Biological Evaluation of Some 6-dihydro-2, 4-di(substituted phenyl)-pyrimid-5-one derivatives

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Abstract : Microwave radiation facilitated synthesis of di(substitutedphenyl)-pyrimid-5-one (I_a-I_j) by condensation of substituted amide(0.01M), aromatic aldehyde (0.015M)and amino acid(0.01M) in presence of metal salt as a catalyst. The reaction mixture was irradiated under scientific microwave oven for 1-2 minutes. The synthesized compounds were characterized by elemental analysis and IR, NMR, CMR, UV and Mass spectrum. Melting point are uncorrected and carried out on Thieles apparatus.The synthesized compound was screened for antimicrobial activities against Proteus vulgaris, Staphylococcus aureus, Escherichia coli and Salmonella typhi. The compounds showed good to moderate activity against the pathogens.

IndexTerms - Condensation, Pyrimidine, microwave irradiation, Antimicrobial activities.

I. INTRODUCTION

Pyrimidine derivatives are important class of heterocyclic compound due to their therapeutic and pharmacological properties like antibiotic[1], antiinflammatory[2], antineoplastic[3-5], antiviral[6-8]. Pyrimidines show significant biological activities such as antitumor, antimicrobial and cardiovascular agent[9-11].The pyrimidine derivatives such as 5-(5-amino-1, 3, 4-thiadiazole-2-yl)-3,4-dihydro-6-methyl-4-phenyl-pyrimidin-2(1H)-one and of 3,4-dihydro-5-(5-mercapto-4H-1,2,4-triazol-3-yl)-6-methyl-4-phenylpyrimidin-2(1H)-one shows significant antibacterial activities against three different species namely, *Pseudomonas aeruginosa*(Gram –ve), *Staphylococcus aureus* (Gram +ve) and *Escherichia coli* (Gram –ve)[12,13].

II. MATERIALS AND METHODS:-

All solvents and reagents are purchased from Merck chemical. All the reactions were carried out in scientific microwave oven (Scientific microwave system model RG311L1, 700w, 2450MHz). Melting ranges of synthesized compounds were determined by open capillary method and are uncorrected. IR spectra were recorded on instrument Perkin Elmer – Spectrum RX- FTIR spectrometer. ^{1}H NMR and ^{13}C NMR spectra were recorded on Advance II 400 NMR spectrometer in $CHCl_3$ using TMS as internal standard. Mass spectra were recorded on a mass spectrometer. The elemental analysis was carried out using Themofinnigan CHNS analyzer. The homogeneity of compound was determined by TLC on silica gel using an eluent acetone. The migrated compounds were visualized by iodine vapour.

2.1 Experimental method

A mixture of substituted amide (0.01M), aldehyde (0.015M), and amino acid (0.01M) in presence of catalyst irradiated in microwave on medium power for appropriate time. After completion, reaction mixture was cooled to room temperature and poured over crushed ice, filtered out and crystallized in ethanol as a solid with maximum yield and appropriate melting point[14].

Ph' :- C_6H_5 [I_a – I_e], C_6H_4N [I_f – I_j]
Ph :- C_6H_4Br[I_a], $C_6H_4NO_2$ [I_b,I_g], C_6H_5[I_c], C_6H_4Cl [I_d], $C_6H_3Cl_2$[I_e,I_h], C_6H_4Cl [I_f], C_6H_5O[I_i], C_7H_7O[I_j]

2.3 Antimicrobial Screening

Disc diffusion method is used for Antimicrobial screening of synthesized compounds and for screening MH agar media utilized. For antimicrobial Screening E.coli, S. aureus, P. vulgaris, S. typhi culture prepared.

2.3.1 Muller Hinton agar (composition)

Ingredients	Gm/L
a. Beef extract	2.0
b. Acid hydrolysate of casein	17.5
c. Starch	1.5
d. Agar	17.0
e. Distilled water	1000 ml
f. pH	7.3± 0.1 at 25°C,

The agar was sterilized by autoclaving at 121^{0}C for 1 minute and was allowed to cool. MH agar was poured in sterile Petri Plates and were allowed to solidify, store the plates at 2-8^{o}C till use.

