



A Review: Biological Importance of Heterocyclic Compounds

Abbas Al-Mulla *

Department of Chemistry, Faculty of Sciences, Kufa University, Iraq

ABSTRACT

Heterocyclic compounds constitute the largest and most varied family of organic compounds. Today there are a lot of heterocyclic compounds are known, day by day the number is increasing rapidly due to the enormous synthetic research and also their synthetic utility. Heterocyclic compounds have a role in most fields of sciences such as medicinal chemistry, biochemistry also another area of sciences. In this review, we cover most biological active heterocyclic compounds that it's recently synthesized or extracted from the plants such as antifungal, anti-inflammatory, antibacterial, antioxidants, anticonvulsant, antiallergic, herbicidal and anticancer.

Keywords: Heterocyclic compounds, Biological activity, Medicinal chemistry

INTRODUCTION

Heterocyclic compounds are the cyclic organic compounds which contain at least one hetero atom, the most common heteroatoms are the nitrogen, oxygen and sulphur but heterocyclic rings containing other hetero atoms are also widely known. Carbocyclic compound a cyclic organic compound containing all carbon atoms in ring formation. Heterocyclic compounds considered one of the vital classes of organic compounds, which are used in many biological fields, due to it is activity in multiple illnesses. Biological molecules such as DNA and RNA, chlorophyll, hemoglobin, vitamins and many more contains the heterocyclic ring in major skeleton. There are a lot of heterocyclic compounds which are have application in many common diseases such as; triazine derivatives have been used as antimicrobial herbicides, urinary antiseptics and anti-inflammatory agents. Benzimidazole derivatives have been reports to possess wide range of biological activities such as antibacterial, antifungal, antiviral and anthelmintic, etc. [1].

Medicinal chemistry which is becomes an important field in chemistry because the joining between chemistry and the medical life issues by trying to study the common diseases and how should we solve it. This branch of the modern chemistry has been beginning when isolating and purifying active materials from plants and animals tissues and taken from microorganism and their fermentation products has become the focus of attention of researchers around the world. The medical chemistry based on the classical branches of chemistry especially organic chemistry and biology and some area of physics [2]. According to the literature review heterocyclic compounds represents important place in medical chemistry.

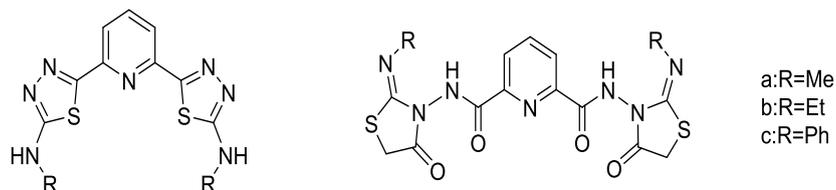
BIOLOGICAL IMPLICATIONS

Heterocycles have been found a key structural in medical chemistry and also they are frequently found in large percent in biomolecules such as enzyme, vitamins, natural products and biological active compounds including antifungal, anti-inflammatory, antibacterial, antioxidant, anticonvulsant, antiallergic, enzyme inhibitors, herbicidal activity, anti-HIV, antidiabetic, anticancer activity, insecticidal agents.

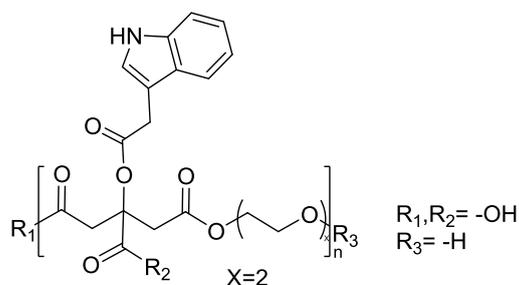
Antifungal activity

It is substances or medications that used to treats the fungal infection which is most commonly located on the skin, hair and nails. There are some common fungal infections such as ringworm and athlete's foot, etc. The effect of antifungal medicine either by killing the fungal cells due to affecting on the substances of the cell membrane which is lead to cells components leak out and cell die. Another way by preventing the growth and reproduction of the fungal cells.

