

Review Article

A Mini Review: Biological Significances of Nitrogen Hetero Atom Containing Heterocyclic Compounds

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Abstract: Heterocycles have vital interest in the pharmaceuticals and agrochemicals. Synthetic chemistry provides wealth of heterocyclic systems. More than 90% of drugs contain heterocycles ring and the interface between chemistry and biology. Scientific insight, discovery and applications are taking place by heterocyclic compounds. This review article covers the active heterocycles that have shown considerable biological actions such as antimicrobial, anti-inflammatory, analgesic, cardiovascular, neurological, antiallergic, herbicidal, and anticancer and various other useful activities.

Keywords: Heterocyclic Compounds, Biological Activities, Medicinal Drugs

1. Introduction

Medicinal chemistry had its beginning when chemists, pharmacist and physicians isolated and purified active principles of plants and animals tissues and taken from micro-organism and their fermentation products. These compounds have been associated with therapeutic properties: Medicinal chemistry which has leaned on the classical fields of chemistry, especially organic chemistry and biology. Various natural and synthetic compounds are serving directly as therapeutic agents and some other uses in agriculture. Most of the drugs belong to the class of heterocyclic compounds. These heterocyclic compounds played a vital role in the metabolism of all living cells; large numbers of them are five and six membered heterocyclic compounds having one, two and three hetero atoms in their nucleus. The compounds may be pyrimidine and purine basis of genetic material DNA, and these heterocyclic compounds may be isolated or fused heterocyclic systems. Some of the common heterocyclic compounds used in the medicines are as amino acids like proline, histidine and tryptophan, the vitamins and coenzymes precursors such as thiamine, riboflavin, pyridoxine, folic acid, biotin, vitamin B₁₂ and vitamin E. There are various pharmacologically active heterocyclic compounds, many of which are in regular clinical use. The pyrimidines and its derivatives have vital role in biological properties like

2-Sulphanilamidopyrimidines (Sulphadiazine, Sulpha-methoxy-diazine and Sulphadiazine) are well known antibacterial agents. Pyrimidinetrinitrones commonly known as barbituric acids have important role in the biological field. The 5-alkylated pyrimidinetrinitrones have show antispasmodic, muscle relaxant and anticonvulsant activity. Substituted oxadiazoles have shown different types of biological activities such as antimitotic, analgetic, diuretic, antiemetic, hypnotics, sedative and antidiarrhael agents etc [1-10].

2. Biological Activities of Heterocyclic Compounds

The largest and one of the classical divisions of organic chemistry is heterocycles. Heterocycles are of immense importance not only biologically but also industrially. The majority of pharmaceutical products that mimic natural products with biological activity are heterocycles. There were approximately 20 million chemical compounds identified by the end of the second millennium, more than two thirds were fully or partially aromatic and approximately one-half were hetero aromatic. The heterocyclic chemistry provides an

inexhaustible resource of novel compounds [11-18].

2.1. Antifungal Activity

Fungi are heterotrophic microorganisms that are distinguished from algae by lack of photosynthetic ability. A fungus includes both yeast and moulds. The former are spherical, oval and mucosid colonies in agar medium and the latter consists of elongated cells that usually reproduce by budding and forming branches of cells.

2.2. Analgesic and Anti-inflammatory

Non-steroidal anti-inflammatory drugs (NSAIDs) refer to the property of a substance or treatment that reduces inflammation. NSAIDs make up about half of analgesics, remedying pain by reducing inflammation as opposed to opioids, which affect the central nervous system. Some common examples of NSAIDs are: aspirin, ibuprofen, and naproxen. The newer specific COX-inhibitors- although, it is presumed, sharing a similar mode of action is not classified together with the traditional NSAIDs. Apart from aspirin, prescription and over-the-counter NSAIDs also increase the risk of myocardial infarction and stroke.

2.3. Antibacterial Activities

Bacteria are the simplest and smallest unicellular organisms found individually or in clusters. The multitudes of highly effective and relatively non-toxic drugs available for the treatment of bacterial infections have provided tough competition for the medicinal chemist, attempting synthesis of new antibacterial agents.

2.4. Neurological Activities

Various heterocyclic agents prevent the convulsions, depression, psychosis, anxiety and other CNS related disorders.