2.3.2 Cultures

The bacterial cultures used for detection of antibacterial activity were:

a. *Escherichia .coli*
b. *Staphylococcus aureus*
c. *Proteus vulgaris*
d. *Salmonella typhi*

2.3.3. Preparation of cultures:

Two to three colonies from agar medium were inoculated in MH broth (5ml) and kept overnight for incubation at 37^{o}C till the growth attained 0.5 MacFarland unit. (0.5 MacFarland unit turbidity of bacterial culture was prepared using 0.05 ml of 1% (w/v) of $BaCl_2$ and 9.95 ml of Sulphuric acid (1% v/v) and read at 600 nm using water blank). This is prepared to ensure the minimum bacterial concentration (MBC) for the antibacterial analysis. The culture adjusted to 0.5 MacFarland unit (with sterile MH broth) was swabbed on Muller Hinton agar plate using a sterile swab, and the medium was allowed to absorb the medium. The plates were kept in inverted position.

2.3.4.Dilution of Compound:

Initially the extract checked for the solubility in Dimethylsulphaoxide and Dimethylformamide. The extracts soluble in Dimethylformamide and DMF selected as solvent for further analysis. The extracts were weighed and dissolved in Dimethylformamide. The extracts were serially diluted using Dimethylformamide. Sterile disc of Whatman chromatography paper no.1 were dipped in the tubes containing dilution of extract.

2.3.5 Antibacterial activity by disc diffusion method:

Once Sterile disc of Whatman chromatography paper no.1 were dipped in the tubes containing dilution of extract the excess liquid was drained off and the disc was placed on the surface of the agar medium. Standard antibiotic Ampicillin (2 g/ml) was used as standard with each culture. A negative control of Filter paper disc soaked in Dimethylformamide was placed on the plates. The plates were incubated at 37^{o}C for 24 hours. The zone of inhibition was read using antibiotic zone reading scale (Hi-Media). The experiment was performed in triplicate and mean with SD were recorded as results.

III. RESULT AND DISCUSSION:

The zone of inhibition of pyrimidine derivatives I_b, Ie, I_g, I_j against *Proteus vulgaris, Staphylococcus aureus, Escherichia coli and Salmonella typhi* have been recorded. 6-dihydro-4-(4-nitrobenzene)-2-phenyl-pyrimid-5-one(I_b) and 4-(2,4dichlorobenzene)-6-dihydro-2-phenylpyrimid-5-one (Ie) show moderate antimicrobial activities against *Staphylococcus aureus, Escherichia coli* and 6-dihydro-4-(4-nitrobenzene)-2-pyridinepyrimid-5-one(I_g) shows very Strong antimicrobial activities against all four microbes. 6-dihydro-4-(2-hydroxybenzene)-2-pyridinepyrimid-5-one(I_j) unable to show antimicrobial activities. Results reported in table 1.1.

Table 1.1 Antibacterial activities of synthesized compounds on *E.coli, S.aureus, P.vulgaris, S. typhi*

Sr. No.	Compounds	Inhibition zone in mm (MIC in ….mg/ml)			
		E.coli	S.aureus	P. vulgaris	S.typhi
1.	4-(2,4dichlorobenzene)-6-dihydro-2-phenylpyrimid-5-one (Ie)	11(700)	13(500)	-	-
2.	6-dihydro-4-(4-nitrobenzene)-2-phenyl-pyrimid-5-one(I_b)	17(200)	18(500)	25(500)	
3	6-dihydro-4-(4-nitrobenzene)-2-pyridinepyrimid-5-one(I_g)	12(100)	15(100)	13(100)	10(100)
4	6-dihydro-4-(2-hydroxybenzene)-2-pyridinepyrimid-5-one(I_j)	-	-	-	-

IV. CONCLUSION: -

The compound 2,4-di(substitutedphenyl)-6-dihydropyrimid-5-one (Ia-Ie) and 4-substitutedphenyl-6-dihydro-2-pyridinepyrimid-5-one (If-Ij) is very efficient to synthesized. The prepared compounds showed significant antimicrobial activities and these are promising compounds for further pharmacological studies.

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