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Synthesis and Antifungal Activities of 2-Hydroxy-4,6-Substituted Phenyl Pyrimidine

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ABSTRACT

Flavones and chromanones are known to be biologically important compounds over 4000 chemically unique flavanoids have been identified in plant sources. These low-molecular-weight substances, found in all vascular plants, with an assortment of basic structure of phenyl benzopyrones (phenyl chromones). In the present work 2-hydroxy pyrimidine and 2-mercapto pyrimidine were prepared from phenol i.e. o-chlorophenol as a starting material. The compounds were characterized on the basis of elemental analysis their IR, ^{1}HNMR and screened for their antifungal activity. Some of these compounds showed significant antifungal activity. The activity was correlated with the structure.

Key words: Chalcone, Pyrimidine, Antifungal activity.

INTRODUCTION

Flavonoids have important effect in plant biochemistry and physiology, acting as antioxidants, enzyme inhibitors, precursors of toxic substances and pigments and light screens. In addition, these compounds are involved in photosensitization and energy transfer, the actions of plant growth of hormones and growth regulators, defence against infection means prevention of disease by the development of active treatments that control illness with minimum side effect. Pyrimidines have been the subject of substantial attention by synthetic and medicinal chemists because of the role of this heteroatomic ring in many biological activities such as anticancer, antiviral, antitumor, anti-inflammatory, antifungal, antimicrobial, anthistaminic analgesic properties were widely cited.

The antifungal activity and antioxidant activity of several plant material have early times, chemical agents, antibiotic, antifungal and antibacterial agents have been effectively used as remedies for the treatment, prevention and diagnosis of the disease. Sickness has been the man's heritage from the beginning and search for remedies to combat, is perhaps equally old. Chemical compounds used are called drugs and their actions on living system are referred to as drug effects. An effective antibiotic must be less toxic for the human being but selectively toxic to the microbial pathogen.

Many plants have been evaluated for the antifungal activity os 2-hydroxyl and 2-mercapto pyrimidine compounds. These plants have been documented to be rich source of flavanoids, flavanones which are interconvertible with isomeric

chalcones. Flowers display as large varieties of colours and they have largest range of components such as anthocyanins, flavones, flavanones, flavanols, chalcones and aurones.

Literature survey reveals that flavanoids are very good antifungal and antioxidant and these play important role in protecting may diseases like cancer, acids, etc. Chromanones are resemble with flavanones in their properties and structure also.

EXPERIMENTAL

Synthesis of compound

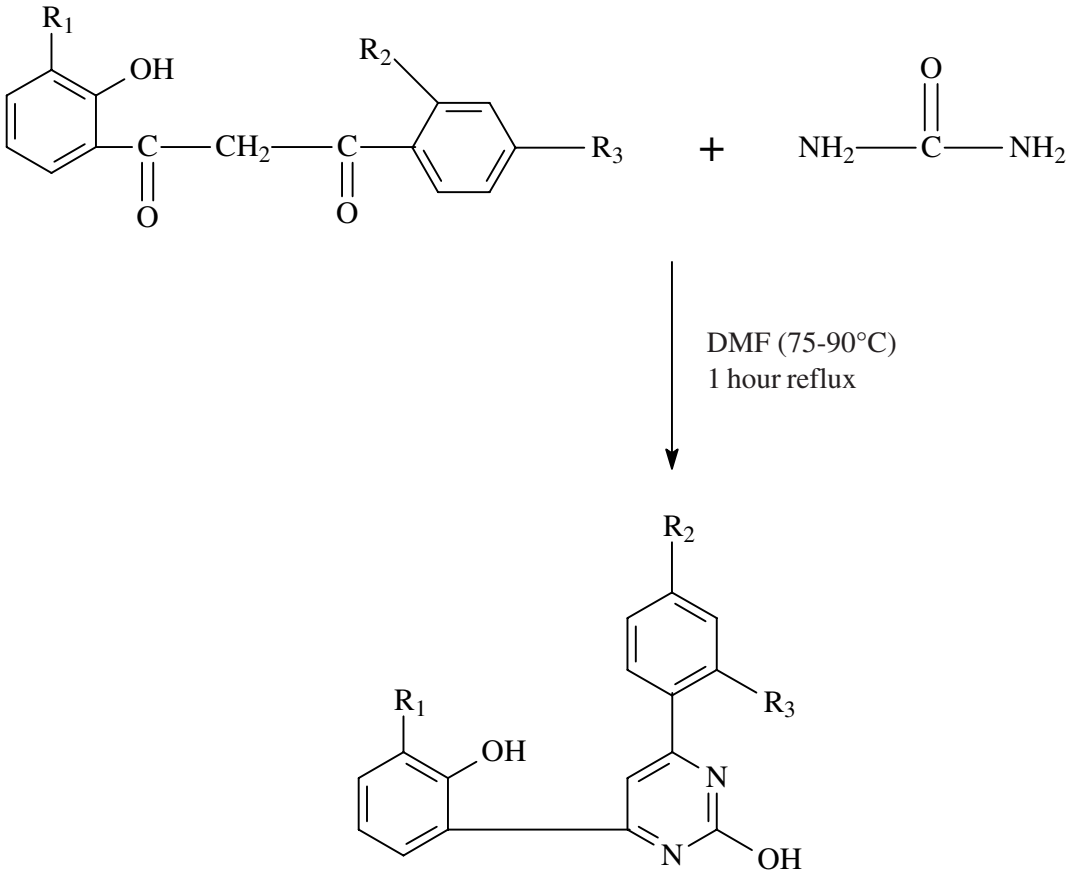
Starting from phenol (o-chlorophenol) and o-cresyl acetate substituted 1,3-propanediones were prepared by acetylation, Fries migration, benzoylation and Baker-Venkatraman transformation by literature method.