2.5. Antiallergic Activities

Various heterocyclic compounds have shown the antiallergic activity.

Herbicidal activity: These are the drugs which destroy the unwanted plants along with some grasses without affecting the food crops. Some substituted heterocyclic systems posses this activity.

2.6. Anticancer Activity

Anticancer refers to a group of disease caused by several agents like as chemical compound, radiant energy. Cancer is characterized by an abnormal & uncontrolled division of cell exhibiting varying degree of malignancy which produce tumor and invade adjacent normal tissue. These agents are used for treatment of cancer or either kill cancer cells or modify their growth.

2.7. Cardiovascular Activities

Various heterocyclic agents prevent the hypertension,

arrhythmia, angina, congestive heart failure, anti-hyperlipidemics, anticoagulant and other cardiovascular related disorders. Substituted heterocycles form a core of vast number of biologically active natural and non-natural compounds. The driving force in the field of synthetic organic chemistry is the heterocycles. The synthesis of various biologically active heterocycles, especially the triazoles, imidazole, benzimidazole, pyrrole/ pyrolidine, pyrimidine, pyrazole, pyranochromene and pyridazine are important. In short there importance can be stated as [1, 2]

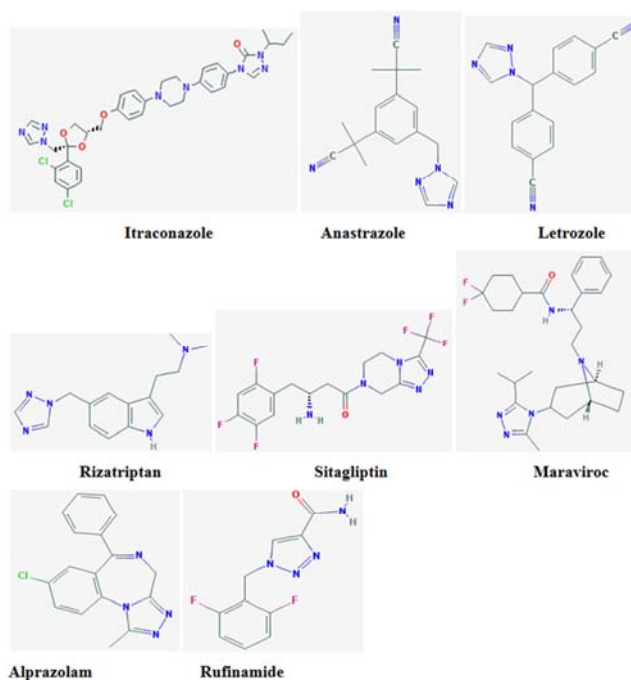


Figure 1. Structure of various triazole ring containing drugs.

3. Triazole

The triazole and its derivatives constitutes an important class of heterocycles that find pivotal position especially in medicinal chemistry due to their varied biological activities as potent antimicrobial, analgesic, anti-inflammatory, local anesthetic, anticonvulsant, antimalarial, and anti-HIV agents. The top selling active pharmaceutical ingredients comprise of triazoles nucleus are itraconazole, anastrozole, rizatriptan, letrozole, sitagliptin, maraviroc, alprazolam and rufinamide.

4. Imidazole

The imidazole ring forms the core of many pharmacologically important molecules. The imidazole derivatives are found naturally, in the amino acid histidine, Vitamin B12, a component of DNA base structure. Imidazole is an important class of heterocyclic molecule having wide array of activities like anticancer, antimicrobial and antioxidant. The top selling active pharmaceutical ingredients comprise of imidazole nucleus are Losartan, Olmesartan and ondasetron.

