

DIVERSE BIOLOGICAL ACTIVITIES OF PYRIMIDINE SCAFFOLDS: A REVIEW

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ABSTRACT

Pyrimidine is a 5-membered heterocyclic ring which is versatile lead compound for designing potent bioactive agents. This interesting group of compound has diverse biological activities such as antimicrobial, CNS depressant, anti-inflammatory, analgesic, anticancer, antihelminthic, antioxidant and herbicidal. In this review, it represents that pyrimidine being heterocyclic planar five membered ring systems has various pharmacological actions. About pyrimidine and its efficacy; there are several researches are performed and many more researches are performing by physiologist and researchers, nowadays also. The review article aims to review the work reported and biological activities of pyrimidines during past year.

KEYWORD: Pyrimidine, CNS depressant, Bioactive agent.

INTRODUCTION

Pyrimidine is a heterocyclic aromatic organic compound similar to benzene and pyridine, containing two nitrogen atoms at positions 1 and 3 of the six-member ring. It is isomeric with two other forms of diazine.

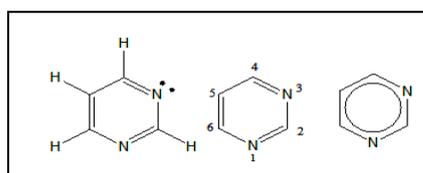


FIG. 1: PYRI.

FIG. 1: PYRIMIDINE

It is a colorless compound, having molecular formula of $C_4H_4N_2$ and molecular weight of 80 dalton having melting point $22.5^\circ C$ and boiling point $124^\circ C$.

Purines and pyrimidines make up the two groups of nitrogenous bases.

1. Purines

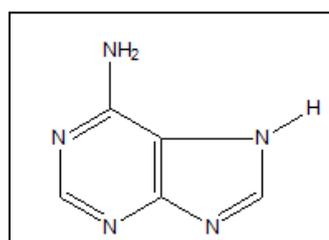


FIG. 2: ADENINE

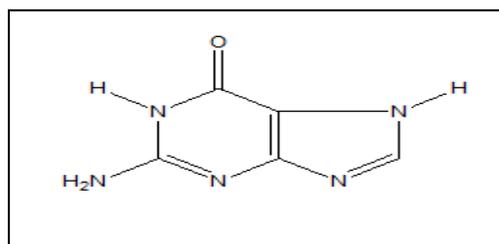


FIG. 3: GUANINE

2. Pyrimidines

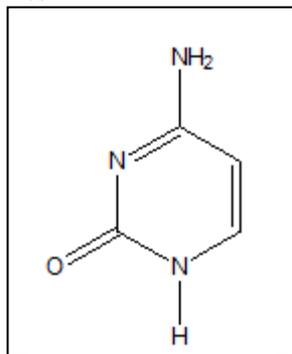


FIG. 4: CYTOSINE

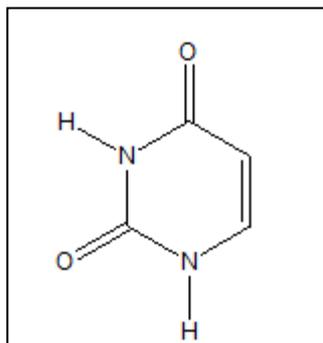


FIG. 5: URACIL

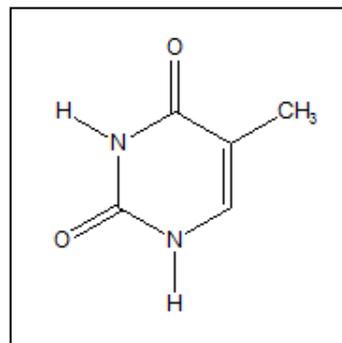


FIG. 6: THYMINE

Pyrimidines are biologically very important heterocycles and represent by far the most ubiquitous members of the diazine family with uracil and thymine being constituents of ribonucleic acid (RNA) and deoxyribonucleic acid (DNA) and with cytosine.

In addition to this, pyrimidines skeleton is also present in many natural products such as vitamin B1 (thiamine) and many synthetic compounds, such as barbituric acid and Veranal which are used as hypnotics.

SYNTHESIS OF PYRIMIDINES

Pyrimidines can also be prepared in the laboratory by synthesis. The classical method for the synthesis of pyrimidine is the Biginelli reaction. Many other methods rely on condensation of carbonyls with amines for instance the synthesis of 2-thio-6-methyluracil from thiourea and ethyl acetoacetate or the synthesis of 4-methylpyrimidine from 4, 4-dimethoxy-2-butanone and formamide.

Pyrimidine ring is found in Vitamins like thiamine, riboflavin, folic acid. Pyrimidine derivatives have been found to be possessed diverse biological activities including antiviral, anticancer, antifungal, antimalarial, sedative, hypnotic, anticonvulsant, anthelmintics and antithyroid activities.

