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BIOLOGICAL AND MEDICINAL SIGNIFICANCE OF PYRIMIDINES: A REVIEW

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ABSTRACT: One useful starting molecule for the development of powerful bioactive drugs is pyrimidine, a 5-membered heterocyclic ring. The biological effects of this intriguing class of compounds are as varied as their names suggest: antibacterial, central nervous system depressant, anti-inflammatory, analgesic, anti-sedative, anti-herpes, anti-cancer, antioxidant, and herbicide.The available evidence suggests that pyrimidines, which are heterocyclic and consist of five-membered rings, have a wide range of pharmacological effects .The next sections cover the pharmacological effects of pyrimidine derivatives and how to synthesize them. Various pharmacological actions of these pyrimidine derivatives are examined in this study. Pyrimidine derivatives, which are detailed in this review, are very useful in biology and pharmacology.

Keywords: Pyrimidine derivatives, Pharmacological Significance

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

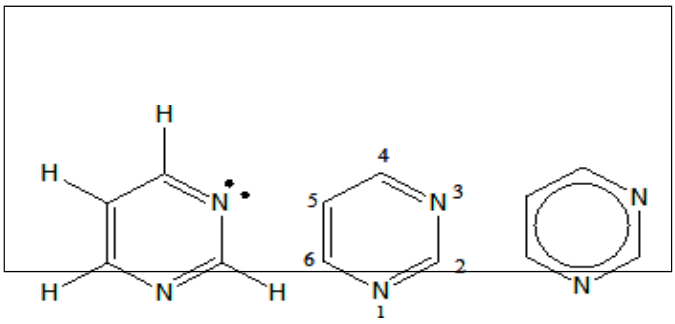
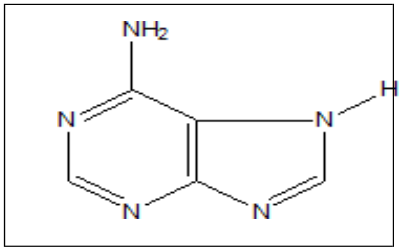


FIG. 1: PYRIMIDINE

Whereas purine is a heterocyclic aromatic organic compound, consisting of a pyrimidine ring fused to an imidazole ring. Purines and pyrimidines make up the two groups ofnitrogenous bases. These bases make up a crucial part of both deoxyribonucleotides and ribo- nucleotides, and the basis for the universal genetic code. The general term purine also refers to substituted purines and their tautomers. The purine is the most widely distributed nitrogen-containing heterocycle in nature notable purines. The quantity of naturally occurring purines produced on earth is enormous, as 50% of the bases in nucleic acids, adenine and guanine are purines. In DNA, these bases form hydrogen bonds with their complementary pyrimidines thymine and cytosine. This is called complementary base pairing. The beginning of the pyrimidine chemistry may be traced back to the isolation of alloxan [1].

1. Purines:



2. Pyrimidines:

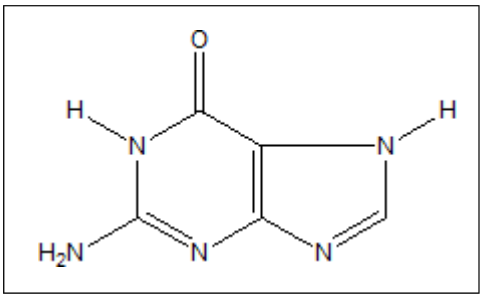


FIG. 3: GUANINE

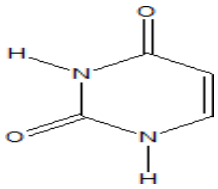


FIG. 4: CYTOSINE

Chemical Properties: A pyrimidine has many properties in common with pyridine, as the number of nitro gen atoms in the ring increases the ring pi electrons become less energetic and electrophilic aromatic substitution gets more difficult while nucleophilic aromatic substitution gets easier. An example of the displacement of the amino group in 2-aminopyrimidine by chlorine and its reverse. Reduction in resonance stabilization of pyrimidinesmay lead to addition and ring cleavage reactions rather than substitutions. One such manifestation is observed in the Dimroth rearrangement. Compared to pyridine, N-alkylation and N-oxidation is more difficult, and pyrimidines are also less basic.ThePk_a value for protonated pyrimidine is 1.23 compared to 5.30 for pyridine.

