

BIOLOGICAL ACTIVITIES OF HETEROCYCLIC COMPOUNDS

Dr. Seema Arora

Department of Chemistry , S P N K S Gov. P G College Dausa

ABSTRACT

In the field of organic chemistry, heterocyclic compounds are considered to be of great importance owing to the amazing structural variety they possess and the extensive range of biological activities they exhibit. Because of their capacity to interact with a wide variety of biological targets, these compounds have become crucial in the area of medicinal chemistry. As a result, they are useful agents in the treatment of a wide variety of disorders. The basic structures of many pharmacological drugs are heterocycles, which contribute to the therapeutic potential of these agents in the treatment of disorders such as cancer, epilepsy, inflammation, fungal infections, bacterial diseases, and allergies. The biological relevance of these substances extends to agrochemicals and industrial uses as well. These substances are used as important components in the production of antioxidants, disinfectants, dyes, and corrosion inhibitors. This research sheds light on the significant part that heterocyclic compounds play in the process of drug discovery and development by concentrating on the many and powerful biological actions that they exhibit. The findings of this study highlight the significance of heterocycles as adaptable scaffolds in the process of developing innovative therapeutic medicines. This is accomplished by conducting an exhaustive investigation of current advancements and applications.

Keywords: Heterocyclic compounds, Biological activities

1. INTRODUCTION

The inclusion of a heteroatom, which is often nitrogen, oxygen, or sulphur, inside the ring structure of a heterocyclic compound is what makes it one of the most significant and diverse forms of organic compounds. These compounds are essential to the production of a wide variety of natural and man-made products, medicines, and biomolecules. The presence of heteroatoms has a significant impact on the physical, chemical, and biological properties of these compounds. This is due to the fact that heteroatoms possess different electronic and steric properties. Heterocyclic molecules are crucial in several subfields of biochemistry because to the wide range of structures that they possess. These subfields include medicinal chemistry, agrochemicals, biotechnology, and materials science, amongst others.

A significant amount of interest in the area of medicinal chemistry as a whole has been generated by the amazing ability of heterocyclic compounds to exert control over essential biological processes. This interest has also been fuelled by the biological activity of these compounds. When they interact with certain molecular targets, such as enzymes, receptors, ion channels, and nucleic acids, they often produce powerful pharmacological effects. Anti-inflammatory, anti-fungal, anti-cancer, antiviral, and antidiabetic are some examples of the traits that fall under this category. Some examples of drug classes that use heterocyclic scaffolds are β -lactam antibiotics (such penicillins and cephalosporins), antivirals based on purine, antibiotics belonging to the quinolone class, and anti-tubercular medications based on pyridine. These are

some of the most important medication classes that are utilised today. Because of their efficacy and the precision with which they target the disease, they are essential in the treatment of a wide variety of disorders.

The pharmacologic and pharmacokinetic properties of heterocyclic medicines, such as receptor affinity, metabolic stability, bioavailability, and solubility, may often be fine-tuned by the application of subtle modifications to the heterocyclic core. The fact that they are so versatile makes them attractive scaffolds for use in the production of drugs and platforms for high-throughput screening platforms. Nitrogen-containing rings with five or six members, such as imidazole, pyridine, and thiazole, are used extensively as building blocks in the pharmaceutical industry. This is due to the fact that these rings are biologically significant and can be easily synthesised. Furthermore, the fact that these compounds often perform the functions of enzyme inhibitors, receptor antagonists, or DNA-interacting agents demonstrates that they have the potential to be used as multitargeted therapeutic agents.

In addition to their application in the medical field, heterocyclic compounds are also used in agriculture as fungicides, herbicides, and insecticides, where they have a significant influence on the biological processes involved. Due to the fact that they protect plants from a wide variety of diseases and boost agricultural output, they are completely necessary for ensuring food security. In addition, it is hard to disregard the importance that they have in the field of materials research. In the production of organic semiconductors, liquid crystals, and fluorescent dyes, which are used in imaging and sensor technologies, heterocyclic systems constitute an essential component.

