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BIOLOGICAL ACTIVITIES OF SOME PYRIMIDINE DERIVATIVES

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ABSTRACT

Because they are present in the substructures of medicinal natural products, pyrimidine derivatives have garnered a lot of interest in the chemistry of biological systems. Pyrimidine derivatives have been identified as the most significant structures in nucleic acids due to their notable and strong pharmacological action. The biological activity of annulated pyrimidine derivatives is briefly discussed in this review. Pyrimidine is a nitrogen-containing heterocyclic ring system that is both synthetically and physiologically significant. It has pharmacological and biological properties and is classified as an aromatic six heterocyclic ring with one or three nitrogen atoms. Pyrimidine is important in the domains of chemistry and medicinal chemistry and may be prepared in a variety of ways. Anti-inflammatory, anti-malarial, anti-tumor, cardiovascular, anti-neoplastic, anti-tubercular, anti-HIV, diuretic, antiviral, antimicrobial, and analgesic properties are all shown by pyrimidines and their derivatives. The biological and pharmacological functions of the pyrimidine nucleus are clarified by this review.
Keywords: *Synthesis, Biological Activities, Pyrimidine derivatives.*

INTRODUCTION

The development and formulation of novel, potent medications, as well as their successful use in applicable fields, are the primary goals of forward-thinking and progressive pharmaceutical chemistry research. The primary goal of any research project is to create and construct novel, potent, and unique pharmaceutical ingredients and preparations that can outperform existing drugs more precisely. The discovery and preparation of these medications may have a quantitative or qualitative impact; it is preferable if there are no unwanted side effects, reduced toxicity, enhanced stability, or cheaper cost. A significant component of the heterocyclic family, dihydropyrimidines have a huge number of new derivatives that have an effective pyrimidine ring as the central core or a ring containing heteroatoms like nitrogen. As pyrimidine, this core ring is a crucial component of all diazines and is present in DNA and RNA in the forms of cytosine (1), uracil (2), and thymine (3), as well as purines (4), uric acid (5), and barbituric acid (6). In order to create and find novel molecules that are physiologically and pharmacologically active, they have become particularly interested in the subject of drug research. Because of its many biological actions, including antibacterial and antifungal, antiasthmatic, antiallergic, antihypertensive, cardiotonic, bronchodilator, and anticancer properties, annulated pyrimidine derivatives have drawn a lot of interest in recent years.

Significant synthetic problems arise in the creation of heterocycles with uracil rings. A number of alkaloids derived from marine sources also included semoieties, which contribute to their pharmacological qualities. Because of these heterocycles' broad range of applications and their unique molecules, scientists were inspired to contribute, synthesise several physiologically active new medications, and develop some

effective techniques. The main prerequisite for moving forward with the formulation and design of a safe and effective medication is having enough understanding of the many metabolic processes and endogenous substances that the body goes through. Choosing a certain functional group related to molecular structure is crucial when making a medicine and medicinal chemists' main responsibility is to ensure that the drug has the right pharmacological efficacy rather than determining the internal workings of the organism.

Drugs are evaluated frequently in laboratories to determine their precise and effective pharmaceutical value since they can have appropriate pharmacological action but an unsatisfactory pharmacokinetic profile (absorption, distribution, metabolism, and excretion). A drug's reactivity is thought to result from its interactions with enzymes, receptors, and other molecules present in the biological system. The stability of the drug-enzyme complex, the percentage of active and allosteric sites that the drug occupies, and the correct binding of drug molecules with the enzymes all influence the drug's pharmacological effect. Because of their unique chemical reactivity, heterocycles play a significant role in pharmacological phenomena. They may either impede the normal action of biological receptors or give misleading synthons in the biosynthetic process. Plants contain the majority of nitrogenous bases, which are naturally occurring alkaloids, and many antibiotics, such as streptomycin and penicillin, also comprise heterocyclic rings. The greatest degree of competence is shown by all classes and groups having distinct heteroatoms in the core ring. Six-membered molecules called pyrimidines have a variety of biological and pharmacological properties, such as the ability to prevent the progression of certain deadly illnesses.