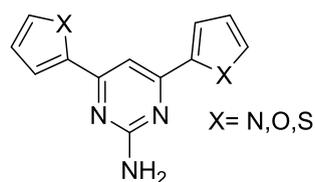
Molnar et al. [3] have synthesized a series of dipicolinic acid derivatives, some of it show antifungal activity against fungal strains called *Aspergillus flavus*, *Aspergillus ochraceus*, *Fusarium graminearum* and *Fusarium verticillioides*.



Chitra et al. [4] have synthesized indole 3-acetic acid based biopolymeric hydrogels, this compounds also show activity against fungal infections and tested of several type of fungi including, *Aspergillus fumigates*, *Rhizopus oryzae* and *Candida albicans* at different concentrations using ketoconazole as positive control and Dimethyl Sulfoxide (DMSO) as negative control for antifungal activity.



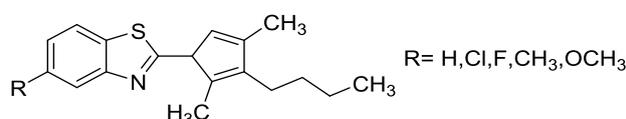
Wahbi et al. [5] have synthesized heterocyclic derivatives based on chalcone that contain five membered rings including pyrrole, furan and thiophene. The purpose of that is to increase the property of antifungal activity of some prepared compounds, also they were studied these compounds with theoretical programs and shows it is new activity as antifungal agents.



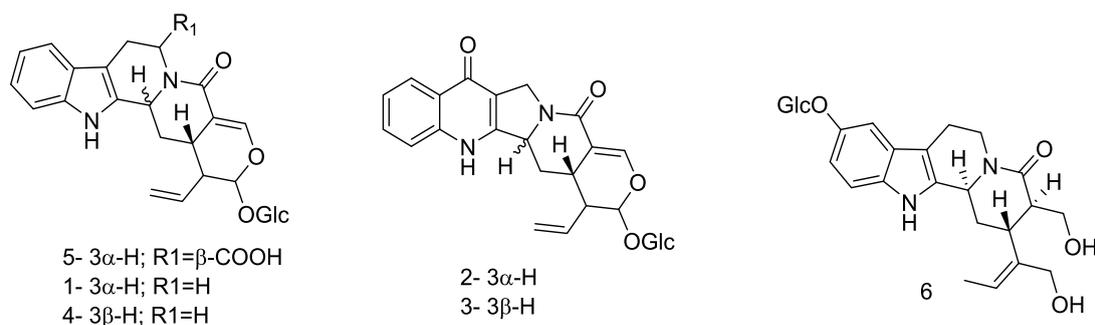
Anti-inflammatory activity

Is a term referring to the substances that used to treatment or reduces inflammations or swelling. Analgesic makes up about half of anti-inflammatory drugs. Relieving pain by reducing inflammation as opposed to opioids which affect the central nervous system, to block pain signaling to the brain. The most common anti-inflammatory drugs are aspirin and ibuprofen and naproxen, this type of anti-inflammatory called Non-steroidal Anti-inflammatory Drug (NSAIDs), this term recognizes these drugs from steroids. The mechanism of actions of these drugs includes inhibiting the activity of Cyclooxygenase (COX) enzymes. The activity of these enzymes is in the metabolism of arachidonic acid. Isoenzymes of cyclooxygenase may be the target of certain NSAIDs.

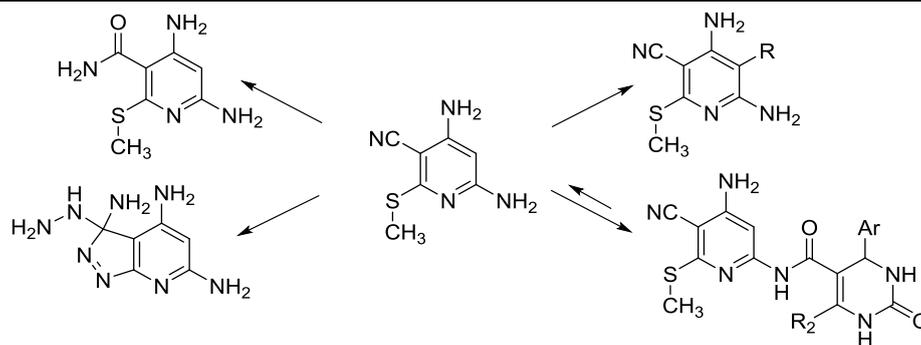
Sawhney and Bhutani [6] have prepared some novel 2-(2-benzothiazolyl)-6-aryl-4, 5-dihydro-3(2 H)-pyridazinone and found that they possessed low to moderate anti-inflammatory activity.