The comound namely 2-hydroxy pyrimidine was prepared by refluxing a mixture of diketone and urea in DMF solvent on water bath at 75-90°C for one hour. Similar way 2-mercapto pyrimidie was also prepared by refluxing a mixture of diketone and thiourea in DMF as solvent with same temperature condition.

The melting poings were determined by melting point apparatus and are uncorrected. IR spectra were recorded on Perkin-Elmer (FTIR)-202 spectrometer using KBr pellets. The purity of compounds was tested by Thin Layer Chromatography on Silica gel-G layers.

Antifungal activity

The literature survey indicated that the research work has been done over many years for the study of antifungal activity of fungus. The substituted diketones shows diverse biological activity.



The biological activities are significantly shown by N-heterocyclic nucleus which incorporated with -OH in pyrimidines, some substituted pyrimidines are found to have antifungal activity.

The disc-fusion using dextrose agar medium was employed to study the preliminary antifungal activity of pyrimidine against 3 pathogenic organisms i.e. *Alternaria alternata, Fumigatus aspergillus* and *Pencillium notatum.*

The agar medium was purchased from laboratory of Botany Department, V.B.M.V., Amravati, during investigation Potato Dextrose Agar (PDA), media was used, that PAD medium was employed to study the preliminary antifungal activity of the 2-hydroxyl pyrimidines against *A. alternata, F. aspergillus* and *P. notatum*. Preparation of PDA medium were done as per standard procedure (i.e. 200 gm peeled potatoes, 20 gm, dextrose, 15 gm Agar-Agar, 0.2 gm streptomycin and distilled water 1000 ml as constituents.

The petri disc for the inoculation of fungal organism were sterilized. 1 ml of organic compound (2-hydroxyl pyrimidine) was mixed to the potato, dextrose agar medium and this medium was poured in sterilized petri disc for the inoculation of fungal organisms. The petri disc were incubated at room temperature for 4 days (at 37±1°C) for antifungal activity and also the (48 hours) antibacterial activity study keep it at 24 hours at room temperature. Zone of inhibition produced by each compound was measured fungus/organisms were taken.

RESULTS AND DICUSSION

All the two/three fungus studied are human pathogen from the results of screening, conclusions were drawn.

The 2-hydroxyl pyrimidine was strongly active against *Alternaria alternata.* In view of the structure activity relationship the appreciable enhancement of the antifungal activity was observed, it has also been found that antifungal activity of the compound increases with increase in structure complexity.

Similar way 2-mercapto pyrimidines were found to be more effective against the fungi: Hence, these heterocycles can easily be used for the treatment of diseases caused by test fungi only when they don't have any toxic effect. From the survey it is clear that pyrimidines may help to right the cancer. It is clearly observed that, the growth of fungus were completely stopped by pyrimidines.

CONCLUSION

The structrue activity relationship suggested that pyrimidines containing electron releasing groups like - OH, CH_3 showed higher antibacterial and antifungal activity than the corresponding chalcones because pyrimidines directly inhibits folate metabolism which plays a crucial role in the biosynthesis of nucleic acid precursors in cancer, microbial and protozoan cells. Literature reveals that presence of phenolic content is responsible are easily convertible to chalcones possessing phenolic -OH group. Due to presence of N-atom in the heterocylic show extra heterocyclic ring exhibits higher antioxidant activity.

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