Biological Activity of Heterocyclic Compounds

The amazing function that the pyrimidine ring plays in dihydropyrimidine, which is thought to be a fundamental component of nucleic bases, vitamins, enzymes, haemoglobin, hormones, chlorophyll, and a broad variety of medicinal qualities, has led to the development of new physiologically active anti-dots in the pharmaceutical business. Following is a brief description of the vast variety of activities that were shown by the biological analysis of these many changes and altered derivatives, as well as a few examples of acknowledged cases and the structures that correspond to them.

Pyrimidine nuclei are molecules that are essential in the fields of agriculture and medicine due to the fact that they possess antibacterial capabilities. Pyrimidines are a family of antibacterial drugs that have had a considerable impact on the field of antibacterial chemotherapy, particularly in recent years. They constitute a fascinating and substantial class of antibacterial treatments. In addition to their role as chemotherapeutic agents, pyrimidine nuclei possess anticancer characteristics.

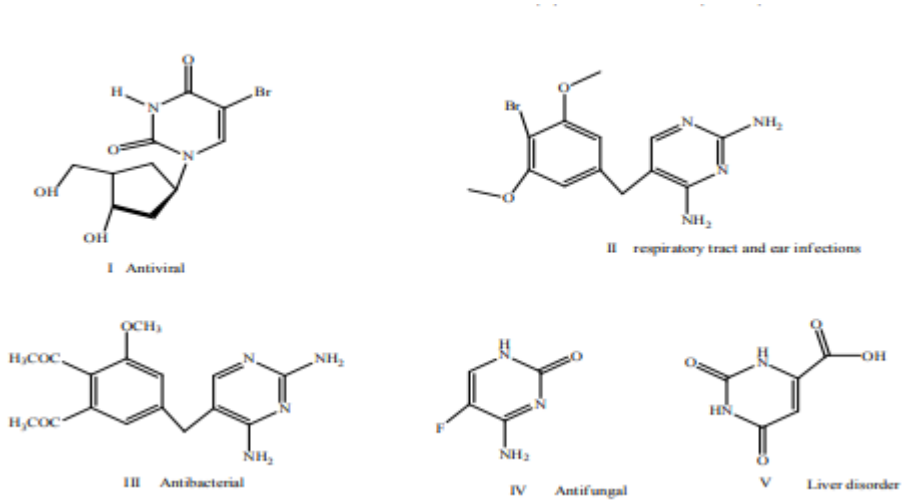

Fig. 1. Pyrimidine compounds that show pharmacological activity

Pyrimidine derivative synthesis and biological functions The equivalent (3) reacts with sulphonamide derivatives when diazonium salts (1) and (2) react in a NaOH solution. Both pyrimidine derivative azo dyes and thiazolyl azo dyes showed good properties on polyester fabrics, but thiazolyl azo dyes showed better properties than pyrimidine derivatives azo dyes. Diazonium salt yields compounds (4a-c) (Fig 1), and compounds (4b) and (4c) show good results against anticancer and antifungal efficacies, Gram-negative and gramme positive respectively. Because of their pharmacological properties, sulphonamidediazobenzene derivatives are employed in nontextile applications.

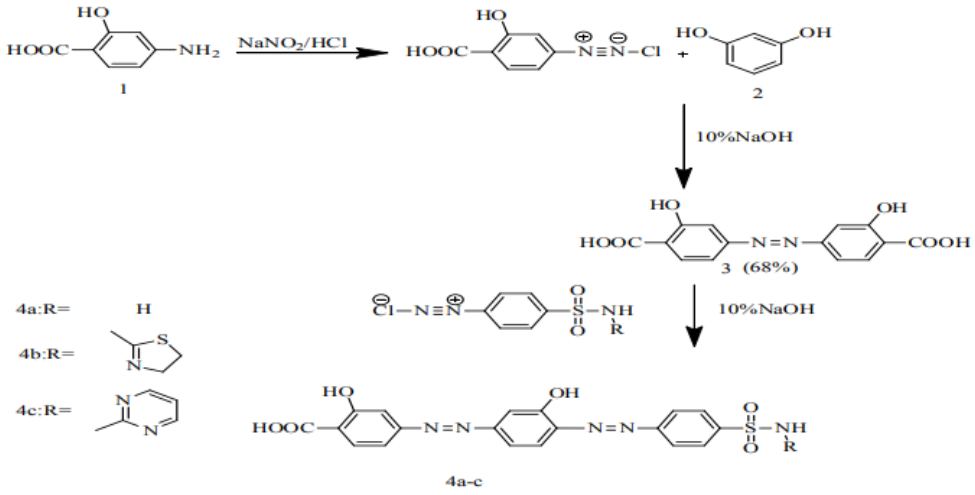

Fig. 1: Synthesis of diazobenzene dyes (4a-c), 4a (81%), 4b (77%), 4c (79%).