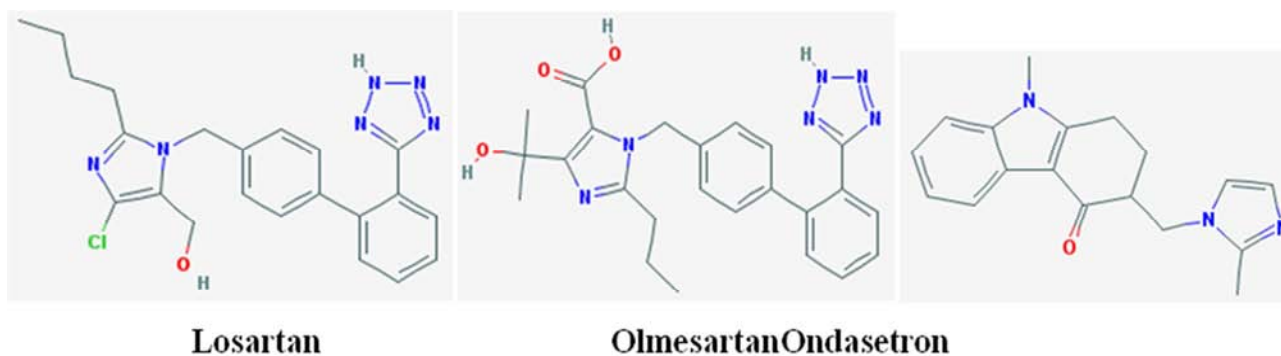


Figure 2. Structure of various imidazole ring containing drugs.

5. Benzimidazole

The benzimidazole and their analogues are considered as important bioactive heterocycles found to possess a wide range of biological activities, such as anticancer, antiHIV, antiulcer, antihypertensive, antibacterial, anti-inflammatory, antihistamine, antioxidant, antiproliferative, antiallergic. The top selling active pharmaceutical ingredients comprise of benzimidazole nucleus are telmisartan, esomeprazole, pantoprazole and candesartan.

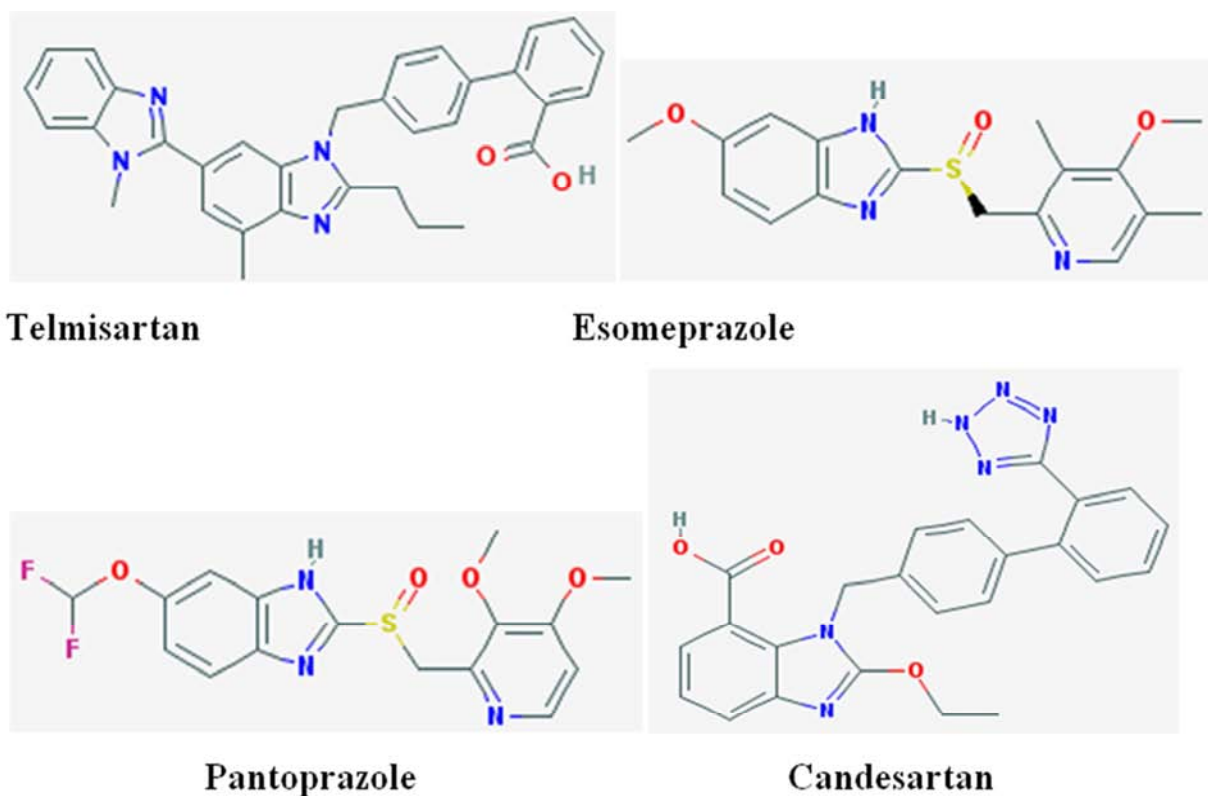


Figure 3. Structure of various benzimidazole ring containing drugs.

