

AN EXPLORATORY STUDY OF HETEROCYCLIC COMPOUNDS IN MEDICINAL CHEMISTRY

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Abstract

Heterocyclic compounds are important in many scientific fields, including biochemistry and medicinal chemistry. The point of interaction between chemistry and science, where so much new logical knowledge, revelation, and application is occurring, is crossed by heterocyclic compounds in over 90% of new medications. Compounds derived from heterocyclic rings used in various industries, including agriculture, medicine, plastics, and polymers. The majority of dynamic heterocyclic have impressively demonstrated natural properties like antifungal, sedative, antibacterial, anticonvulsant, and anti-allergenic, as well as herbicidal and anticancer action.

They are typically used in human medicine to treat ailments like cough, asthma, clogging, migraine, tobacco, fever, and skin problems. The majority of medications that doctors recommend also because adverse side effects, like digestive problems. As a result, there is a pressing need for the development of effective new anti-diabetic medications with fewer side effects. Since diabetes is a global pandemic, there is a constant need for new anti-diabetic medication types.

There are currently combinations of heterocyclic compounds. Because of extensive engineering research and in addition to their industrial utility, heterocyclic compounds are rapidly increasing in number. These substances serve a wide range of functions in the study of medicinal chemistry. Additional notable applications include dyestuff, sanitizers, consumption inhibitors, cancer prevention agents, and copolymer combinations. The characteristics of an efficient

method for generating novel heterocyclic compounds and their moieties are constantly being recognised. According to a previous analysis, the creation of over 90% of prescriptions containing heterocyclic compounds followed the careful logical grasp of the natural framework.

Keywords: *Heterocyclic Compounds, Medicinal Chemistry, Diabetes, Classification of Heterocyclic Compounds.*

1. Introduction

The most traditional categories in natural chemistry are heterocycles, which have enormous organic and contemporary significance. The majority of organically active drugs and agrochemicals are heterocyclic, as are many of the additives and modifiers used in business, including plastics, reprography, data storage, and beauty care products. The ability of heterocycles to display substituents in given three-layered pictures by a central platform is a striking primary property that the pharmaceutical industry greatly exploits. For more than a century, heterocycles have been one of the important areas of focus in natural chemistry. Heterocycles have sparked the organic and financial development of human progress as well as the awareness of the life-supporting systems that are geared toward enhancing personal satisfaction. Of the 20 million substance compounds discovered before the second millennium, more than 66 percent are completely or partially fragrant, and about half are heterocyclic.

Engineered heterocyclic have been widely used for beneficial purposes such as antibacterial, antifungal, antimycobacterial, trypanocidal, hostile to HIV, against leishmanial, genotoxic, antitumoral, calming, strong relaxants, anticonvulsants, against malignant growth, and lipid peroxidants. There are also more manufactured heterocyclic compounds with other fundamental purposes, such as fungicides, herbicides, counter acting, and preventing transfers. The monocyclic and bicyclic heterocycles of pyrimidine (cytosines, uracils, and thymines) and purine (adenine and guanines) each contain two to four nitrogen atoms. Deoxyribonucleic acid (DNA) atoms are fundamental components that connect directly when unravelling genetic material.

The scientific field of study known as medicinal chemistry develops treatments either through disclosure or design. In addition, remedial science includes the unmistakable evidence, portrayal, and mixture of substances that can be applied to medicine for the prevention, treatment, and correction of disorders (Davis An and Ward SE, 2014). Clinical science has converged on natural therapeutic agents, whether they are common or integrated. Alkaloids, glycosides, vitamins, synthetic compounds, immunisation poisons, and other substances are obtained from traditional sources. Some of them, like supplements and synthetic substances, are coordinated, but others, like alkaloids, glycosides, various disease-causing agents, and a few synthetics, like insulin, are purchased from regular sources. Semi-designed drugs, like semi-produced penicillin, can be created by fundamentally altering the development of common medications. By observing changes in the designs of common and manufactured drugs, numerous novel analgesics, local tranquillizers, sympathomimetics, and various solutions have been developed.