Li et al. [7] have isolated six compounds *Nauclea officinalis* (Pierre ex Pit.) and compared the activity of it.



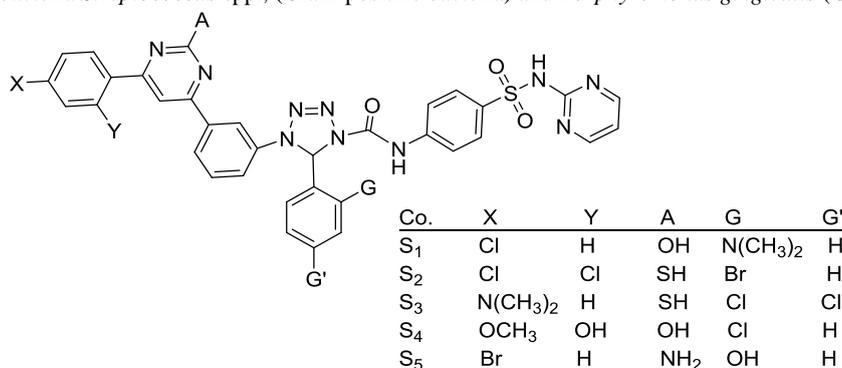
Ghattas et al. [8] have synthesized some of 4,6-Diamino-3-cyano-2-methylthiopyridine derivatives and proved this compounds have anti-inflammatory by carrageenan-induced paw oedema standard method in rats.



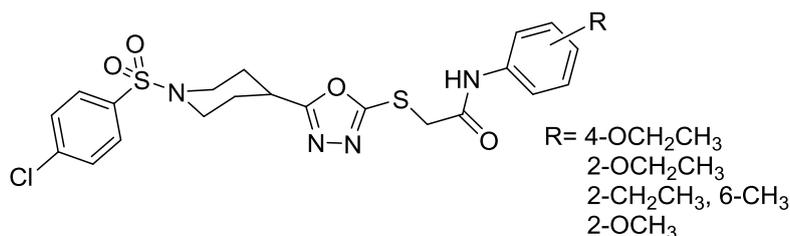
Antibacterial activity

Antibacterial or antibiotics is a term that used to describe the drugs which are used for prevention or treatment of bacterial infections, either by killing or inhibit the growth of bacteria. The antiprotozoal activity also related to some of the antibiotics. Antibiotics do not effective against viral infections such as the common cold or influenza. The emergence of resistant organisms may happen if the using of antibiotics was inappropriate. The classification of antibiotics is according to the mechanisms of actions or chemical structural. Aromatic heterocyclic derivatives represent an important part of antibiotics chemical structure such as β -lactam derivatives, and there are a lot of chemists' have been synthesis many compounds have this type of activity and tested it on several types of bacteria. We will review some of this works in recent two years.

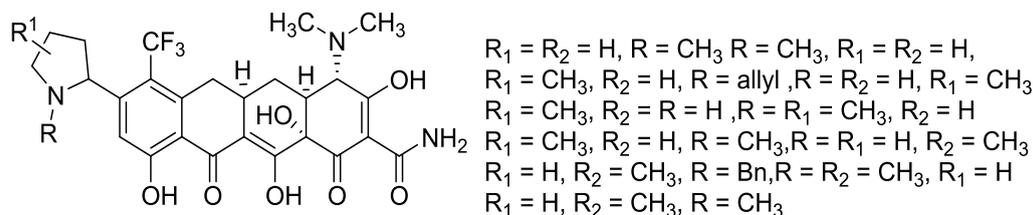
Abbass and Zimam [9] have been synthesized some new pyrimidine and 1,2,3,4-tetrazole derivatives based on sulfadiazine and tested these compounds on two types of bacteria *Streptococcus* spp., (Gram-positive bacteria) and *Porphyromonas gingivalis* (Gram-negative bacteria).