Significance of Pyrimidines

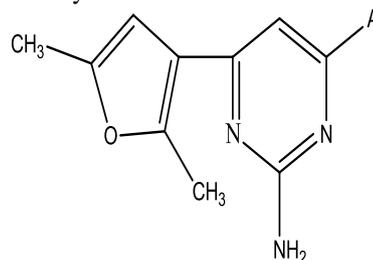
In medicinal chemistry pyrimidine derivatives have been very well known for their therapeutic applications.

- 1. Pyrimidines as Antineoplastic (Anticancer) Agents:** Cancer is not just one disease, but a large group of almost one hundred diseases. The main target of anti-tumor chemotherapies is DNA. As DNA unfolding is a preliminary step in cell replication, a ligand capable of inducing structural alterations to DNA could be used as a chemotherapeutic.
- 2. Pyrimidine as Anti-inflammatory and Analgesic Agents:** There are large numbers of pyrimidine derivatives found to exhibit anti-inflammatory and analgesic activity. New lipid soluble forms of thiamine (Vitamin-B1) such as Acetamine, bentamine and fursultiamine are used for beriberi, polyneuritis, encephalopathy and pain.

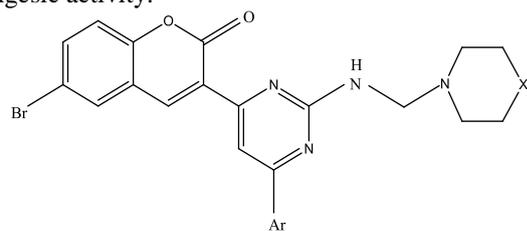
- 3. Pyrimidine Analogues as Antibiotics:** Pyrimidine derivatives are also known for antibiotic properties. Pyrimidine analogs which acts as antibiotic are bacimethrin.
- 4. Pyrimidine as Antibacterial Agents (Sulfa Drugs):** A number of pyrimidine derivatives have been found to be useful as chemotherapeutic agent. Among the sulfonamide, sulfadiazine, sulfamerazine and sulfadimidine are pyrimidine analogues of sulfa drugs which are more superior clinically antibacterial agent and are also used in the treatment of acute UT infections, cerebrospinal meningitis and for patients allergic to penicillins.
- 5. Pyrimidine as Anthelmintic Agents:** Pyrimidines, sulphonamides and carboxamides have shown large number of pharmacological properties against different types of diseases among which is helminthiasis.
- 6. Pyrimidine as Antifungal Agents:** Pyrimidines also exhibit antifungal properties. Flucytosine is a fluorinated pyrimidine and is an orally active antifungal agent which is used for the treatment of serious systemic infections caused by susceptible strains of *Candida* and *Cryptococcus* and hexetidine is mainly used for the treatment of aphthous ulceration.
- 7. Pyrimidine as Cardiac agents:** Fused pyrimidines, quinoazolines are used as antihypertensive agents.
- 8. Pyrimidine as antioxidant and herbicidal.**

LITERATURE REVIEW

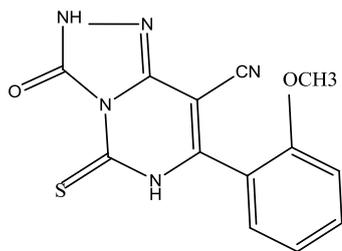
1. Sridhar et al. (2011) had been reported with the synthesis of novel pyrimidine derivatives for their anticancer activity.



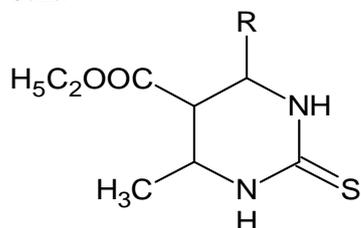
2. Anshu Chaudhary et.al (2011) had been reported with synthesis of novel pyrimidine derivatives for their analgesic activity.



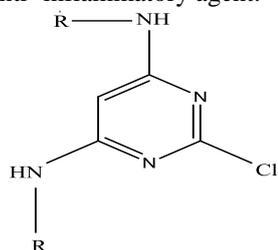
O.A. Fathalla et.al (2009) had been reported for synthesis, antibacterial and anticancer evaluation of some novel pyrimidine derivatives.



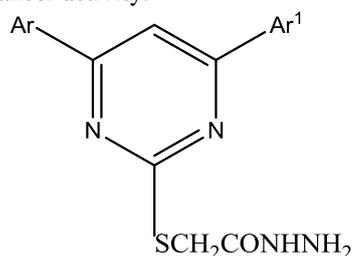
El-Gaby et al (1999) prepared some new pyrimidine-2-thiones. Some of these compounds were tested for in vitro anticancer activity against *Ehrlich Ascites Carcinoma* Cells.