According to data, more than 85% of all physiologically dynamic substance compounds contain heterocycles. This emphasises the significance of heterocycles in the current treatment regimen. All heterocycles, both synthetic and natural, have pharmacological action. Heterocyclic compounds, which are dynamic in terms of physiology and pharmacology, have developed a notable quality in the medical review. Heterocyclic particles are used in the creation of many natural substances that are connected to living things, including nutrients, chemicals, and anti-infection substances. Among physiologically active structures, natural products, and synthetic compounds typically used in medicinal chemistry, heterocyclic compounds with nitrogen atoms in their designs are regarded as the significant class of synthetic substances. Quinoline, indoles, pyrroles, and pyrrolidines are among these nitrogen-containing heterocyclic compounds that have grown in importance in a variety of research fields, including natural combination and medicine. The synthesis of heterocyclic compounds has evolved into a point of convergence in natural combination because of their diverse uses. Before many years, a number of precise delivery methods for heterocyclic compounds containing nitrogen were considered and developed. Researchers have demonstrated a remarkable interest in various heterocycles, particularly sulfur-containing heterocyclic particles, despite the extensive exploration of heterocycles, particularly those based on nitrogen heteroatoms. Sulfur-containing heterocyclic

compounds are widely used in FDA-approved drugs and therapeutically effective designs. These synthetics have been shown to have numerous other natural benefits, including antifungal, antibacterial, anticancer, antiviral, antimicrobial, calming, antimalarial, antihypertension, and hostile to diabetes. Heterocyclic compounds with sulphur are frequently used in drug research and can be found in many everyday items and medications. Additionally, a variety of heterocyclic compounds containing sulphur are used to season foods like meat, vegetables, peanuts, coffee, and coco. Some FDA-approved medications contain sulphur heterocycles, such as clopidogrel, raloxifene, and rosiglitazone, which are used to treat diabetes, bosom disease, and peripheral vascular disease, respectively. Ritonavir is also a well-known antiviral expert. Thiabendazole is also an effective antifungal medication. In addition, only a small number of sulphur heterocycle-containing drugs are approved by the FDA and are used to treat a variety of clinical issues.

1.1. Diabetes

Hyperglycemia, a metabolic infection, is a symptom of diabetes mellitus. When the body doesn't produce enough insulin or when cells don't react to the insulin produced as a result of abnormalities in insulin creation, insulin hailing, or both, hyperglycemia results. 1'3 One of the most serious dangers to human prosperity in the twenty-first century is considered to be diabetes mellitus.

Persistent hyperglycemia brought on by insulin insufficiency causes some problems with protein, fat, and starch digestion. Now that diabetes mellitus has become a global pandemic, India has been dubbed the "diabetes capital."

Type 1 diabetes: Because the pancreas lacks beta cells, it is unable to produce enough insulin. This condition was previously known as "young adult diabetes" or "insulin-dependent diabetes mellitus" (IDDM). Beta cells are destroyed by a robust framework reaction. The aetiology of this resistant framework response is unclear.

Type 2 diabetes: Cells that are insulin resistant do not respond to insulin as it should. As the condition worsens, an absence of insulin could happen. Until recently, this condition was referred to as "adult starting diabetes" or "Non-Insulin-Dependent Diabetes Mellitus" (NIDDM). The most common cause is a result of both high body weight and insufficient activity.

Gestational diabetes: The third type, which is the most typical, occurs when pregnant women who have never had diabetes promote high glucose levels.

In this review, which is based on heterocyclic combinations and composite courses, as well as produced heterocyclic auxiliaries dependent upon hidden game plan, we detail the separation, blend, and anti-diabetic properties of these heterocyclic compounds.

2. Literature Review

2.1. Heterocyclic compounds

The combination, properties, and functions of heterocyclic combinations—which are particularly important in the development of new medications—are the focus of heterocyclic chemistry. A carbocyclic compound is a cyclic regular molecule in which the carbon atoms are all organised into a ring structure. When a portion of the ring structure other than carbon is present, the compound is said to be heterocyclic. Nitrogen, oxygen, and sulphur are the most persistent heteroatoms, but heterocyclic rings with additional heteroatoms are also noteworthy. Numerous heterocyclic combinations are known, and new ones are constantly being discovered. The study of heterocyclic particles is actually as predictable of aliphatic or fragrant combinations, depending on their electronic beauty care products. From a theoretical and utilitarian standpoint, their investigation is fascinating. There are many heterocyclic combinations in nature, and they are important for life in a variety of ways. Alkaloids, antimicrobials, basic amino acids, supplements, haemoglobin, synthetic materials, and a vast array of manufactured medicines and varieties are just a few examples of the many different combinations in which heterocyclic ring structures can be found (Rees CW, 1992).