Recent advancements in computational chemistry, molecular docking, and quantitative structure-activity relationship (QSAR) modelling have made it much simpler to optimise and rationally build heterocyclic compounds that exhibit biological activity. This has made the process of designing these compounds even more straightforward. When these technologies are utilised to foresee how heterocyclic compounds will interact with biological targets, there is less of a need for rigorous trial-and-error procedures in the process of developing new drugs. In addition, novel heterocyclic scaffolds that have acceptable pharmacological profiles have been swiftly found using the integration of bioinformatics and cheminformatics, which has allowed for the discovery of new medicinal procedures that go beyond the limitations of the present methods.

In spite of these developments, research into novel heterocyclic compounds that have better or unique biological activity is continuing to make significant progress. Extensive study into their potential therapeutic applications, structure-activity correlations, and action mechanisms ought to result in the development of innovative medications for the treatment of complex and developing illnesses. In spite of the fact that the global ailment burden is shifting, it is predicted that heterocyclic compounds will continue to play a crucial part in the pipelines of cutting-edge medication development.

2. OBJECTIVES

1. To look into the pharmacological potential and biological characteristics of heterocyclic molecules.
2. To investigate how heterocyclic chemicals may be used to create medicinal medicines.

3. METHODOLOGY

To study the methods of manufacturing and biological uses of heterocyclic compounds, a thorough and methodical approach is used. To kick out the research process, a comprehensive literature evaluation is conducted using prestigious scientific databases including Web of Science, PubMed, and Scopus. Careful searches of these databases provide patents, peer-reviewed studies, and news about current developments in heterocyclic chemistry. To provide a complete picture of the area, the review covers both past and present achievements. A variety of synthetic methods for building heterocyclic frameworks are investigated in the research. Green chemistry procedures, microwave-assisted synthesis, metal-catalyzed transformations, multicomponent reactions (MCRs), and conventional cyclisation reactions are all part of this category, along with more contemporary and environmentally friendly approaches. The beginning materials, catalysts, solvents, temperature, pressure, reaction time, and total yield of each synthetic technique are analyzed. The benefits and drawbacks of each method are examined, drawing attention to their usefulness in both academic and commercial contexts. There is a strong focus on making sure the synthetic processes are efficient, scalable, and environmentally friendly. An evaluation of the environmental effect of heterocyclic compound manufacturing is conducted via the integration of green chemistry concepts. These principles include decreased waste creation, use of non-toxic reagents, and energy-efficient procedures. To further clarify their structural variety, the technique incorporates heterocycle categorization according to ring size, heteroatom kinds, and substitution patterns. This work takes a multipronged strategy, which allows it to both record the present status of heterocyclic synthesis and prove a causal relationship between synthetic methods and the biological effects of the resultant molecules. Future developments in medicinal chemistry may be advanced with the help of this analytical approach, which identifies interesting heterocyclic structures with prospective pharmacological uses.

4. RESULT

Medical chemistry relies on macromolecules like enzymes, vitamins, natural products, and physiologically active chemicals that include heterocyclic compounds.[1-8]

1. Antifungal activity

There might be a single cell or several cells in a fungal organism. The great majority of them live in habitats that are either plant-based or terrestrial. Few fungi have the potential to really cause sickness in mammals. Mould and yeast are also examples of fungal creatures. When grown on agar medium, mould, which has long cell units, expands by budding and forming new cell branches. Yeast, on the other hand, may form colonies that are round, oval, or mucosid. The purpose of antifungal treatment is to eliminate fungal cells by modifying their membranes in such a manner that either kills the contents of the cell or causes the contents to leak out of the cell. It is for S.V. Using fluconazole as a positive control, Blokhina et al. [9] developed new thiazole [4,5-d] pyrimidine derivatives and (1H-1,2,4)-traizol, and then investigated the antifungal efficacy of these compounds in vitro against a variety of different cultures (Fig. 1). It is Miss L.S. Through the use of fluconazole as a positive control and the application of different doses, Ming et al. [10] were able to develop heterocyclic chalcones based on thiophene that demonstrated antifungal activity against fungus (Fig. 2). Mr. Charles K. For the purpose of their research, Ryu and colleagues [11] developed heterocycles of benzo-[d]oxazole-4,7-iones and examined the antifungal effects of these compounds on pathogenic fungi. They compared their findings to those obtained with 5-fluorocytosine, which is a typical drug that is often used (Fig. 9).