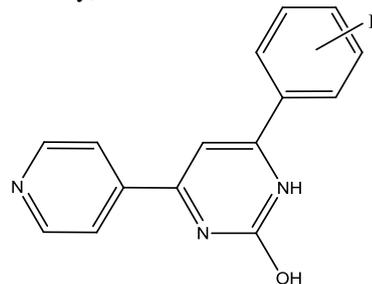
P.K. Singour et.al (2012) had been reported for synthesis and biological evaluation of novel pyrimidine derivatives as anti-inflammatory agent.



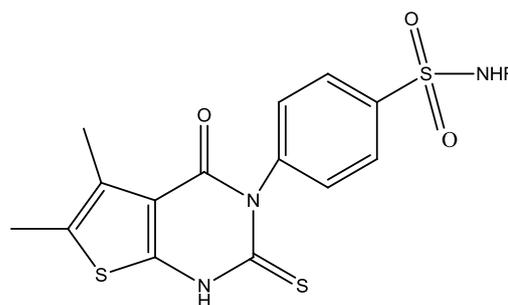
Sonia D.Arikkat et al. (2014) had been reported for their synthesis of novel pyrimidine derivatives for their potent anticancer activity.



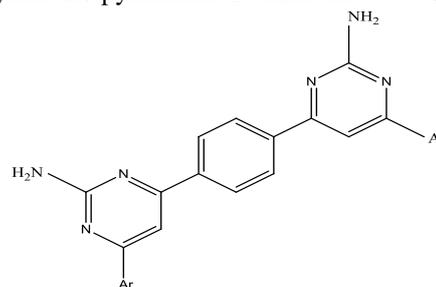
Monica Kachroo et.al (2014) had been reported for synthesis and biological activities of some new pyrimidine derivatives from chalcone for their anti-TB, anti-inflammatory, anti-oxidant activities.



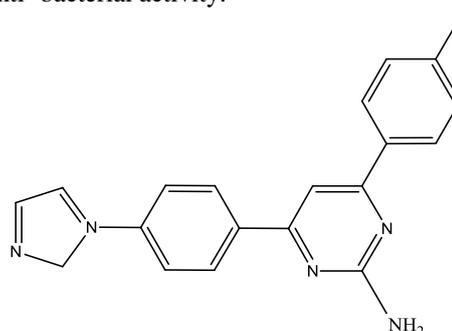
Mostafa M Ghorab et.al (2016) had been reported for anticancer activity of some novel thieno pyrimidine derivatives.



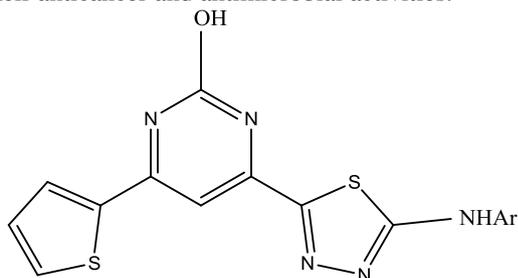
Meliha Burcu Gurdere et al (2016) had been reported for the synthesis and in-vitro anticancer evaluation of 1,4-phenylene-bis-pyrimidine-2-amine derivatives.



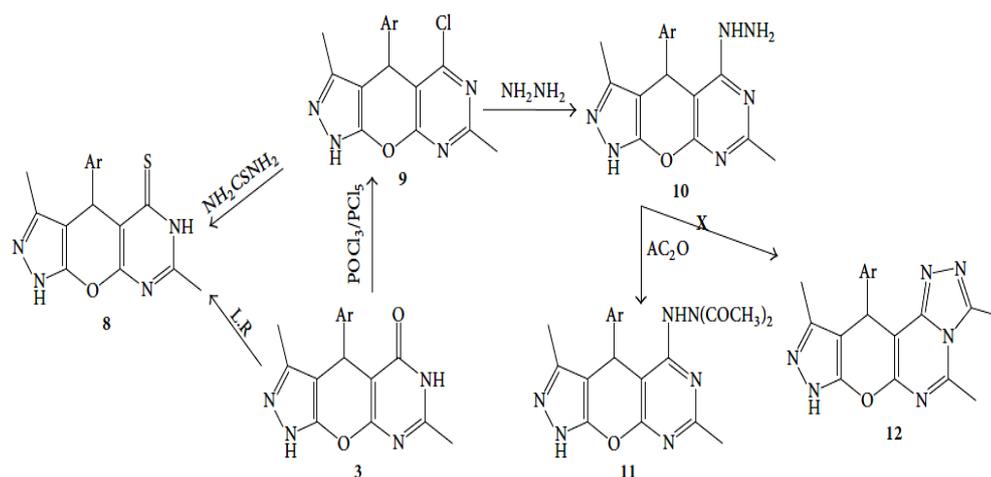
Eswara Rao G. et.al (2016) had been reported for synthesis and biological evaluation of pyrimidines for their anti-bacterial activity.