2.2. Indole compounds with potential anti-diabetic activity

The properties of designed indole subordinates are the same as those of typical indole alkaloids, according to Zhu Y, et al. Over the past twenty years, more indole auxiliaries have been created and included to study their bioactivities. His article summarises systems that are isolated from normal sources or by produced procedures and examines the counter-diabetic effects and mechanisms of action of indole compounds with likely adversaries of diabetic development, including customary indole alkaloids and designed indole subordinates. Additionally, his blueprint shows the combination techniques for various gigantic indole subordinates right away.

By administering alloxan monohydrate at a dose of 0.9 mg/egg on the fourteenth day of suffering, Srividya L and Reddy AR demonstrated that diabetes was established in chicks. This was shown by the transport of chicks with elevated blood glucose levels when contrasted with chicks who didn't seek alloxan treatment. Data were analysed in a single way using one-way analysis of variance (ANOVA). According to the test substance's relationship, it was discovered that glucose levels drastically decreased in segments of 10 and 30 mg kg⁻¹. Thiocarbohydrazone was subordinate to picked indole.

According to Kanwal K. et al., indole-3-acetamides (124) were produced by combining indole-3-acidic destructive with various substituted anilines inside of the presence of the coupling reagent 1,1-carbonyldiimidazole. To find the designs of manufactured combinations, specific spectroscopic systems, such as electron ionization-mass spectroscopy (High-Resolution Electron Ionization Mass Spectrometry (HREI-MS)), were used. The confinement of made particles with the compound's strong site was verified by in silico tests. In the stream research, various lead particles were identified as potential adversaries of experts in hyperglycemia and cell support.

According to research by S. Fattaheian-Dehkordi et al., supportive plants, such as removed and purified dynamic parts, have a crucial limit in blood glucose regulation. Due to the extraordinary to splendid results depicted in the composition, they have become a crucial focus for developing and disseminating Diabetes mellitus remedies and updates. The encouraging results encouraged

us to reconsider whether it was feasible to plan for the development of local antagonists to diabetic medications.

2.3. Novel triazole compounds have anti-diabetic action

According to Mohamed MA and colleagues, new sulfonamide and Thiazolidinedione (TZD) 5a–c, 7a–c auxiliaries were transported from amino acids associated triazole subordinates 1a–h under green science conditions. The recently mentioned substances exhibited potent anti-diabetic activity both in vitro and in vivo. The developments of the recently discovered combinations were represented using the reach and standard data.

2.4. Scope of nitrogen-based compounds in medicine

According to Kerru N. et al., the diversity of nitrogen-based iotas in pharmaceuticals is fostering a regular schedule, and their various analogues provide a potential and crucial pathway for the disclosure of treatments with a variety of conventional vocations. His overview paper aids in advancing the hidden model and development of reliable nitrogen-based treatments for a variety of ailments with few unfavorable side effects.

In their paper, Flefel EM, et al. revealed the creation of novel spirothiazolidene auxiliaries and their combined analogues, which were made and understood using both reach and fundamental examinations. When in doubt, the heterocyclic design type had an effect on the blends' anticancer and anti-diabetic potency. Human liver and chest cell lines were used to test the mixed combinations' potential anticancer effects. Additionally, it was demonstrated that heightens, which combine amino spirothiazolopyridine-carbonitrile and parasol spirothiazolidine social occasions, had significant development against alpha-amylase and alpha-glycosidase proteins at all bits.

Additionally, three cross-assortments containing benzimidazole and thiazolidine-2,4-dione have been combined, according to analysts (Gutierrez Hernandez A, et al.), with advantages over the current antagonist of diabetic glitazone medications.

Using amylase limitation development, Manoharan D, et al. tracked down the counter diabetic effect of indoline subordinates in this audit. To create a movement of indoline subordinates, the pioneer N-(4-aminophenyl) indoline-1-carbothiamide was used. In order to verify the created compounds, Fourier-Transform Infrared Spectroscopy (FT-IR) was used. The in vitro effectiveness of manufactured indoline auxiliaries as a diabetic countermeasure was evaluated using the common amylase restriction test.