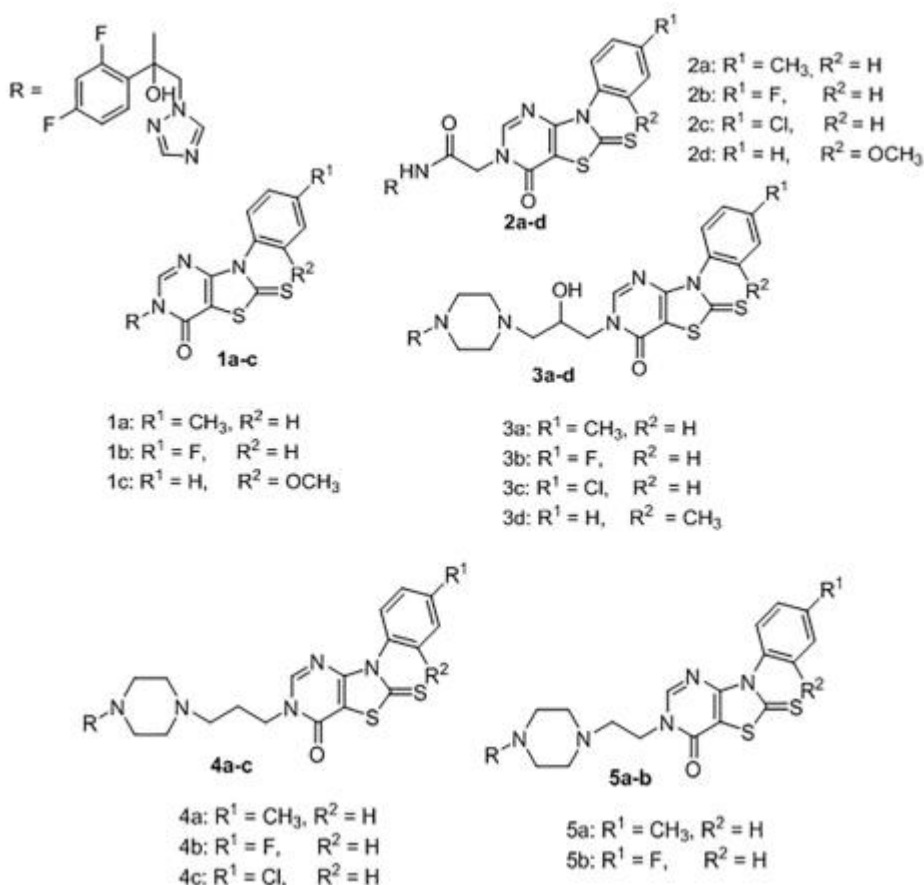


Figure 1. Thiazole [4,5-d] pyrimidine derivatives having (1H-1,2,4)-traizol structures.

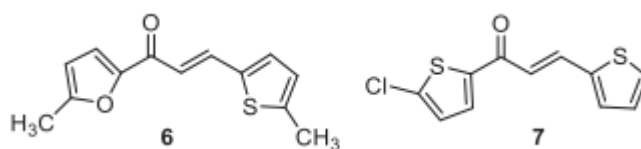


Figure 2. Thiophene-based heterocyclic chalcone structures.