Organic Synthesis: Pyrimidines can also be prepared in the laboratory by organic synthesis. One method is the classic Biginelli reaction. Many other methods rely on condensation of carbonyls

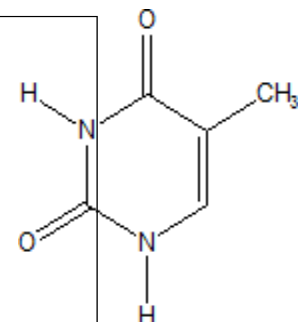


FIG. 5: URACIL

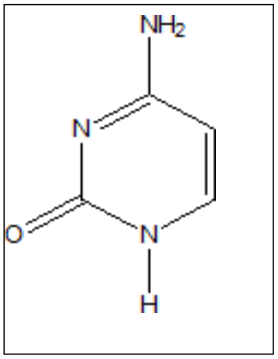


FIG. 6: THYMINE

In DNA and RNA, these bases form hydrogen bonds with their complementary purines. Thus the purines adenine (A) and guanine (G) pair up with the pyrimidines thymine (T) and cytosine (C), respectively. In RNA, the complement of A is U instead of T and the pairs that form are adenine: uracil and guanine: cytosine. These hydrogen bonding modes are for classical Watson-Crick base pairing. Other hydrogen bonding modes ("wobble pairings") are available in both DNA and RNA, although the additional 2'-hydroxyl group of RNA expands the configurations through which RNA can form hydrogen bonds. Pyrimidines can also be prepared in the laboratory by synthesis. The classical method for the synthesis of pyrimidine is the Biginelli reaction [2]. with amines for instance the synthesis of 2-thio-6- methyluracil from thiourea and ethyl acetoacetateor the synthesis of 4-methylpyrimidine from 4, 4- dimethoxy-2-butanone and formamide.

Pyrimidine ring is found in Vitamins like thiamine, riboflavinand 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.

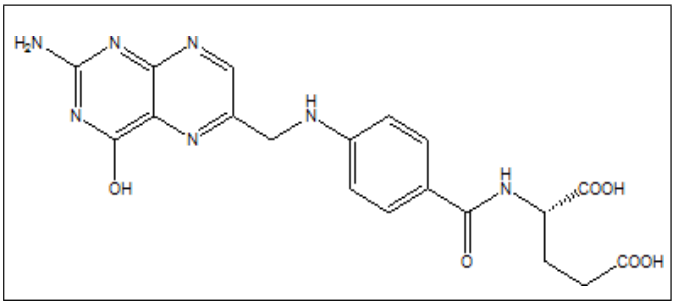


FIG. 7: FOLIC ACID

Further some hetero-fused pyrimidines are known to exhibit promising antiviral, [3] antibacterial, [4] anti-AIDS [5] activities. It is found that fused pyrimidinesare selective inhibitors for multidrug resistance (MDR) [6, 7]. Folate metabolism as antitumor agents [8]. Atherothrombotic coronary artery disease, givingrise to a number of cardio circulatory disorders such as myocardial infarction (MI), unstable angina(UA), or acute stroke associated with deep vein thrombosis (DVT), is one of the most important causes of death worldwide. The relevance of fused pyrimidines as anti-platelet and antithrombotic drugs [9] has been firmly established by clinicaltrials.