2.5. Diabetic complications

Sun L. et al. made and distributed these tyrosine kinase inhibitors, which exhibit selectivity for verifiable Receptor Tyrosine Kinases (RTKs). To replace the bioisostere, oxindole is coordinated (Sun L, et al., 1998). Few studies have been done to determine whether the removal of insulin resistance in peripheral tissues is the cause of the improvement of metabolic issues in naturally plump rodents and mice caused by M16209, a diabetic professional's enemy. The investigation of crucial requirements for thiadiazolidinone subordinates as non-ATP reliable Glycogen Synthase Kinase 3 (GSK-3) inhibitors was revealed by Castro A, et al. The main modifications of 1, 2, 4-thiadiazole are maintained, relative to one of the carbonyl parties, but additions are made independently in positions 3 and 5. The GSK-3 development of the newly created thiadiazole assistants showed IC50 respects in the micromolar range from this point on, for an extended period of time the mixtures. New spirohydantoin compounds derived from tetrahydroquinolines have been viewed as helpful in the treatment of some persistent diabetes issues.

3. Classification of Heterocyclic Compounds

We have categorised the heterocyclic compounds according to the heterocyclic atoms (N, S, O, Se...) and the number of members.

3.1. Aromaticity of heterocyclic compounds

Perhaps the most important quality in synthetic science, aromaticity is particularly interested in understanding the gem structure of heterocyclic compounds. Heterocyclic compounds power the organic cycles. To improve the quality of human existence, researchers work to understand the chemistry of heterocyclic compounds. Understanding aromatics requires a special focus on the structure and properties of heterocyclic compounds. Recently, it has become possible to lay out the sweet-smelling characteristics using quantitative aromaticity analysis, including the polycyclic combination of heterocyclic compounds.

Nanostructures and the point of chemistry and science's interaction, which is connected by heterocyclic compounds to an excessive amount of new logical exploration and use, are present in more than 90% of modern medications.

By cycloaddition reactions to the new heterocyclic compounds in the five, six, and seven areas, numerous other new heterocyclic derivatives, such as hydrazine hydrogenic and its derivatives as well as aniline and dynamic methylene substances, have been identified.

- **Medicinal significance of Heterocyclic compounds:**

There are many pharmacologically dynamic heterocyclic compounds in many common illnesses. There are countless pharmacologically dynamic heterocyclic compounds used in specific common illnesses, such as anti-toxins, herbicides, urinary germ-killers, and mitigating specialists. Some heterocycles have antitumor and anti-microbial properties as well as mitigating, stimulating, anti-malarial, anti-HIV, and post-HIV activity.

- **The biological significance of Heterocyclic compounds:**

The 5-part bull diazole core of a few heterocyclic compounds has a few beneficial organic side effects. Because of its distinctive organic behavior, moieties are important. The heterocyclic core is used in the following types of medications to treat various illnesses. Allergy medication that is immunomodulatory, pain-relieving, mitigating, antifungal, pain-relieving, local sedatives,

antiepileptic, and antimalarial. Epileptics' enemies, antiviral, and antihypertensive. Antimicrobials like Cephalosporin and Penicillin.

- **Other versatile applications of Heterocyclic compounds:**

These heterocyclic compounds have notable solvate chromic, photographic chromic, and biochemical properties. Particularly in formed polymers used in material sciences such as dyes, fluorescence, luminance, data capacity, plastic, and scientific reagents, the enormous applications of primary heterocyclic are really sub-atomic. They frequently serve as organic conduits, functional information transporters, organic light-emitting diodes, semiconductors, atomic wires, photovoltaic cells, light-gathering frameworks, and substances that can be controlled. Glassy fluid compounds.

3.2. Regulatory affairs

Regulatory Affairs (RA) professionals play a crucial role in the drug industry because they are concerned with the pattern of clinical medications' existence. They also provide political, strategic, and hierarchical direction for administrative work to make it easier to create and deliver safe and viable health products to people all over the world. It is very common and can be challenging to create and market medications due to the street to medication enlistment advertising freedom. Things are still changing.

