable structural units in organic chemistry. By creating novel compounds with desired structural characteristics and showcasing their potential via a variety of analytical and biological tests, this endeavour sought to further our current understanding. To ensure efficiency, yield optimization, and sustainability, the hetero-cycles were synthesized utilising both conventional and eco-friendly techniques. One of the main tactics used in inclinations procedures is the use of ecologically friendly chemicals. Reaction time and waste might be reduced by using a microwave with solvent-free settings. synthetic paths with many steps that provide structural variation. Spectral studies revealed that all of the synthesized compounds were very pure and produced in good to outstanding yields. Functional groups were strategically changed and substituted in order to assess the connections between structure and activity.

REFERENCES

1. *Sebastián Montalvo-Vázquez (2023), "Synthesis of Novel Heterocyclic Ferrocenyl Chalcones and Their Biological Evaluation", ACS Omega, ISSN 2470-1343,Vol.8,Issue.38*
2. *Ali H. Alsadoon (2024), "Creation of Novel Heterocyclic Compounds from (Triazole) Derivatives and Assessment of Their Biological Functions", central Asian Journal of Theoretical and Applied Science,ISSN 2660-5317, Vol.5, issue.7*
3. *Monir Uzzaman (2022), "A review on biological and medicinal impact of heterocyclic compounds", Results in Chemistry,ISSN: 2211-7156, Volume.4, https://doi.org/10.1016/j.rechem.2022.100606*
4. *Jitendra N. Borase (2021), "Design, synthesis and biological evaluation of heterocyclic methyl substituted pyridine Schiff base transition metal complexes", SN Applied Sciences,ISSN : 2523-3971,Volume.3,vol.197*
5. *Mohammed S. Farhan (2015), "Synthesis of some Novel Nitrogenous Heterocyclic Compounds with Expected Biological Activity as Antimicrobial and Cytotoxic Agents", Novel nitrogenous heterocyclic compounds with biological activity, Iraqi Journal of Pharmaceutical Sciences, ISSN:2521-3512, Vol.24,issue.(1)*
6. *Nilima Dnyanadeo Mahajan (2021), "Heterocyclic Compounds And Their Applications In The Field Of Biology: A Detailed Study", Natural Volatiles and Essential Oils, vol. 8,issue.(4)*
7. *P.Anvar Kasim (2018), "Synthesis And Characterization Of Some Novel Heterocyclic Chalcone Derivatives", Journal of Emerging Technologies and Innovative Research,ISSN-2349-5162, Volume.5,Issue.11*
8. *Rasim Farraj Muslim (2019), "Synthesis, Characterization and Evaluation of Biological Activity of Novel Heterocyclic Derivatives from Azomethine Compounds", Oriental Journal Of Chemistry,ISSN: 0970-020 X, Vol.35, issue.(4), Pg. 1360-1367*
9. *S. Syed Shaf (2014), "Synthesis, Characterization And Biological Study Of Novel Heterocyclic Compounds", Rasayan J. Chemistry, ISSN: 0976-0083, Vol.7,issue.4,pages.370 – 374*
10. *Simin Vazirimehr (2017), "Ultrasonic synthesis, characterization, and antibacterial evaluation of novel hetero cycles containing hexahydroquinoline and pyrrole moieties", Heterocyclic Communications, ISSN: 2191-0197, Volume.23,Issue.1*