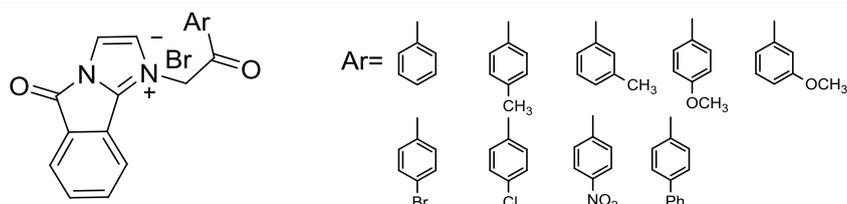
Iqbal et al. [10] have been synthesized some of N-substituted acetamide derivatives of azinane-bearing 1,3,4-oxadiazole nucleus derivatives and screening it is antibacterial activity against five types (*Salmonella typhi*, *Escherichia coli*, *P. aeruginosa*, *S. aureus* and *Bacillus subtilis*) of bacterial strains. All the synthesized compounds are moderate inhibitors but relatively more active against Gram-negative bacterial strains. 5-[1-(4-Chlorophenyl)sulfonyl]piperidin-4-yl]-2-[[N-(2-methylphenyl)-2-acetamoyl]thio]-1,3,4-oxadiazole is the most active growth inhibitor of all the strains except *S. aureus*.



Deng et al. [11] have synthesized a series of new derivatives of tetracyclines. 1,7-trifluoromethyl-8-pyrrolidinyltetracyclines as broad spectrum antibacterial agents with enhanced activity against *P. aeruginosa*.



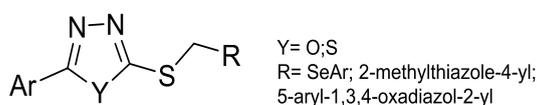
Narsimha et al. [12] synthesized excellent new broad spectrum antibacterial agents which is a novel substituted imidazo[2,1-a]isoindole derivatives and tested it *in vitro* against for types of bacteria two Gram-positive bacteria such as *S. aureus* and *B. subtilis* two Gram-negative bacteria such as *E. coli* and *Proteus vulgaris* with streptomycin as standard drug (positive control) for comparison.



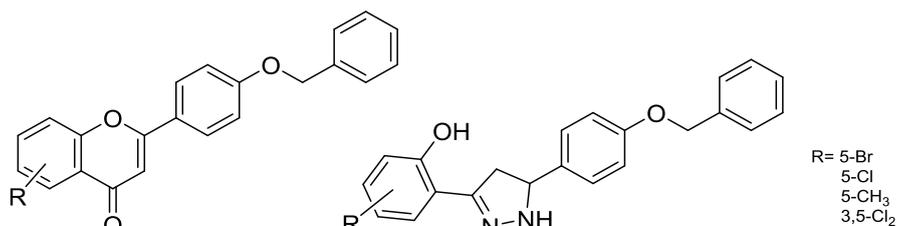
Antioxidants activity

Oxidation is the chemical reaction that can produce free radicals and cause cell damage by chain reactions. Antioxidant is molecules that inhibit oxidation reaction of other molecules such these compounds thiols or Ascorbic acid (vitamin C) can terminate these chain reactions and prevent cell damage, antioxidant is a term mainly used for two different groups of substances which are added products to prevent oxidation and natural chemicals found in foods and body tissue which are said to have beneficial health effects. There are a lot of researchers try to synthesized chemical compounds have this types of biological activity, we will review some of these researchers.

