SUBMISSION OF THE FINAL REPORT OF THE WORK DONE ON THE PROJECT

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- **TITLE OF THE PROJECT** : Synthesis and study of novel flavone derivatives as antimicrobial and antioxidant Agent

SUMMARY OF THE PROJECT

- **WHETHER OBJECTIVES WERE ACHIEVED :**

The objective of the present work is focused on the synthesis of novel heterocyclic entities possessing flavones, flavanols and flavanones are based through chalcone derivatives with the aim of significant antimicrobial and antioxidant screening. Based on previous literature survey, we have modified the important scaffold leading to specific structural changes and extended for synthesis of new chemical entities.

As per the proposed work plan I have synthesized flavanoid molecules. All the synthesized compounds were crystallized and purified by column chromatography. Compounds were obtained in moderate to good yield. They are off white to light yellow coloured compounds freely soluble in chloroform, dimethylformamide and dimethylsulfoxide. Structural characterization of all the compounds was done by various spectroscopic method viz; IR, ^{1}HNMR, ^{13}CNMR and Mass Spectral studies.

The minimal inhibitor concentration method (MIC) of synthesized compound has been send for evaluation of their biological activity against two representatives Gram positive organisms viz. *S.aureus*(MTCC 96), *S.pyogenus* (MTCC 442) and two Gram-negative organisms viz. *E.coli*(MTCC 443) *,P.aeruginosa* (MTCC 1688) by the broth dilution method recommended by National Committee for Clinical laboratory (NCCL) standards. All the newly synthesized compounds were also tested for their *in vitro* growth inhibitory activity against the yeast-like pathogenic fungus *C. albicans.* The strains used for the activity were procured from Institute of Microbial Technology, Chandigadh. DMSO was used as diluent/vehicle to get desired concentration of drugs to test upon standard strains. . Standard anti bacterial agents like Ampicillin and Chloramphenicol and anti fungal agent like K.Nystenin were screened under identical conditions for comparison. The minimal inhibitor concentrations (MIC) of synthesized compounds are found to have significant activity when compared with standard drugs.

All compounds synthesized were recrystallised and adequate spectroscopic data IR, ^{1}H NMR, ^{13}C NMR and Mass supported the constitution of the newly synthesized compounds.

➢ ACHIEVEMENTS FROM THE PROJECT

In order to discover novel and potent bactericides, the best way to overcome bacterial resistance, properties of substituted flavone derivatives. On basis of the results of antimicrobial activity of the synthesized compounds it can be concluded that compounds which substitute with chloro, bromo, methoxy and hydroxy groups in flavone derivatives skeleton furnishes active antimicrobial activity, however, best antimicrobial activity can be obtained with halogen and alkoxy substitution. Thus, it appears that most potential antimicrobial activity of compound can be achieved with appropriate combination of heterocyclic moiety substitution with halogen and alkoxy group.

It seems that the substitution of methoxy might influence activity. According to the data of the MIC value number of compounds are the most active compounds against all bacteria. Few compounds is an attractive candidate for development as a novel antimicrobial agent. Presence of two methoxy group in the phenyl ring which linked with the flavone ring , results, in a significant increase in activity, particularly against, *S. aureus, S. typhi, E. coli and B. subtilis* as compared to standard drug Gentamycin.

It is also observed that some of the compound with halogen group causes overall decreases in activity good to moderate particularly against *S.aureus, S. paratyphi, E. coli.* While From antifungal results it seems that compounds exhibits promising activity against *C.albicans*. It can be concluded that presence of halogen leads the enhancement in the fungal activity.

Among all the synthesized compounds, 14 compounds were screened for their in vitro antioxidant activity by various methods such as scavenging of hydrogen peroxide, scavenging of nitric oxide radical, and lipid peroxidation inhibitory activity. The investigation of antioxidant screening revealed that some of the tested compounds showed moderate to good antioxidant activity.

➢ SUMMARY OF THE FINDINGS

Today a large number of dieses are cured or at least controlled by drug therapy. To fight against bacterial and fungal infections has been largely won and significant progress has been made in treating disturbed mental, cardiovascular, gastrointestinal condition. To boast it, can be claimed that certain form of causes can be cured by chemotherapy but even today these irritate physician all times when coupled with other chronic conditions and also due to the resistance offered by acting to various form of therapy.

The great expansion in medicinal research in past has contributed much to the unparalleled progress in medicine during that period. Improved and basically more meaningful biological tests, procedures and methods of diagnosis have provided better guidance in drug discovery by pointing out suggestive observations which could be used in the design of new prophylactic and therapeutic agents. The growth of molecular biology with its chemical insight in to experimental biology has contributed more significant pharmacological theories.

Heterocyclic compounds have to potential for having good activity against bacteria, antitumor, anti inflammation, antiseptic, diuretics, analgesics etc. Among a wide variety of heterocyclic that have been explored for developing pharmaceutically important molecule like chalcones and flavanoids have played an important role in medical chemistry.

Part-1 deals with the synthesis of chalcones. This part is further divided in to two sections. Among the reported methods, the method adopted has found fruitful since yield is in the range of 83-95%. Besides the other heterocycles, the parent compounds were also screened for antimicrobial activity for comparison. Some of the chalcones containing halogen, nitro group have showed excellent antimicrobial activity and rest of the compounds have shown moderate to good anti bacterial activity. Similar trend was observed against fungal strain, perhaps some of the compounds found inactive also.

Part-2 & 3 deals the chemical and biological study of flavone derivatives. Again both the parts are divided into three sections. Yield of all the synthesized flavone derivatives were obtained ranging about 48-71%. Among them, hydroxy group at 3-

position on flavone nucleus showed remarkable antimicrobial activity in comparison with flavones and flavanones.

Newly synthesized entities with number of derivatisations and evaluation of antimicrobial screening against representative bacteria namely gram positive and gram negative strains and fungal strain. Results of the biological activity are reported in the form of MIC (Minimal inhibition concentration). Comparatively, results of the antimicrobial activity of synthesized compounds of section-2.2 and section-3.2 were better in compare to other sections.

The few novel flavone derivatives showed more promising antioxidant activity as compared to that of standard, ascorbic acid. This could be due the availability of free hydroxyl group at 3-position of flavone nucleus. In scavenging of nitric oxide radical techniques, some compounds have shown more potent activity in scavenging of hydrogen peroxide. This may be due to electrodonatig group on benzene ring.

All the compounds selected for antioxidant screening showed higher IC_{50} value than the standard by lipid peroxidation inhibitory activity. Derivatives with electrodonatig group on benzene ring having good antioxidant activity compared with the other compounds in their series. Rest of the compounds exhibited moderate to good antioxidant activity.

- **CONTRIBUTION TO THE SOCIETY**

From the present studies, the transformation products of chalcones viz; flavones, flavanols and flavanones have emerged as potential biologically active systems.We have identified novel potential antimicrobial model as a target. Antimicrobials in this study should be inexpensive to produce using the convenient chemistry that we have developed; cost of production is a critically important consideration if the resulting compounds are ever to be developed into therapeutic agents for the world's developing countries. Our preliminary SAR data and molecular efforts will further direct efforts and even more potent antimicrobials in the future. . Further structural modification in these structures will be of interest and may result in compounds having a better therapeutic and biological activity.