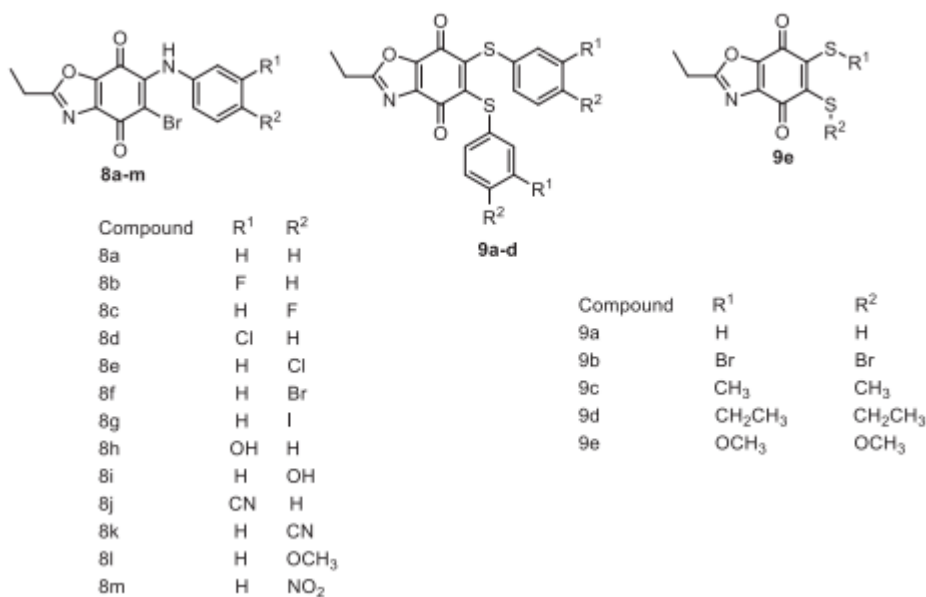


Figure 3. Benzo-[d]oxazole-4, 7-ione heterocycle structures.

2. Anti inflammatory activity

Any pharmaceutical material that has anti-inflammatory effects is considered to be an anti-inflammatory agent, according to one definition. Anti-inflammatory drugs make up almost half of all analgesics. Opioids, on the other hand, are pharmaceuticals that have an effect on the central nervous system. As a result of their ability to reduce inflammation, they mitigate discomfort. Some of the most widely used and effective anti-inflammatory medications are aspirin, ibuprofen, diclofenac, and ketoprofen. Naproxen is another common medication. The term "non-steroidal anti-inflammatory drugs" (NSAIDs) is used to refer to these kinds of chemicals. As a result of chronic usage of nonsteroidal anti-inflammatory medicines (NSAIDs), a disease known as gastro intestinal erosion (GIT) may develop, which can result in the development of peptic ulcers. NSAIDs, both those available by prescription and those available without a prescription, are also associated with an increased risk of heart attacks. A number of novel heterocyclic derivatives of furan, pyrrol, 4-oxabutanamide, 1-phenyl-1,4-dihydropyridazin-3(2H)-one, 4-oxo-butanehydrazide, 1H-pyridazin-6-one, 3-(3,4-dichlorophenyl)- 1Hpyridazin-6-one, and 3-(2-thioxo-4,5-dihydro-1,3,4-oxadiazol-5-yl)but-3-en-1-one were synthesised by E. I. Hameed and colleagues [12]. They then tested the anti-inflammatory properties of all of the drugs that they had synthesised, as shown in Figure 4. Following the synthesis of the pyrano[2,3-d] pyrimidine analogues by Abdel azim et al. [13], the researchers compared the anti-inflammatory effectiveness of these compounds to that of celecoxib, the medicine considered to be the gold standard. According to the findings shown in Figure 5, the investigation demonstrated that chemicals 17 and 21 exhibited a significant inhibition of cyclooxygenase-2 (COX-2) enzymes, lipoxygenase (LOX) enzymes, and tumour necrosis factor alpha (TNF- α) enzymes, hence showing a powerful anti-inflammatory activity in vitro.