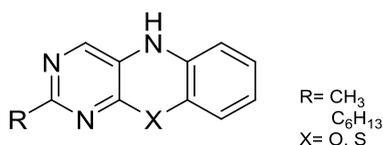
Sauer et al. [13] have synthesized some new heterocyclic complexes of organosulfur and organoselenium compounds derived from 5-substituted-1,3,4-oxadiazole/thiadiazole-2-thiols which are showed antioxidant activity when screened for *in vitro* antioxidant activity as reflected by free radical scavenging against 2,2-Diphenyl-1-Picrylhydrazyl (DPPH) and reduction of molybdenum(VI) to molybdenum(V). The compounds have significant antioxidant properties in both applied methodologies.



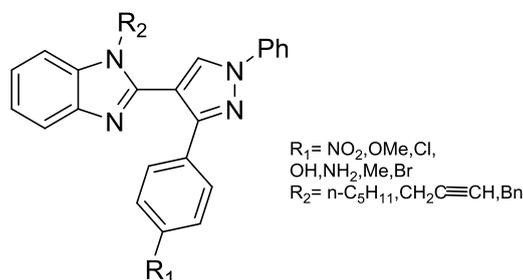
Jahan et al. [14] have been submitted their works which is include synthesis new derivatives of flavones and pyrazolines derived from chalcones. Tested of these compounds *in vitro* showed significant antioxidant activities were also shown by flavones and pyrazolines.



Haidasz and Pratt [15] have synthesized diazaphenoxazines and diazaphenothiazines compounds which they are highly reactive radical trapping antioxidants. This activity was proved by preliminary kinetic studies.



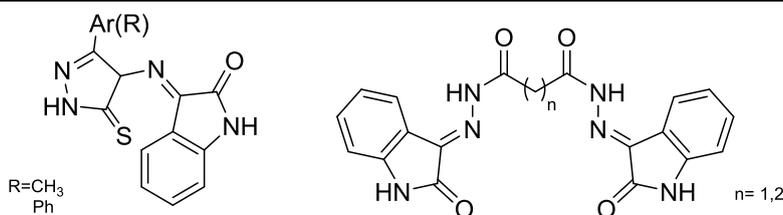
Bellam et al. [16] have synthesized a new series of N-substituted pyrazole-containing benzimidazoles and tested for antioxidant activity by using DPPH method and H₂O₂ method.



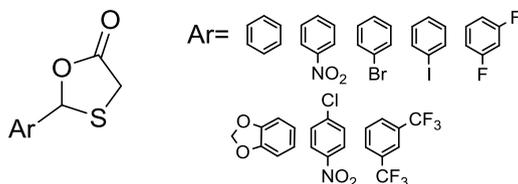
Anticonvulsant

Are varied groups these chemicals may be called antiepileptic drugs or as antiseizure drugs of pharmacological agents used in the treatment of epileptic seizures. These drugs may be called as antiepileptic drugs or as antiseizure drugs. The mechanism of actions of this drugs showed that it is block sodium channels or enhance γ -aminobutyric acid (GABA) function. There are a lot of articles focuses on the synthesized new generations of these drugs.

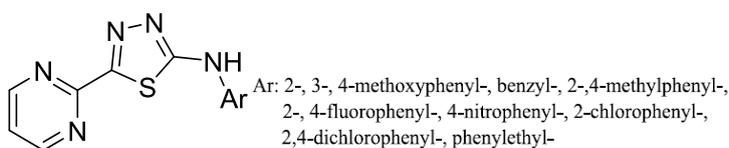
Nami et al. [17] synthesized new heterocyclic compounds containing 3-iminoisatin and 1,2,4-triazole using Fe₃O₄ magnetic nanoparticles and study it is anticonvulsant activity.



Thakare et al. [18] have been synthesized new anticonvulsant compounds which is 1,3-oxathiolan-5-one and tested it for anticonvulsant activity.

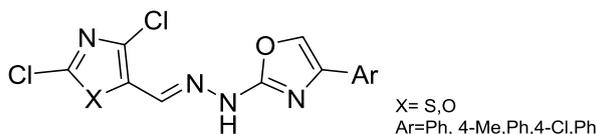


Cavus et al. [19] have been synthesized new 1,3,4-thiadiazole compounds including pyrazine moiety and investigate it's anticonvulsant activity.