A treatment of paracetamol (5) with 2,3-di chlorobenzaldehyde (6) in an OH solution at a temperature of 298 kelvin results in the production of chalcones (7). In methyl alcohol, chalcones (7) undergo a reaction with potassium hydroxide and urea, which results in the production of the equivalent (8). Chalcone (7) may also be handled with thiourea and OH in methyl alcohol to make chemical (9), chalcone (7) and hydrazine monohydrate in acetic acid to produce the equivalent (10), and triazole (11) as a byproduct. All of these reactions can be used to produce chemical (9).

In the process of reaction between (12e) and triazole (11) results the production of unsubstituted triazolo pyrimidine (18e). The formation of triazolo pyrimidine (22) was accomplished by the reaction of chemical (20) with triazole (11). The reaction was carried out by cyclizing (21) and refluxing in the presence of DMF/2CO3 in order to complete the reaction. It was recrystallised using ethanol28 as the solvent. Triazolo pyrimidine (15a) or (18a) are generated when the combination is reacted in DMF with reflux and heat in the presence of potassium carbonate anhydrous. However, there is no reaction that takes place when triazole (11) and (12a) are reacted with other solvents such as methanol/HCl, ethanol, or acetic acid at the same time. In order to verify the validity of (18a), the reaction between malononitrile and (19) was carried out under the same circumstances and with the same sample of (18a). For the production of triazolo pyrimidine (18b), triazole (11) is subjected to the reaction with (12b). In addition, the combination of amino acids (11) and (12c) results in the production of amino derivatives (18c). Through the reaction of (12) with (19), the compound (18d) was produced. On the other hand, compound (18b, c) may also be made through the reaction of benzyl cyanide and cyanoacetate with (19).

In order to create triazolopyrimidine (23), the chemical (22) is subjected to a reflux reaction with substituted 1, 4-benzoquinone and acetonitrile (three equations) (Graph 3). As a consequence of the reaction between equimolecular quantities of compound (11) and β-enaminones (24a) in the presence of DMF/2CO3 and the subsequent refluxing process lasting for two hours, the outcome is the formation of compounds (25a) and (26) in similar proportions. Substituted pyrimidines are produced by the process of cyclocondensation of β-enaminones (24a–c) with 11 and acetic acid with the use of reflux.

According to Fig 4, compounds (24b, c) were subjected to the treatment of compound 11, which resulted in the formation of compounds (25b, c). Pyrimidine derivatives (30a–n) were produced by treating three components (27), (28), and (29) in ethanol. These pyrimidine derivatives are listed in Table 131 below.

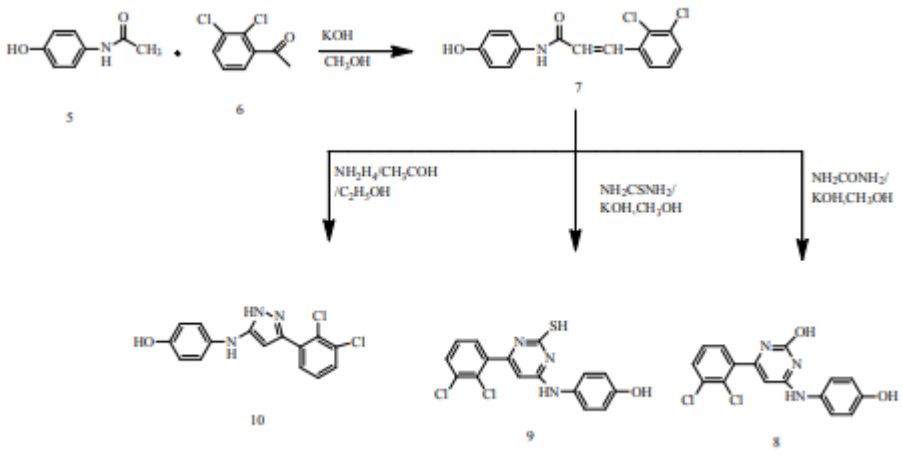

Fig 2: Synthesis of pyrimidine (8) and (9)