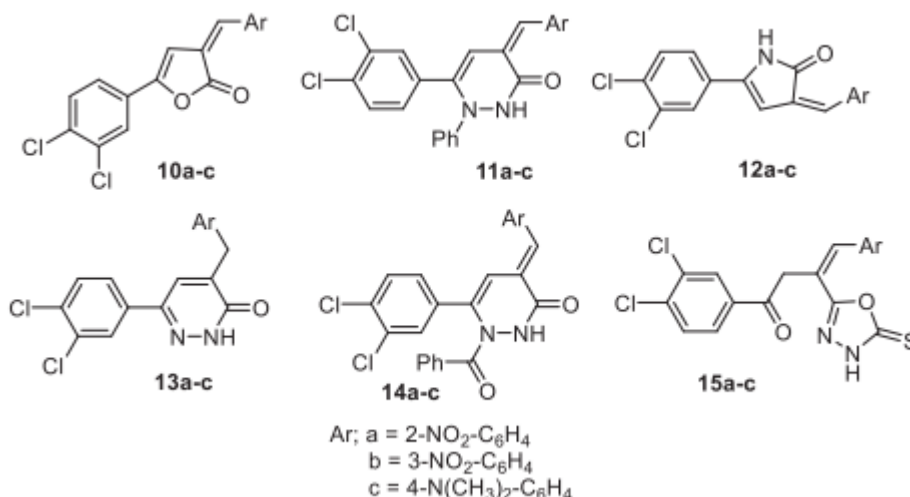


Figure 4. Furan, pyrrol structures 4-oxabutanamide, 1-phenyl-1,4-dihydropyridazin-3(2H)-one, 4-oxo-butanehydrazide, 1H-pyridazin-6-one, 3-(3,4-dichlorophen -1Hpyridazin-6-one, But-3-en-1-one derivatives of 2-thioxo-4,5-dihydro-1,3,4-oxadiazol-5-yl

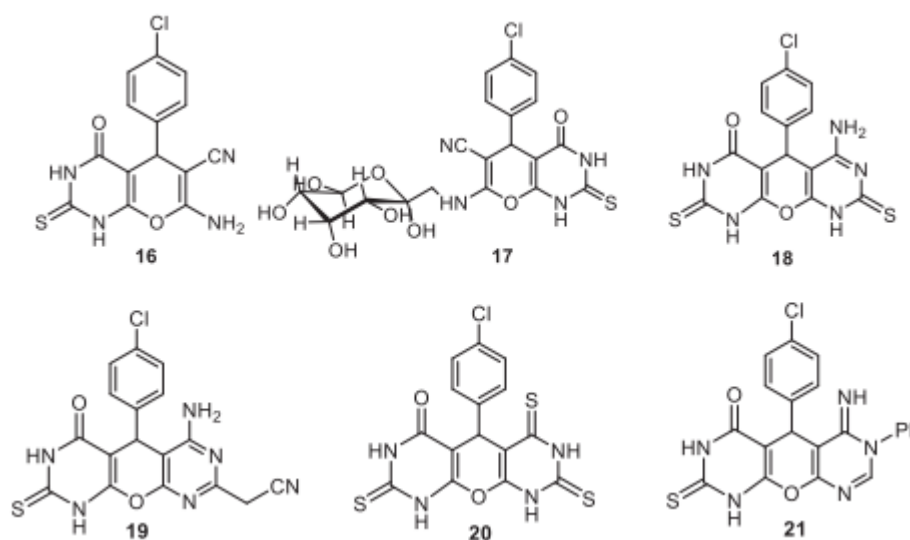


Figure 5. Pyrano [2,3-d] pyrimidine derivative structures.

3. Antibacterial activity

Chemicals that inhibit the growth of pathogenic microorganisms are referred to be antibacterial or antimicrobial substances. By misusing antibiotics, there is a possibility that microbes may become more resistant to them. There are aromatic heterocyclic compounds that constitute a component of the chemical structure of antibiotics. These molecules include -lactam derivative compounds. In the treatment of a wide variety of common illnesses, there are a few compounds that seem to possess all of these features, and tests conducted on a number of different kinds of bacteria have showed positive results. Two experiments were conducted to investigate the antibacterial properties of coumacine and its derivatives. The first study focused on aerobic bacteria and compared the performance of these compounds to that of ciprofloxacin,

which served as a positive control. The second study focused on anaerobic bacteria and used metronidazole as a positive reference. In their study [14], Y. F. Mustafa and colleagues were successful in synthesising the novel heterocycles of coumacin derivatives. Figure 6 demonstrates that both analogues were believed to be effective antibacterial agents until recently. T. D. Tran and colleagues [15] used the Claisen Schmidt condensation technique in order to synthesise the derivatives of heterocyclic chalcones. For the purpose of screening all medications, the methicillin-sensitivity of bacteria that were derived from a human sample was used (Fig.7). 23e, 24f, and 25e were the compounds that, when coupled with oxacillin and vancomycin, had the highest potential for inhibiting the growth of methicillin-resistant *Staphylococcus aureus*. Using this, it is possible that new drugs that treat infections caused by *Staphylococcus aureus* may be produced.