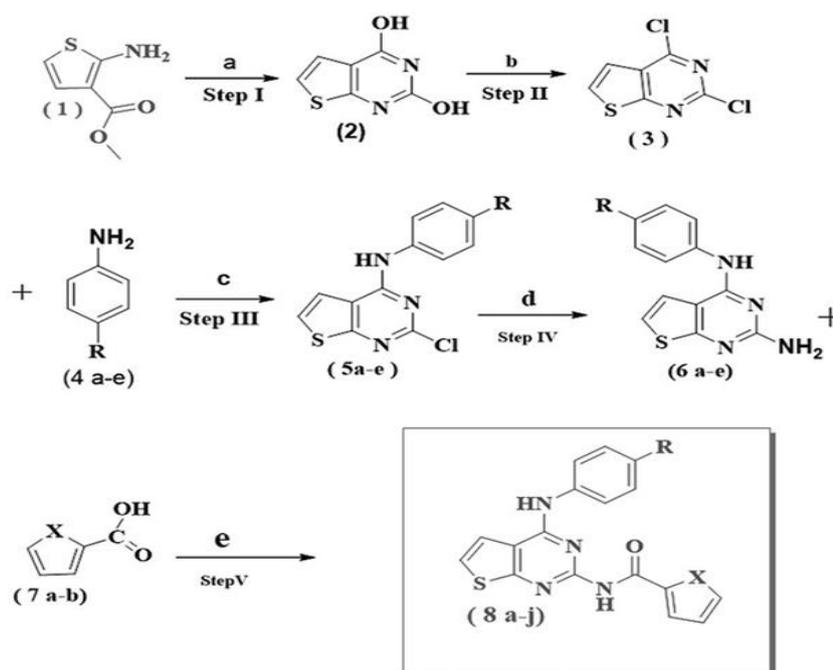
Nermine A Osman et.al (2016) had been reported for synthesis of new pyrimidine derivatives and evaluation of their anticancer and antimicrobial activities.



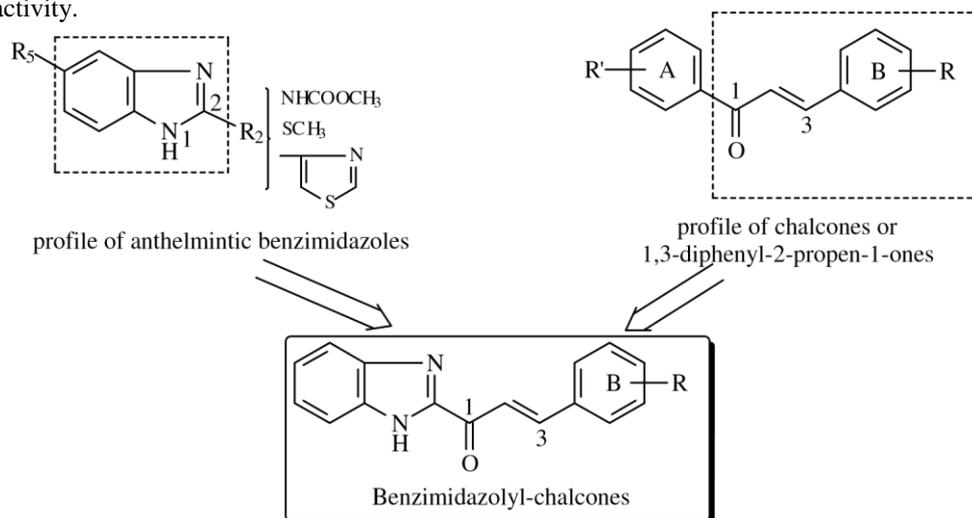
Naglaa F. H. Mahmoud et al (2017) has synthesized various fused oxazine such as pyrazolopyranopyrimidinones and pyrazolopyranopyrimidines which were screened for anticancer activity.



Virupakshi Prabhakar et al (2017) has reported a new series of N-(4-(substituted amino) thieno[2,3-d]pyrimidin-2-yl) thiophene/Furan-2-carboxamide (7 a-j) derivatives which were screened for antibacterial and antifungal activity.



Mahama Ouattara et al (2011) has synthesized hybrid benzimidazolyl-chalcone derivatives, evaluated their anthelmintic activity.



DAVID I. UGWU et al (2017) Synthesised pyrimidine derivatives bearing carboxamide and sulphonamide moieties and reported anthelmintic activity.

CONCLUSION

Pyrimidine's showed diverse biological activities such as antimicrobial, CNS depressant, anti-inflammatory, analgesic, anticancer, antihelminthic, antioxidant and herbicidal. As a result; a vast literature has been accumulated over the years and significance of pyrimidines. It would also be interesting to see development of pyrimidines as potentially active therapeutic compound.

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