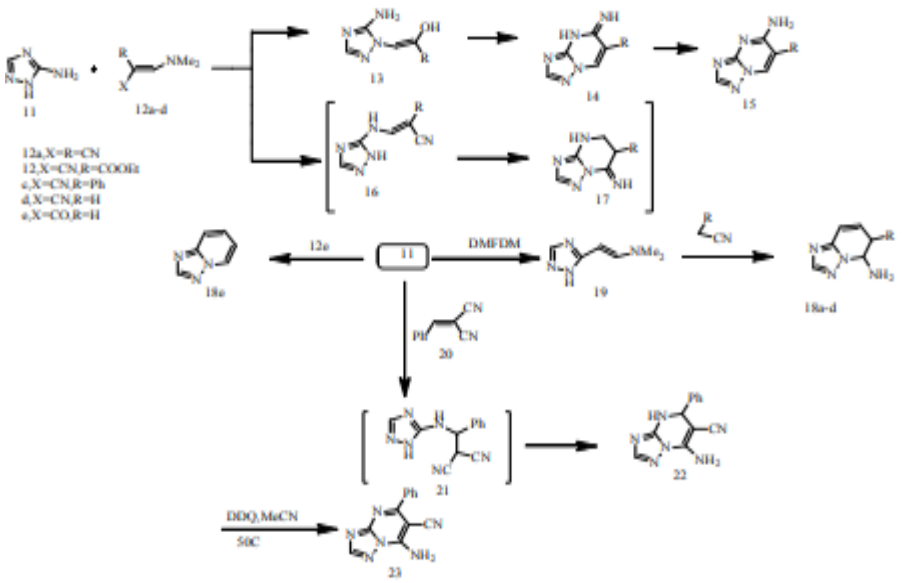

Fig 3: Synthesis of pyrimidine 22 and 23

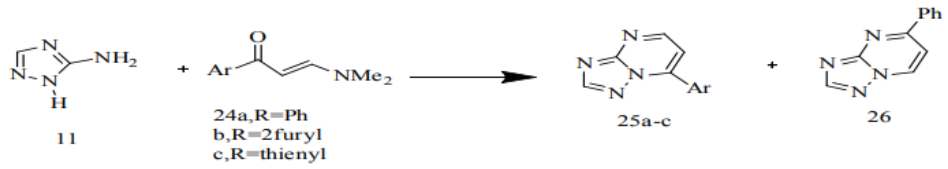

Fig 4: Synthesis of pyrimidine derivatives 25a-c and 26

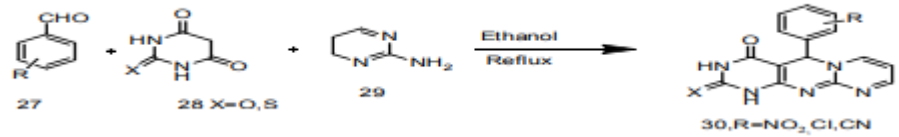

Fig 5: Synthesis of pyrimidines (30a–n)

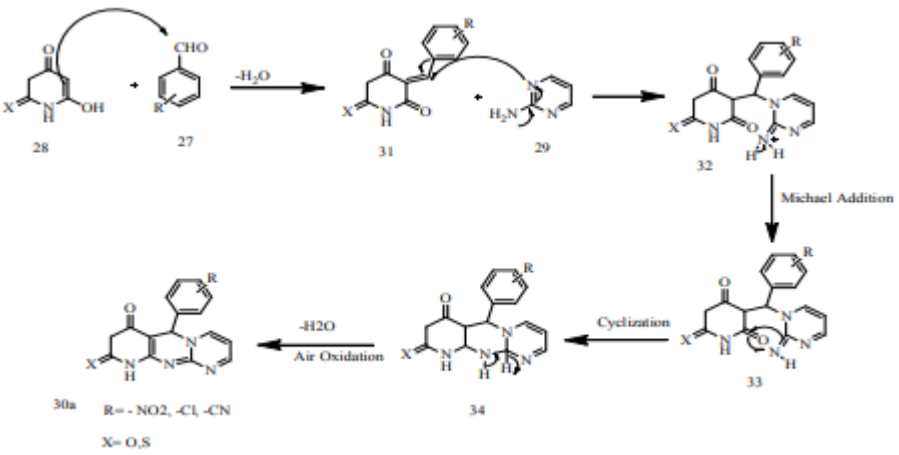

Fig 6: mechanism for synthesized pyrimidines (30a–n).