3.3. Regulatory affairs in R&D

The administrative team creates novel products in relation to showcasing and R&D that take advantage of recent administrative and technological developments to shorten the time to market. Humble reductions in advertising time are matched by significant pay and benefit growth as a result of the anticipated expansion of new products to significant deals. Utilizing adaptable clinical investigation techniques, quick controller wiggle room, and process accident prevention can hasten the development of new products and help to prevent expensive mistakes and delays.

4. Biological Importance of Nitrogen Containing Heterocyclic Compound

4.1. Chromeo Pyrimidines

Chromeno moiety is the essential underlying element in organically dynamic and regular compounds. Alkaloids, flavonoids, tocopherols, and anthocyanins are the components of chrome. Although poly-fractionalized pyrene subordinates are a common sub-unit in a wide range of basic everyday products, including alkaloids, sugars, anti-microbials, bug sprays, and herbicides, pyrimidines continue to be a crucial area of research for scientists around the world. The extraordinary position of chrome Due to their significant natural and pharmacological properties, such as anticoagulant, spasmolytic, diuretic, and antagonistic to anaphylactic effects, 4H - Chromeno subsidiaries are a vast class of heterocyclic that have attracted enormous interest. Primary components of many common assets, 4H-Pyrans have advantageous photochemical properties. Given this important component, it is not surprising that long-term solutions to deal with these ring structures have been manufactured. Additionally, the widespread drug value of heterocycles containing nitrogen justifies our ongoing efforts to investigate engineered systems that result in structures made from the combination of heterocycles and that can provide important information on primary action relations in this area.

The researcher identified fully engineered methods in a variety of 4H-pyrene heterocyclic designs, as represented by the compound in the title that was thus used as intermediates and building blocks for additional heterocycles.

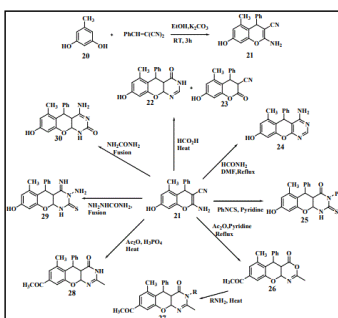


Figure: 1. Synthesis of 4 H -pyrans containing heterocycles

4.2. Chromeno- Oxadiazoles

Oxadiazole is a heteroaryl group with a wide variety of aryl groups that is occasionally used in medicinal chemistry. It is referred to as a carboxylic bio isoster and can be used in place of an ester group to produce compounds that are resistant to chemically catalysed hydrolysis. Bioisosters are also distinguished from oxydiazoles for amides and esters. Improved pharmacokinetic and in vivo productivity are frequently noted as a result of the improved bull diazole ring hydrolytic and metabolic strong qualities, turning these heterocycles into a fundamental primary theme in the pharmaceutical industry.

Heterocyclic ring framework-containing compounds have enormous mechanical and medicinal potential. Five-member ring heterocyclic with two carbon molecules, two nitrogen iotas, and one oxygen atom, also known as bull diazoles, are crucial in the fields of drug chemistry, pesticide research, polymers, and material sciences.

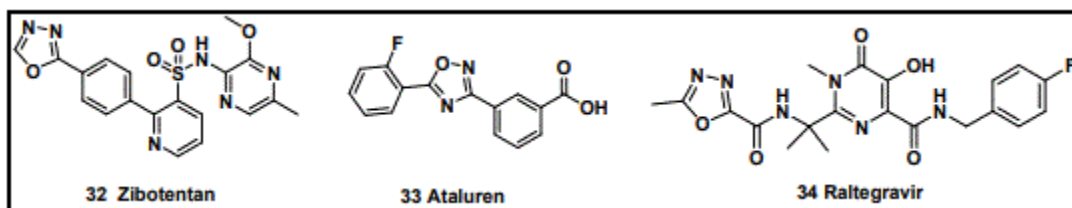


Figure: 2. Drugs containing Oxadiazole ring

4.3. Pyrazolo- ox diazole

With the adjacent nitrogen iotas, the ring's single twofold unsaturated compound—which has two nitrogen and three carbon atoms—is designated pyrazole? No pyrazole subordinates were long present in nature, but in 1959 alanine was extracted from the watermelon seeds using -(1-pyrazolyl) as a catalyst (*Citrullus lanatus*). Although tautomerism shouldn't be visible in the pyrazole itself, it can be derived into pyrazole subordinates. Pyrazole is a tautomeric substance. Among the various heterocyclic, the pyrazole groups of compounds play a significant role in medicinal chemistry. Pyrazole and its offshoots, a class of well-known heterocyclic nitrogen with