6. Pyrroles

Pyrroles are an important class of organic compounds, found in many natural products like heme, chlorophyll, bile pigments and vitamin B₁₂, contain functionalized pyrroles subunits as the building blocks. Pyrrole is an important

heterocyclic ring explored mainly after the discovery of the blockbuster atrovastatin and many compounds containing it exhibit interesting biological activities such as antibacterial, antifungal, anti-inflammatory, antioxidant and antitumor effects. The top selling active pharmaceutical ingredients comprise of pyrrole nucleus are, Atrovastatin, Sunitinib, fluvastatin, rosuvastatin, nitrofurantoin and pitavastatin.

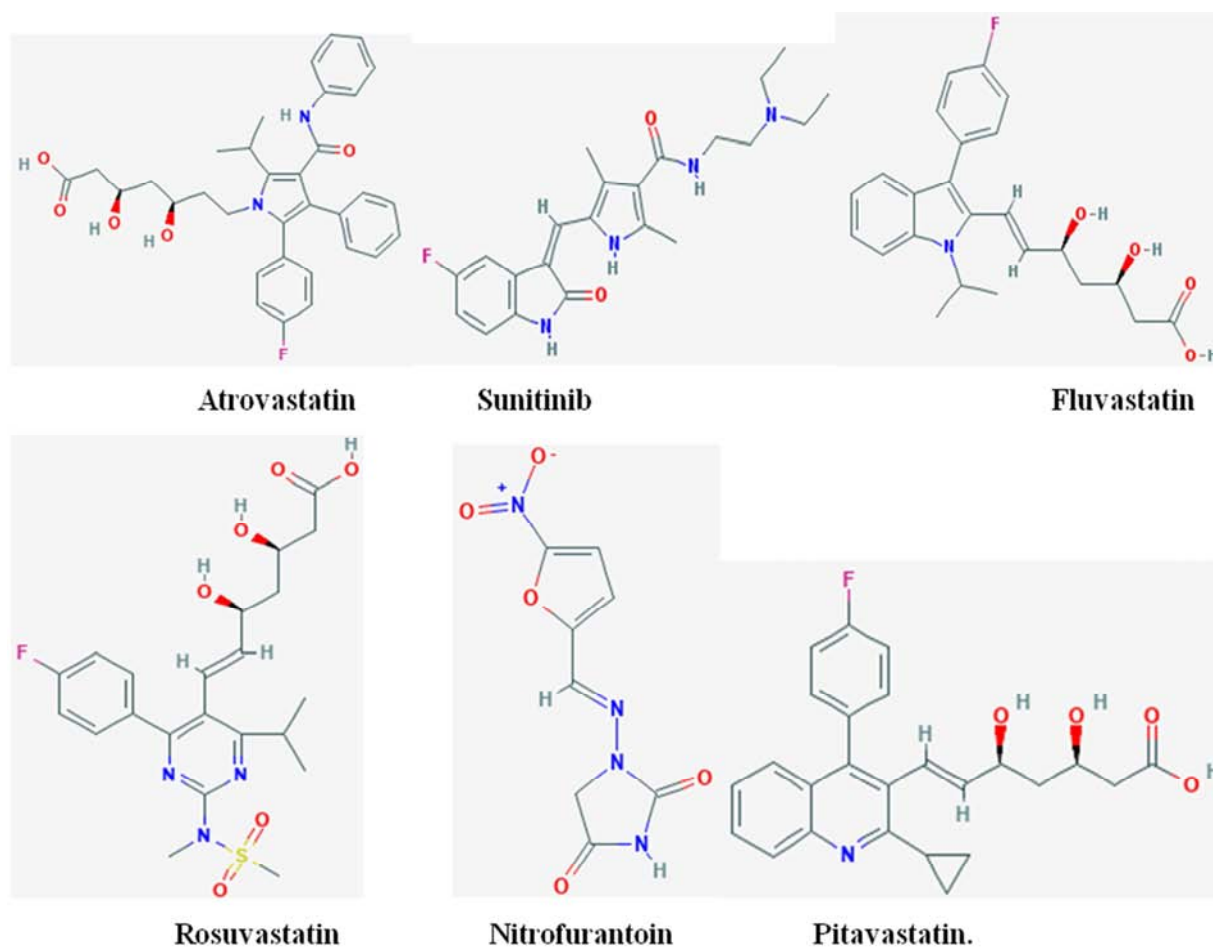


Figure 4. Structure of various pyrrole ring containing drugs.