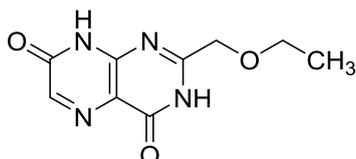


Antiallergic

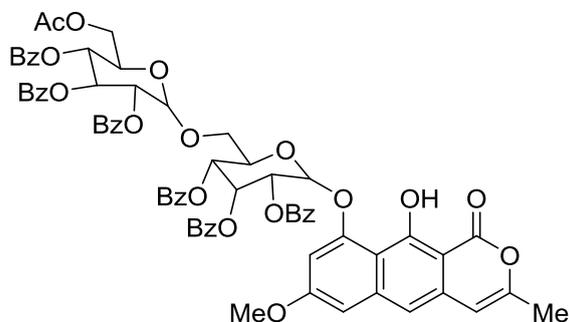
There are a lot of synthesized heterocyclic compound that showed antiallergic activity when tested. Putta et al. [20] have been synthesized of new Bis-heteroarylhydrazines as effective anti-allergic agents and these compounds do not cause cytotoxicity of the cells at 50 and 100 μ M and also significantly inhibit β -hexosaminidase release stimulated by immunoglobulin E/silver at 50 and 100 μ M.



Chem et al. [21] have been synthesized pteridinones and related compounds and the antiallergic activity was confirmed, It was therefore selected for further development as a human therapeutic agent, below one of the prepared compounds.



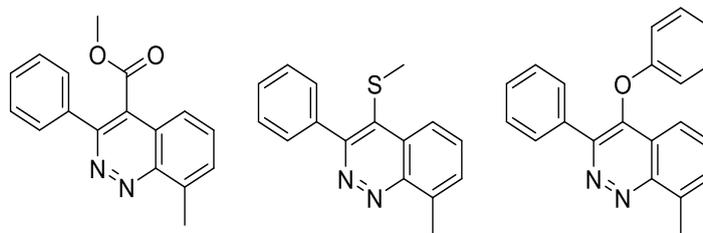
Zhang and Yu [22] have been synthesized antiallergic naphtho-r-pyrone Tetraglucoside, cassiaside C2, isolated from cassia seeds.



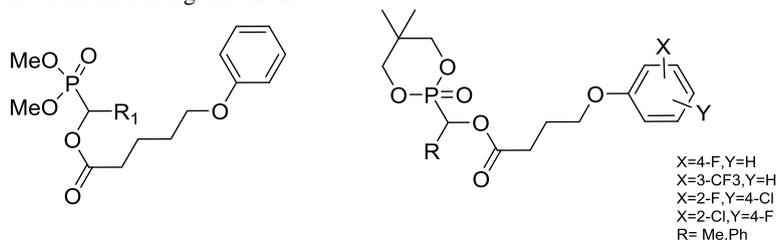
Herbicidal activity

There are a lot of drugs which can destroy undesired plants along with some grasses without affecting the food crops, some of the heterocyclic derivatives possess this activity and we will review the recent synthetic compounds of this kind.

Ana and Luminita [23] have combined molecular docking and Quantitative Structure-activity Relationship (QSAR) study of fused heterocyclic as a herbicide inhibitors of D1 protein in photosystem II of plants. Here is one on the compounds under this study.



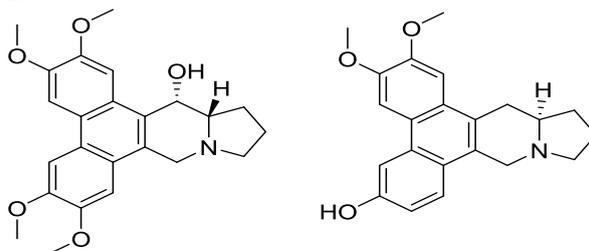
Wang et al. [24] have been synthesized a-[(substituted phenoxybutyryloxy or valeryoxy)]alkylphosphonates and 2-(substituted phenoxybutyryloxy)alkyl-5,5-dimethyl-1,3,2-dioxaphosphinan-2-one containing fluorin. These compounds have showed herbicidal activities against some species of weeds were evaluated in a green house.