a wide range of bioactivities, are essential in medicinal chemistry and pesticide chemistry. The nitrogen heterocyclic that make up the pyrazole core exhibit significant strengths for substances that move naturally, such as analgesics, fungicides, and herbicides. Recently, dynamic pyrazolyl herbicide was identified.

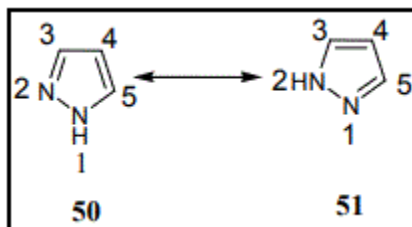


Figure: 3. Resonance structure of pyrazole

There aren't many pyrazole subordinates right away because living organic substances have a difficult time forming a N bond. The assessment of pyrazoles and their subsidiaries through combination and organic movement has been the focus of increased research due to their numerous and varied applications, as revealed in voluminous writing on the subject.

The newest oxadiazole-diarylpyrazole 4-carboxamides have been identified as ligands for the CB1 cannabinoid receptor.

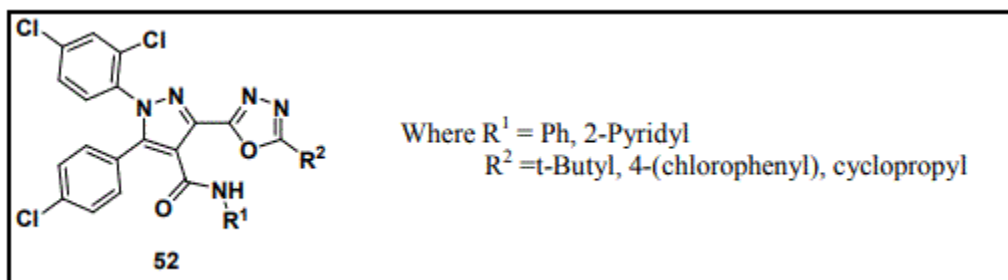


Figure: 4. Oxadiazole-diarylpyrazole 4-carboxamides

5. Conclusion

Heterocyclic chemistry is a vast field with a lot of current interest, and it should be apparent in a few exam papers in cited diaries, as well as in the abundance of monographs and investigations of different points like photochemistry, pharmacology, and the business, to name a few. Only a natural scientist is currently attempting to comprehend the progression of a sizable portion of its fundamental fields due to the difficulties this expansion in awareness and execution presents for education. To combine new particles, however, whose underlying action connections will recall applications for the clinical sciences, etc., a natural scientist can use the heterocyclic district.

One of the most common types of natural atoms in medicinal chemistry are heterocyclic compounds, which are used as medications for a variety of illnesses. Numerous significant discoveries have demonstrated the wide range of therapeutic uses for heterocyclic compounds. Due to their fascinating organic activities, heterocyclic compounds are adaptable manufactured targets and essential fundamental elements in natural combination and medicinal chemistry. The potential uses of heterocyclic as anticancer, sedative, antifungal, antibacterial, harmful to Alzheimer's, antiviral, insect diabetic specialists, etc. have sparked a great deal of interest in the pharmaceutical industry. Strangely, a growing number of heterocyclic have been identified as potential drug candidates in continuous drug development.

Despite all medical advancements, diabetes remains a major cause of illness and mortality worldwide. We have observed that efforts to combine heterocyclic subordinates known to be harmful to diabetics are ongoing in the study. The review information reveals the drug neighborhood in the path of convincing, amazing inhibitors for the treatment of diabetic mellitus with a short-term aftereffect. The physical and engineering resources necessary to gather all of the best particles for the treatment of diabetes mellitus free from the adverse effects caused by common adversaries of diabetic medications may also help advance the work.

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