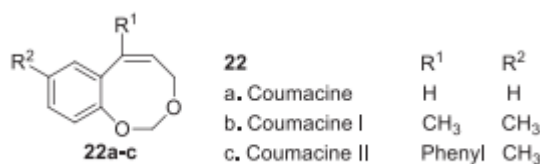


Figure 6. Coumacin derivative structures.

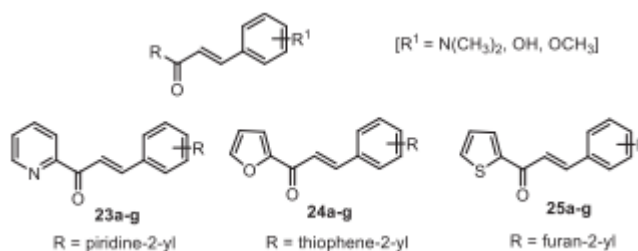


Figure 7. Heterocyclic chalcone derivative structures.

4. Antiviral activity

At their core, viruses are RNA or DNA strings bonded together by a protein covering, which may or may not include lipids. The immune response to viruses may manage illness or cause major health issues or death. Doctors employ antivirals to treat viruses. A. E. Hameed et al. [16] tested their synthesised pyridazinones for antiviral activity in Figure 8. Rotavirus and adenovirus were tested. A. Gigante et al. [17] found CHIKV-fighting properties in synthesised [1,2,3] triazolo[4,5-d]pyrimidin-7 (6H)-ones (Fig. 9). F. M. Almutairi et al. [18] developed 8,9-dihydro-4H-thieno[2,3-g]-chromene derivatives to fight COVID-19 and examined their antiviral activity in relation to Mpro, SARS-CoV-2's major protease. Figure 10 demonstrates that medicinal chemistry has focused on the halogenated heterocyclic compounds 31a, 31b, 31c, 31e, 31f, 31g, and 31h due to their high SARs-COV nsp 14 and COVID-19 inhibition. M. Horchani et al. [19] created heterocyclic compounds from Pyrazolopyrimidinone. Pyrazolopyrimidinone coupled to 2,5-pyrrolidinedione and unconjugated carboxylic acid inhibited Omicron SARS-CoV-2 (Fig. 11). Spectral and micro-analytical data support N. H. Zaher et al.'s synthesis of new halogenated triazole compounds [20]. Researchers tested compounds 46 and 50 for MERS-CoV helicase resistance (Fig. 12). T. K. Venkatachalam et al. [21] synthesised and tested several thiazolyl thiourea derivatives, which

suppressed HIV replication with sub-nanomolar IC₅₀ values, were mildly toxic to PBMC, and had CC₅₀ values from 28 to >100 g. The most effective chemical was N-[1-(1-furoylmethyl)]. N'-[2-(thiazolyl)] thiourea (51f) was more effective than nevirapine, delavirdine, HI-443, and HI-244 against both wild-type and NNRTI-resistant HIV-1 isolates (A17 and A17 variant) at nano-molar to small micro-molar concentrations (Fig. 13). Its selectivity index exceeded 100,000. A. S. Sokolova et al. [22] synthesised new nitrogen and sulphur heterocycles such 1,3-thiazolidin-4-one and thiazoles coupled to a 1,7,7-trimethylbicyclo[2.2.1]heptan framework and studied Orthopoxvirus antiviral potential. The bioassay demonstrated that replacing 52b, 52c, and 52e thiazoles with benzene rings may suppress Orthopoxvirus reproduction with IC₅₀ values of 2.4 to 3.7 micro-molar and average cytotoxicity. Thiazolidin-4-one derivative (55b) inhibits well with an IC₅₀ of 9.5 M and low toxicity (Fig. 14).