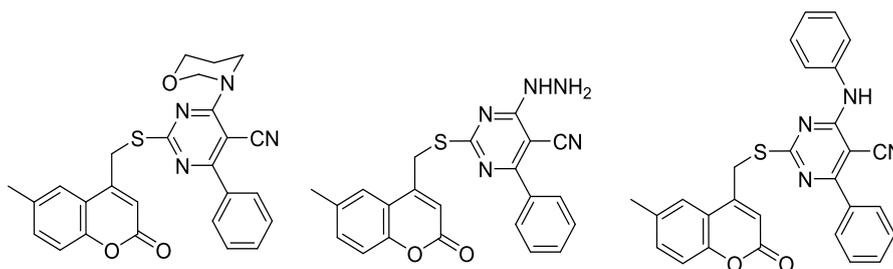
Anticancer activity

Cancer is a group of diseases involving abnormal cell growth with the potential to invade or Spread to the other parts of the body. This disease caused by varied agents such as, chemical compound, radiant energy. There are a lot of drugs which is used for treatment of this disease either by kill cancer cells or modify their growth. We will review the latest synthetic compounds that used for this purpose.

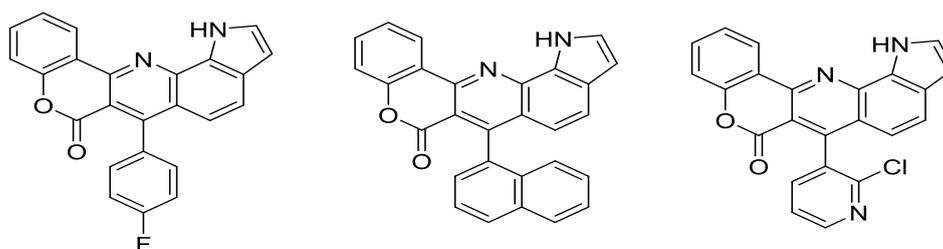
Liu et al. [25] have been synthesized 6-OH-Phenanthroquinolizidine alkaloid and its derivatives, which are exert a potent anticancer activity by delaying the S phase progression of the cell.



Morsy et al. [26] have been synthesized new derivatives of coumarin containing compounds which showed anticancer activity by screened biologically against two human tumor cell lines, breast carcinoma Michigan Cancer Foundation-7 (MCF-7) and hepatocellular carcinoma (HepG-2), at the National Cancer Institute, Cairo, Egypt using 5-fluorouracil as standard drug. Below the structure of some of the synthesized compounds.



Thigulla et al. [27] have been synthesized fused chromeno[4,3-b]pyrrolo [3,2-h]quinolin-7(1H)-one and test anticancer activity of the prepared compounds. Here we show some of these compounds.



CONCLUSION

Heterocyclic compounds one of the important sorts of organic compounds, which is taking a wide range in the medicinal chemistry this due to the huge number of heterocyclic compounds that used in medicine as drugs for varied diseases. The drugs which contain the core of heterocyclic its skeletons such as Antifungal activity, anti-inflammation, anti-bacterial, antioxidants, anticonvulsant, antiallergic, herbicidal activity and anticancer, etc.