7. Pyrimidine

Pyrimidines and their analogues are considered as important bioactive heterocycles exhibiting interesting biological activities like antiviral, antiinflammatory and muscarinic agonist activities. Tetrahydro-pyrimidine is an important heterocyclic ring responsible for salt and heat sensitivity of protein–DNA interactions. The top selling active pharmaceutical ingredients comprise of pyrimidine nucleus are, 5-fluoro flucytosine, Floxuridine, Lopinavir, Lamivudine, Zidovudine, Pyrimethamine and Minoxidil.

8. Pyrazole

Pyrazoles are possess a wide range of agricultural and pharmaceutical activities. Pyrazoles have wide range of application in polymer chemistry, food industry, cosmetic colorings and as UV stabilizers. The pyrazole nucleus is present in top selling drugs such as Celecoxib, Remonabant and Sildenafil citrate.

9. Pyridazine

The Pyridazine derivatives constitutes framework of the molecule used in herbicides such as credazine, pyridafol and

pyridate. It is also an important pharmacophore of top selling pharmaceutical drugs such as, Azelastine, Ameziniummetalilsulfate, Emorfazone, Cadralazine, Hydralazine, Minaprine and Sulfamethoxypyridazine. Pyridazine molecule and its derivatives are also known to possess a wide range of biological activities, such as anticancer, antiviral, antituberculosis, antidepressant, analgesic, antimicrobial and in platelet aggregation.

10. Coumarin

Coumarin and its analogues form an interesting class of heterocyclic compounds. Coumarin is used as a precursor molecule in the pharmaceutical industry for the synthesis of a number of anticoagulant pharmaceuticals, the notable one being warfarin. The analogues of coumarin, pyranochromenes have also attracted considerable interest due to their biological activities such as spasmolytic, anticoagulant, anticancer, antianaphylactic, antioxidant, diuretic and anti-HIV activity. The coumarin nucleus is present in pharmaceutical drugs such as Warfarin, Acenocoumarol, Dicoumarol, ethyl biscoumacetate, Phenpro-coumon. The popular rodenticides used having the coumarin nucleus are couma-tetralyl, difenacoum, flocoumafene, bromadiolone, coumatetralyl and tiocoumarol.