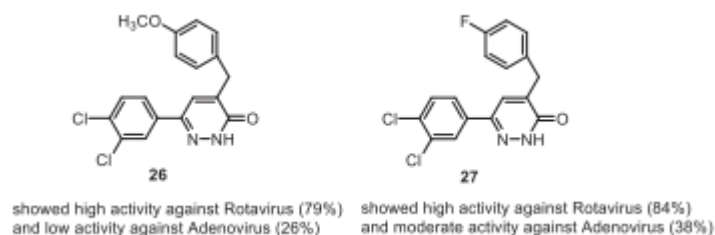


Figure 8. Structures of pyridazinones.

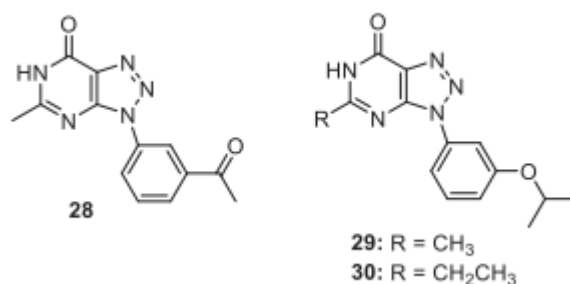
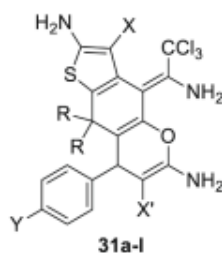


Figure 9. [1,2,3] triazolo[4,5-d]pyrimidin-7(6H)-one structures.



10	a	b	c	d	e	f	g	h	i	j	k	l
R	H	H	CH ₃	CH ₃	H	H	CH ₃	CH ₃	H	H	CH ₃	CH ₃
X	CN	CN	CN	CN	CN	CN	CN	CN	CN	CN	CN	CN
Y	H	H	H	H	Cl	Cl	Cl	Cl	OCH ₃	OCH ₃	OCH ₃	OCH ₃
X'	CN	HCOOEt	CN	HCOOEt	CN	HCOOEt	CN	HCOOEt	CN	HCOOEt	CN	HCOOEt

Figure 10. Structures of 8,9-dihydro-4H-thieno[2,3-g]-chromene.

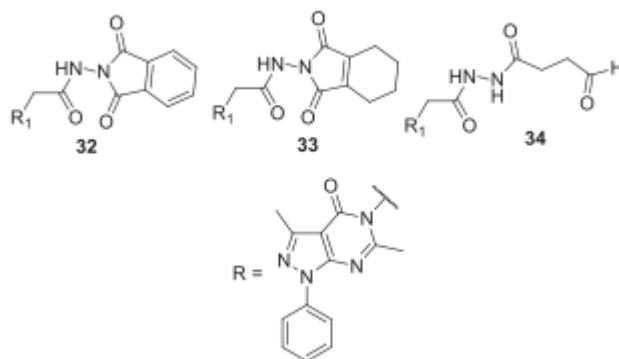


Figure 11. Structures of heterocycles derived from Pyrazolopyrimidinone

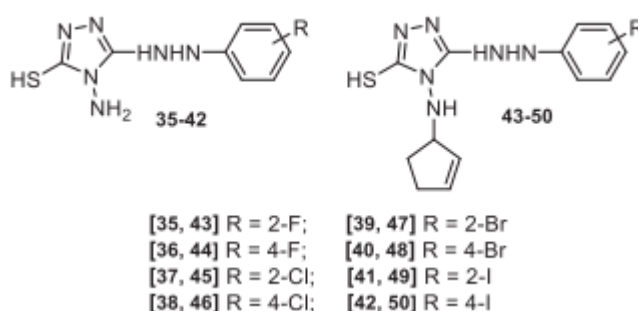


Figure 12. Structures of halogenated triazole derivatives.