The N-alkylation product (38a–c) and (39) are formed as a consequence of the reaction of compound (35) with p-toluene while stirring in the presence of 2CO3 and DMF. This reaction takes place when 2-chloro-N-substituted phenylacetamide (37a–c) is treated with thioxopyrimidine 35 and dimethyl formamide, potassium carbonate. Compound (40) is produced when compound (35) is treated with anhydrous potassium carbonate and ethylacetoacetate. This product then reacts with ethanol and hydrazine hydrate to produce the corresponding compound (41) (Fig 7).

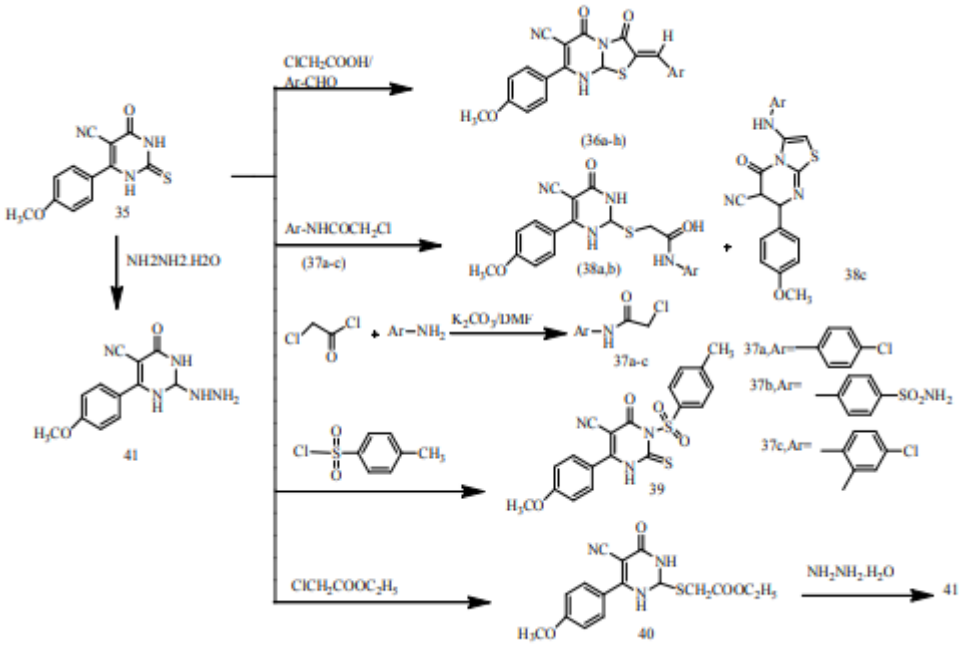

Fig 7: Synthetic pathway of compounds (36-41)

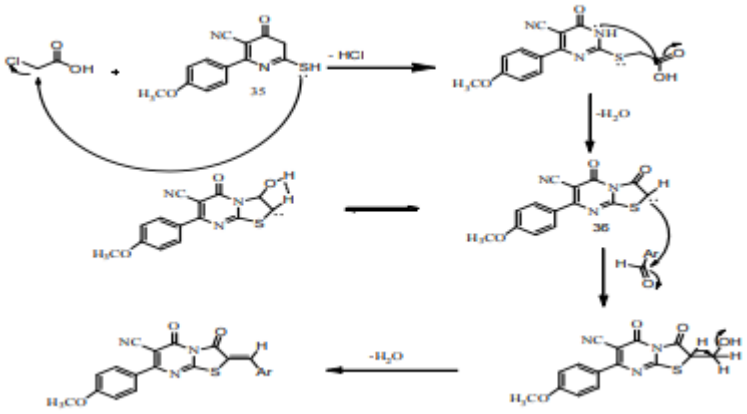

Fig 8: Mechanism for synthesis of (36a-h)

