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Biological Activities of Synthesized Dihydropyrimidine Carboxylates and its Derivatives

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ABSTRACT: Many dihydropyrimidines and its related compounds possess various biological, medicinal and industrial activities. We have synthesized dihydropyrimidines and its derivatives and characterized them by IR, ^{1}H-NMR spectroscopy. The pharmacological activities are studied and reported herewith.

Keywords: Dihydropyrimidine carboxylates; Anti-microbial activity; Antibacterial.

INTRODUCTION: Heterocyclic compounds form a major class of organic chemistry having distinct applications in industry and plays crucial role in many biochemical processes. Heterocyclic compounds containing Oxygen, Nitrogen and Sulphur have various biological activities[1-13] such as antiviral, antibacterial, anticancer, antifungal, antioxidants, antimalarial, anti-HIV etc. Heterocyclic compounds have wide application and are present in nature such as vitamins, drugs, biological vital compounds possessing certain medicinal activities including effective action against virus, bacteria, fungi, insect and cancer. They also possess anti-inflammatory, herbicidal properties also. Some heterocyclic compounds has also found application in material science having brightening agent, dyestuff etc. Heterocyclic compounds play an important role in pharmaceuticals as well as agrochemicals. The exploitation for new biologically active heterocyclic analogues has been continuously used in research and medicinal field.

In view to the varied biological and pharmacological applications, we have synthesized dihydropyrimidines carboxylates [14] and screened for microbial activities by standard method. They showed enhanced and significant biological activities than standard one. Results of the activities reveals that compounds exhibit moderate to good antibacterial activities.

Dihydropyrimidine carboxylates- Its biological importance: Dihydropyrimidine nucleus exhibits numerous pharmacological activities. It is present in many bioactive heterocyclic compounds having various biological and clinical applications. They can be extensively used as adhesives for noble metals in medical treatment, dental field, electronic material[15]. Various drugs like nitractin, Bay-41-4109 have excellent antiviral activity (Hurst and Anna, 1962).

In early 1930's, 4-chlorophenyl-2-thio-dihydropyrimidinones was patented for protection of wools against moth (Ertan *et al*, 1933).

Adhikari *et al* synthesized dihydropyrimidines containing quinoline and showed that it possess highest biological activities against *Escherichia coli*, *Staphylococcus aureus* and *Pseudomonas aeruginosa*.

Some ester, cyanide and other substituted compounds are reported to possess good antibacterial properties[16].

MATERIALS AND METHODS: Dihydropyrimidine carboxylates was synthesized from aromatic aldehydes, urea/thiourea, diethyl malonate and ammonium chloride at 100^{o}C followed by recrystallization from ethanol or ethyl acetate: *n*-hexane (1:3). Structure was confirmed from IR and ^{1}H-NMR spectroscopy. The antimicrobial activity evaluation was carried out using a liquid culture of four bacterial

strains namely *Escherichia coli*, *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Candida sp*. by serial dilution method. The results of biological activities of dihydropyrimidine carboxylates and derivatives are presented in table 1.

RESULTS AND DISCUSSION: The following table show biological activities of dihydropyrimidines and its derivatives. From table 1, it is clear that compound 1 showed no microbial activity for *Escherichia coli*, *Pseudomonas aeruginosa*, *Staphylococcus aureus* and *Candida sp* respectively. Compound 2 and compound 6 showed excellent antimicrobial activity against *Candida sp*. as compared to standard Nystatin. Compound 09 and compound 10 showed moderate antimicrobial activity against *Candida sp*.

Table 1: Biological activities of dihydropyrimidines and its derivatives.

Comp.	*Escherichia coli* ATCC 25922	*Pseudomonas aeruginosa* ATCC 25922	*Staphylococcus aureus* ATCC 25923	*Candida sp*
	No Zone	No Zone	No Zone	No Zone
2	No Zone	No Zone	No Zone	**30 mm**
3	**15 mm**	No Zone	**14 mm**	No Zone
4	No Zone	No Zone	**07 mm**	**07 mm**
5	No Zone	No Zone	**16 mm**	**07 mm**
6	No Zone	No Zone	**12 mm**	**30 mm**
7	No Zone	No Zone	**13 mm**	**08 mm**
8	No Zone	No Zone	No Zone	No Zone
9	No Zone	No Zone	**08 mm**	**15 mm**
10	No Zone	No Zone	**07 mm**	**18 mm**
11	No Zone	No Zone	**20 mm**	**08 mm**
12	No Zone	**14 mm**	**15 mm**	**07 mm**
DMSO	No Zone	No Zone	No Zone	No Zone
Gentamicin	18 mm	33 mm	33mm	-----
Nystatin	-----	-----	-----	24 mm

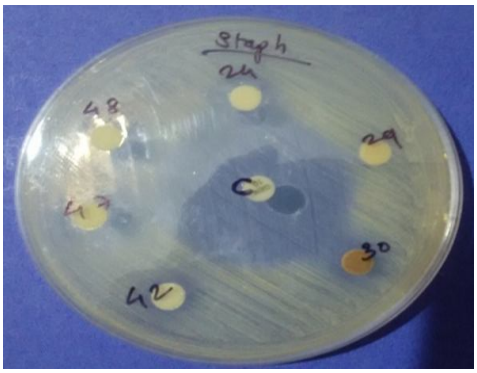

Figure 1: Antibacterial activity against *Staphylococcus aureus.*

Good antibacterial activity against *Escherichia coli* and *Pseudomonas aeruginos* was shown by compound 3 and compound 11 respectively with respect to Gentamicin. Similarly moderate antibacterial activity was associated with compound 3, 5, 11 and 12 against *Staphylococcus aureus* and compound 4, 6, 7 9, 10 showed fairly antibacterial activity against *Staphylococcus aureus*. Compound 4, 5, 7, 11,12 were found to possess fairly antimicrobial activity against *Candida sp*.

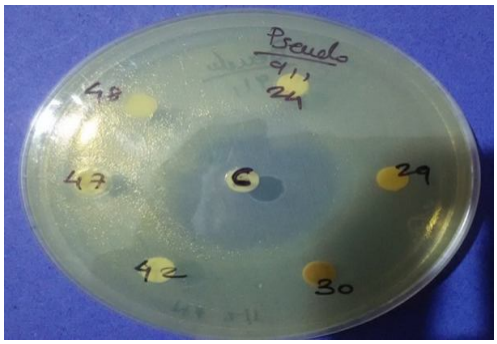

Figure 2: Antibacterial activity against *Pseudomonas aeruginosa.*

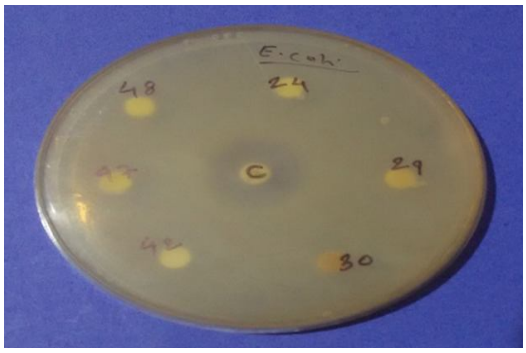

Figure 3: Antibacterial activity against *Escherichia coli.*

CONCLUSION: The present study reveals that dihydropyrimidine carboxylates corresponds to an interesting class of compounds possessing biological activity. On the basis of various literature survey, series of compounds were synthesized by new protocol and further characterized for evaluation of desired pharmacological activity with high potency. Also it will be exciting to observe that the further modification can be utilized as potent therapeutic agent in future and can be evaluated for many diseases whose treatment are difficult in medicinal sciences.

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