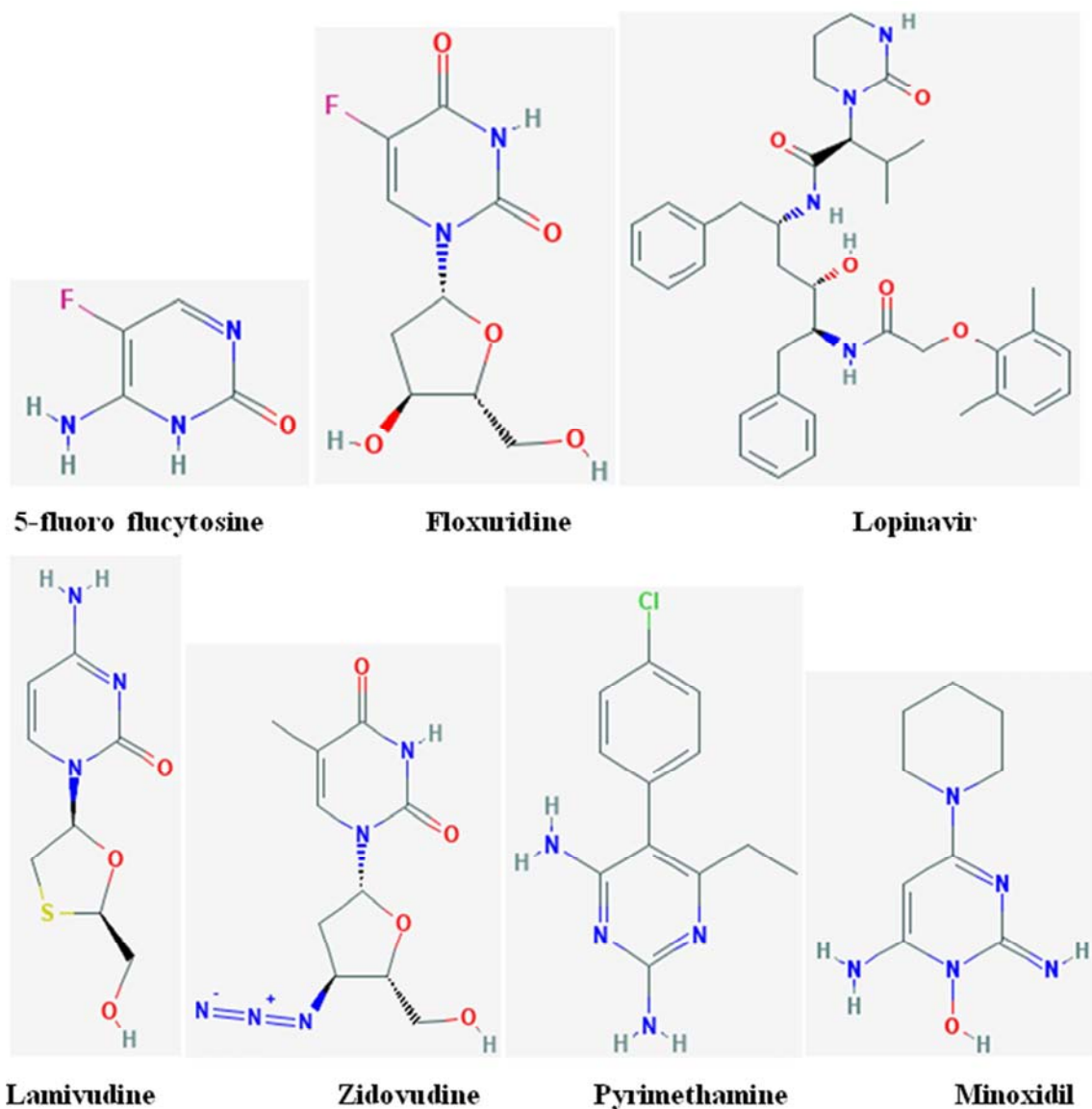


Figure 5. Structure of various pyrimidine ring containing drugs.

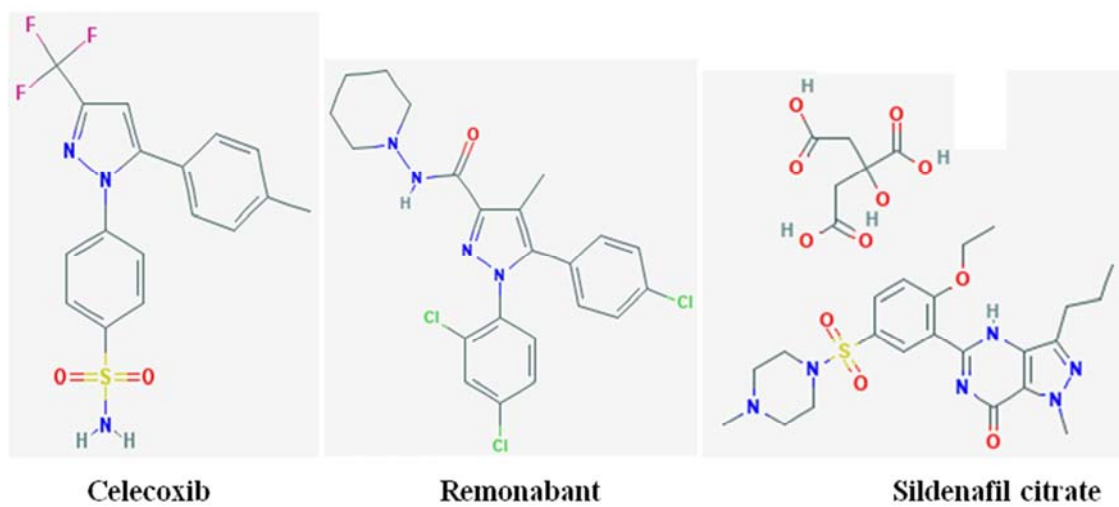
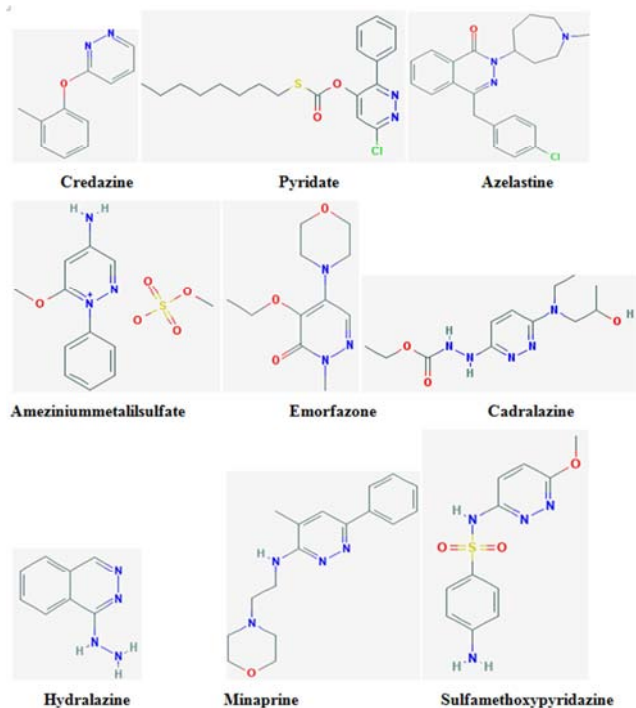