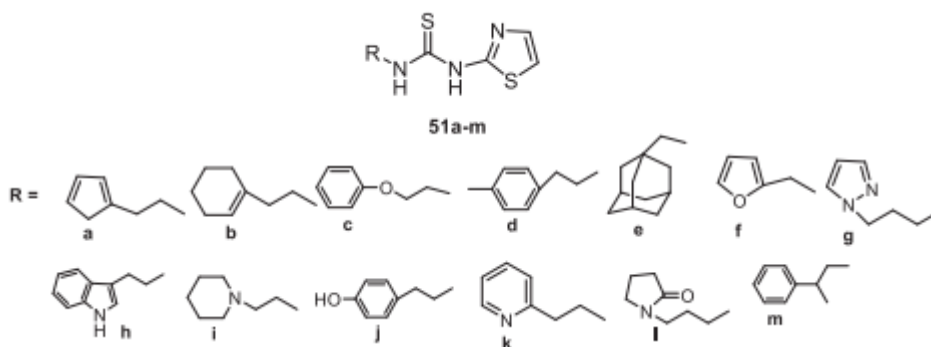


Figure 13. Structures of thiazolyl thiourea derivative

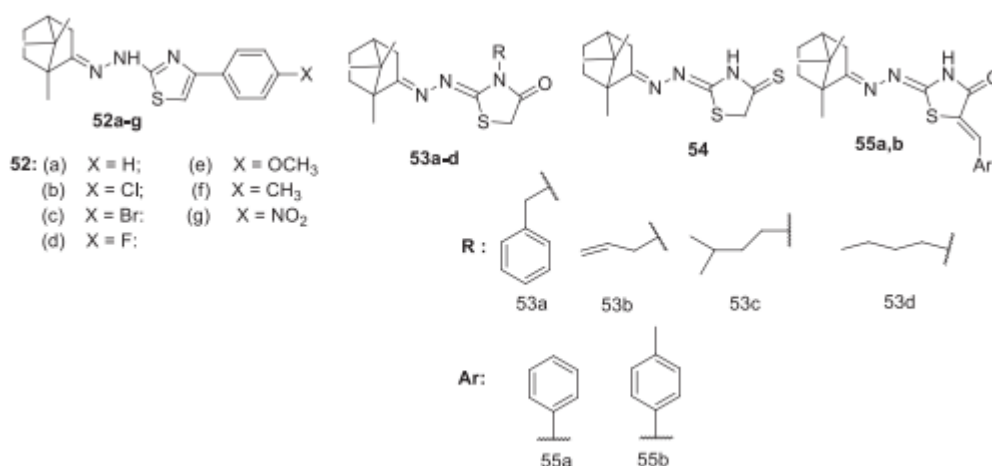


Figure 14. Structures of 1,7,7-trimethylbicyclo-[2.2.1]heptan-2-ylidene)hydrazinyl)thiazole (52a-g), 1,7,7-trimethylbicyclo[2.2.1]heptan-2-ylidene)hydrazono) thiazolidin-4-one (53a-d), 1,7,7-trimethylbicyclo[2.2.1]heptan-2-ylidene)-hydrazinyl)thiazole-4(5h)-thione (54) and 1,7,7-trimethylbicyclo[2.2.1]heptan-2-ylidene)hydrazinyl)thiazol-4(5h)-one (55a,b) derivatives.

5. CONCLUSION

Heterocyclic compounds are an important class of organic molecules due to the fact that they possess a wide range of structural variations and a significant amount of biological activity. Because of their wide variety of applications, particularly in the field of medicinal chemistry, they have the potential to be used as important components in the production of therapeutic drugs that are antibacterial, antiviral, antifungal, anti-inflammatory, and anticancer. They are an important instrument in the area of modern pharmacological research and drug development due to the fact that they are capable of binding to a wide variety of biological targets, including enzymes, receptors, nucleic acids, and other biological targets. Additional evidence of their significance in contemporary medicine is shown by the fact that they are included into a large number of drugs that have been approved for use in clinical settings. The investigation of novel heterocyclic structures and the biological possibilities that they provide will continue to be an essential aspect of pharmaceutical research for as long as there is a need for treatments that are safer, more precise, and more effective. The future of heterocyclic chemistry lies on expanding the chemical space of these compounds and gaining a deeper knowledge of the biological tasks they perform. This pursuit will ultimately result in the development of next-generation medical advancements.

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