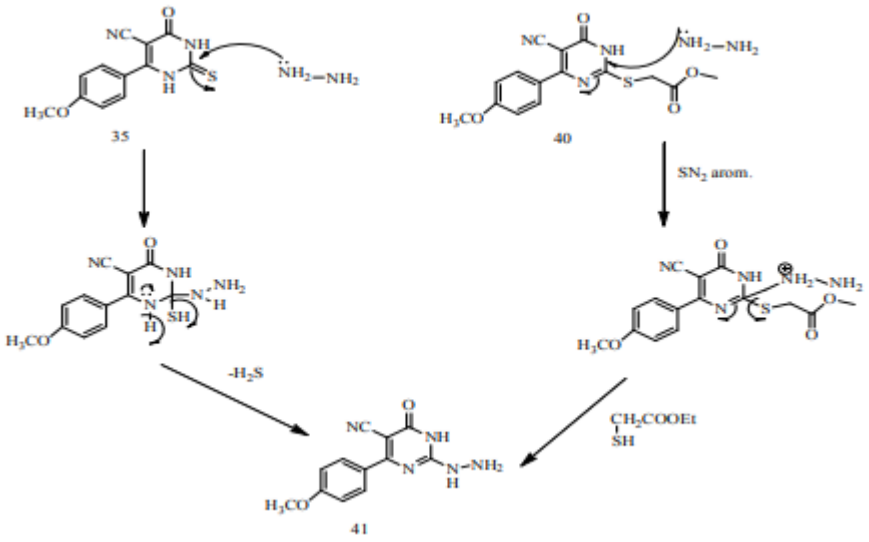

Fig 9: Mechanism for compound (41)

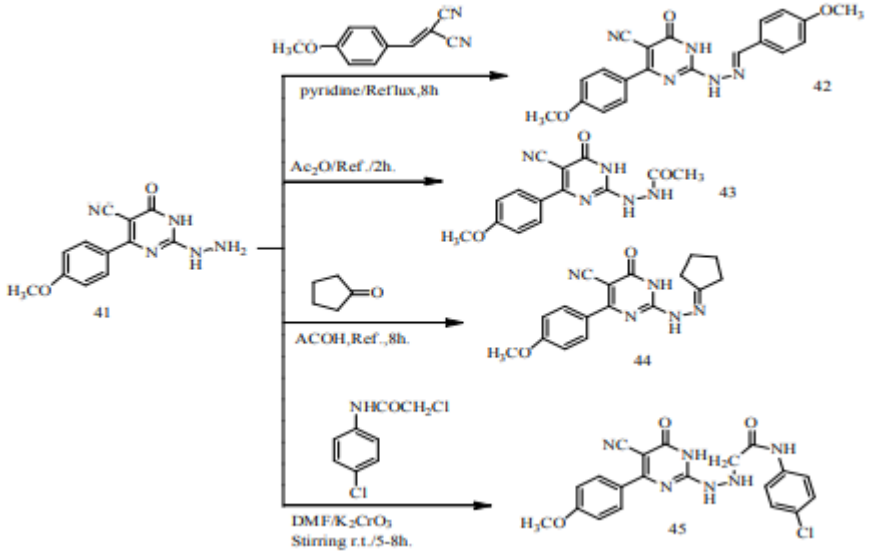

Fig 10: Conversion of (41) to pyrimidine derivatives (42–45)

CONCLUSION

In the present research, the relevance of heterocyclic linked pyrimidine nuclei in terms of both biology and nature is shown. The composition of these pyrimidine units revealed a wide range of significant organic characteristics. Both the cyclocondensation reaction and the reaction of chalcone with a variety of 1, 3-dinucleophiles were used to produce the pyrimidine derivatives that were investigated. derivatives of pyrimidines that have biological activity were also investigated. Adenine, guanine, uracil, thymine, and cytosine are anulated pyrimidine derivatives that are essential components of both DNA and RNA. Anuled pyrimidines are among the most prevalent structures found in nucleic acid. Hence, pyrimidine derivatives are significant heterocyclic compounds due to their role as a building block of all cells and their therapeutic

potential for a wide range of illnesses. It was noted in this study that cyclic N-type structures with distinct electron withdrawing and electron donating substitution groups demonstrated extensive biological act ivities, and that this review focused on the several powerful annulated pyrimidine derivatives.

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