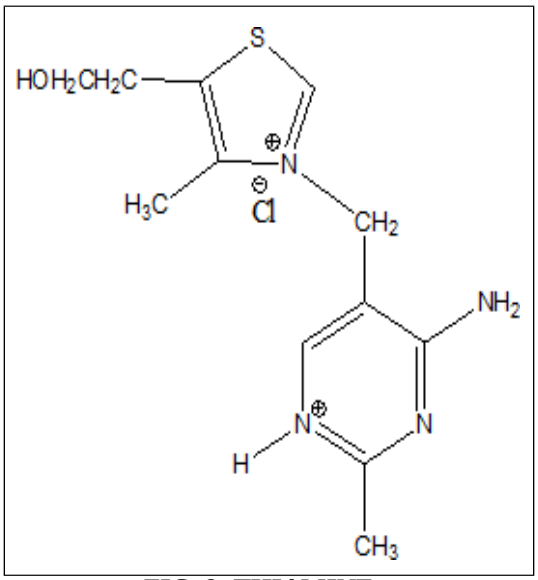


FIG. 8: THIAMINE

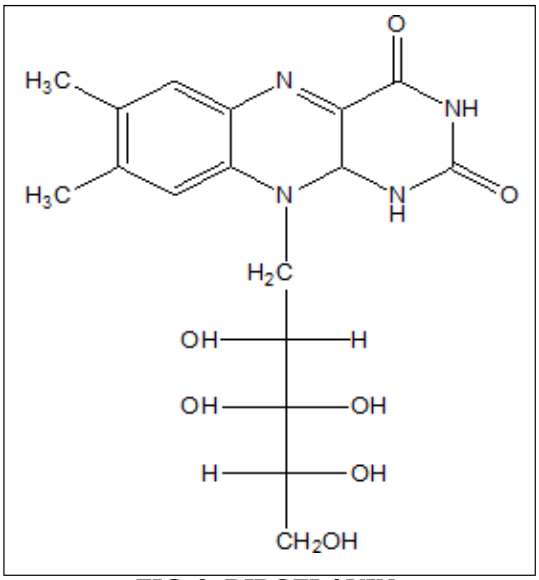


FIG. 9: RIBOFLAVIN

Medicinal Significance of Pyrimidines: In medicinal chemistry pyrimidine derivatives have been very well known for their therapeutic applications. During the last two decades, several

pyrimidine derivatives have been developed as chemotherapeutic agents and have found wide clinical applications, which are as follows.

CONCLUSION: Pyrimidine's showed diverse biological activities such as antimicrobial, CNS depressant, anti-inflammatory, analgesic, anti- convulsant, anticancer, antihelmentic, antioxidant and herbicidal. This review describes variousPyrimidine derivatives have potent biological and pharmacological applications.

REFERENCES:

1. Eussell JA: Annu. Rev. Biochem., 1945; 17: 309.2. Cox RA: Quart. Rev., 1968; 22: 499.
3. Hossain N, Rzewski J, Clercq ED and Herdewijn P: J. Org.Chem., 1997; 62: 2442.
4. Sabnis RW and Rangnekar DW: Indian J. Technol., 1990;28: 54.
5. Joseph S and Burke JM: J. Biol. Chem., 1993; 268: 24515.
6. Bookser BC, Ugarkar BG, Matelich MC, Lemus RH, Allan M, Tsuchiya M, Nakane M, Nagahisa A, Wiesner JB and Erion MD: J. Med. Chem., 2005; 48: 7808.
7. Wang S, Folkes A, Chuckowree I, Cockcroft X, Sohal S, Miller W, kilton J, Wren SP, Vicker N, Depledge P, Scott J, Smith L, Jones H, Mistry P, Faint R, Thompson D and Cocks SJ: Med. Chem., 2004; 47: 1329.
8. Gangjee A, Jain HD, Phan J, Lin X, Song X, McGuire JJ and Kisliuk RL: J. Med. Chem., 2006; 49: 1055.
9. Bruno O, Brullo C, Schenone S, Bondavalli F, Ranise A, Tognolini M, Impicciatore M, Ballabeni V and Barocelli E: Bioorg. Med. Chem., 2006; 14: 121.
10. Neidle S and Thurston DE: Nat. Rev. Cancer., 2005; 5: 285.
11. Wright WE, Tesmer VM, Huffman KE, Levene SD and Shay WJ: Genes Dev., 1997; 11: 2801.
12. Larsen AK, Escargueil AE and Skladanowski A: Pharmacol. Ther., 2003; 99: 167.
13. Marco E, Laine W, Tardy C, Lansiaux A, Iwao M, Ishibashi F, Bailly C and Gago F: J. Med. Chem., 2005; 48: 3796.
14. Giller SA, Zhuk RA and Lidak MI: Dokl. Akad. Nauk. SSR. 1967; 176: 332.
15. Al Safarjalani ON, Zhou XJ, Ras RH, Shi J, Schinazi RF, Naguib FN and El Kouni MH: Cancer Chemother.Pharmacol., 2005; 55: 541.
16. Gauthier B: Ann. Pharm. Fr., 1963; 21: 655.
17. Takeda, US Patent, 1962; 3 016 380.
18. Pirisino R, Bainchini G, Ignesti G and Ramondi L: Pharmocol. Res. Comm., 1996; 18: 241.
19. Modica M, Santagati A, Cutuli V, Mangano N and Caruso A: Pharmazie. 2000; 55: 500.
20. Cenicola ML, Donnali D, Stella L, Paola CD, Constanatio M, Anignwente E, Arena F, Luraschi E and Saturnino C: Pharmacol. Res., 1990; 22: 80.