Figure 6. Structure of various pyrazole ring containing drugs.



Oxygen containing heterocyclic compounds.

Figure 7. Structure of various pyridazine ring containing drugs.

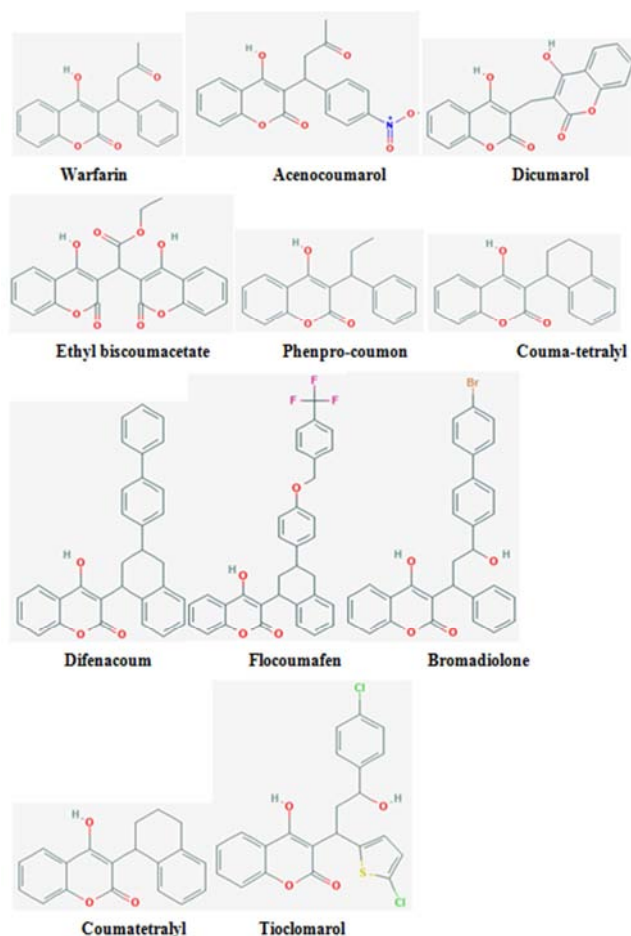


Figure 8. Structure of various coumarin ring containing drugs.

11. Conclusion

Literature survey shows that a number of heterocyclic compounds having condensed ring system possess various types of physiological activities [19-22]. Various heterocyclic derivatives are exhibit various pharmacological activities such as antimicrobial, anti-inflammatory, analgesic, neurological, antiallergic, herbicidal, anticancer, cardiovascular and other activities.

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