REFERENCES

- [1] M. Gupta, *Int. J. Physical, Chem. Mat. Sci.*, **2015**, 4(1), 21-24.
- [2] M.S. Saini, A. Kumar, J. Dwivedi, R. Singh, *Int. J. Pharm. Sci. Res.*, **2013**, 4(3), 66-77.
- [3] M. Molnar, V. Pavić, B. Šarkanj, M. Čačić, D. Vuković, J. Klenkar, *Heterocycl. Commun.*, **2017**, 23(1), 1-8.
- [4] C. Chitra, S. Sudarsan, S. Sakthivel, S. Guhanathan, *Int. J. Biol. Macromol.*, **2017**, 95, 363-375.
- [5] H.I. Wahbi, C.Y. Ishak, A. Khalid, T. Adlan, *Int. J. Pharm. Phytopharmacol. Res.*, **2014**, 4(1), 13-19.
- [6] D.V. Sa whney, S.N.S. Bhutani, *Chem. Inform.*, **1987**, 18(43), 55-62.
- [7] D. Li, J. Chen, J. Ye, X. Zhai, J. Song, C. Jiang, J. Wang, H. Zhang, X. Jia, F. Zhu, *J. Ethnopharmacol.*, **2017**, 196(100), 66-74.
- [8] A.E.A.G. Ghattas, A. Khodairy, H.M. Moustafa, B.R.M. Hussein, *J. Heterocycl. Chem.*, **2016**.
- [9] A.F. Abbass, E.H. Zimam, *Int. J. ChemTech Res.*, **2016**, 9(11), 206-217.
- [10] K. Iqbal, Q. Jamal, J. Iqbal, M. Sadaf Afreen, M.Z. Ahmed Sandhu, E. Dar, U. Farooq, M.F. Mushtaq, N. Arshad, M.M. Iqba, *Trop. J. Pharm. Res.*, **2017**, 429-437.
- [11] Y. Deng, C. Sun, D.K. Hunt, C. Fyfe, C.L. Chen, T.H. Grossman, J.A. Sutcliffe, X.Y. Xiao, *J. Med. Chem.*, **2017**, 60(6), 2498-2512.
- [12] S. Narsimha, K. Battula, N.V. Reddy, *Synth. Commun.*, **2017**, 47(9), 928-933.
- [13] A.C. Sauer, J.G. Leal, S.T. Stefanello, M.T.B. Leite, M.B. Souza, F.A.A. Soares, O.E.D. Rodrigues, L. Dornelles, *Tetrahedr. Lett.*, **2016**.
- [14] N. Jahan, S. Chaitali, M. Idrees, *Ind. J. Adv. Chem. Sci.*, **2017**, 43-49.
- [15] E.A. Haidasz, D.A. Pratt, *Trapping Antioxid.*, **2017**.
- [16] M. Bellam, M. Gundluru, S. Sarva, S. Chadive, *Chem. Heterocycl. Compd.*, **2017**, 53, 2, 173-178.
- [17] N. Nami, D. Zareyee, M. Ghasemi, M. Forouzani, S. Mirzad, S.M. Hashemi, *J. Sulfur Chem.*, **2017**, 112.
- [18] M.P. Thakare, R. Shaikh, D. Tayade, *J. Sulfur Chem.*, **2017**, 1-10.
- [19] M.S. Çavus, M. Gür, S. Nesrin, *J. Mol. Str.*, **2017**, 1139, 111-118.
- [20] R.R. Putta, S.D. V, R. Guda, P. Adivireddy, V. Padmavathi, *J. Heterocycl. Chem.*, **2017**, 4-10.
- [21] E.J.M. Chem, G. Ferrandl, H. Dumasl, J.C. Depin, Y. Quentinl, *Eur. J. Med. Chem.*, **1996**, 273-280.
- [22] Z. Zhang, B. Yu, *J. Org. Chem.*, **2003**, 68(16), 6309-6313.
- [23] S.F. Ana, B. Luminita, *Mol. Divers.*, **2017**, 21(2), 437-454.
- [24] W. Wang, Y. Zhou, H. Peng, H. He, X. Lu, *J. Fluor. Chem.*, **2017**, 193, 8-16.
- [25] Y. Liu, L. Qing, C. Meng, J. Shi, Y. Yang, Z. Wang, G. Han, Y. Wang, J. Ding, L.H. Meng, Q. Wang, *J. Med. Chem.*, **2017**, 60(7), 2764-2779.
- [26] S.A. Morsy, A.A. Farahat, M.N.A. Nasr, A.S. Tantawy, *Saud. Pharm. J.*, **2016**, 1-10.
- [27] Y. Thigulla, T.U. Kumar, P. Trivedi, B. Ghosh, *Chem. Sel.*, **2017**, 7, 2721-2724.