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Research Article

SYNTHESIS, CHARACTERIZATION AND BIOLOGICAL ACTIVITY OF SOME NOVEL ARYL AND HETROARYL CHALCONE ANALOGUES

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ABSTRACT
A new series of Heterocyclic chalcones showed diversified biological activities. In view of potential biological activities of Heterocyclic chalcones derivative were prepared by claisen-Schmidt condensation technique. The compound were screened for anti-inflammatory and antibacterial activity.
KEY WORDS: Heterocyclic chalcones, claisen-schmidt condensation technique, Anti-inflammatory and, Antibacterial activity.

INTRODUCTION

The development of new anti-inflammatory and antibacterial agents has been a very important step for research, most of the research programme efforts are directed toward the design of new drugs, becose of the unsatisfactory status of present drugs side effects and the acquisition of resistance by the infecting organism to present drugs. The resistance of common pathogens to standard antibiotic therapy is rapidly becoming a major health problem through out the world. These is real perceived need for the discovery of new compounds endowed with antibacterial property. Synthesis of chalcones and their derivatives were reported to have potential anti-inflammatory activity.[1] The presence of reactive a, b, unsaturated ketone group in chalcone is responsible for their antibacterial activity,[2-4] and antifungal activity anti-inflammatory anti-miotic activity,[5] important molecules, pyrrole, pyrimidine,[6] pyridine,[7] indole,[8] flavones, [9-10] and pyrimidinethiones,[11] have played an important role in medicinal chemistry.

MATERIAL AND METHODS

Melting points were determined by open capillary method and are uncorrected. The IR (KBr) spectra were recorded on thermo Nicolet IR-200 spectrophotometer. The ^{1}H-NMR spectra were recorded on varian NMR 400 MHz spectrometer using CDCL3 as a solvent and TMS as internal standard. The purity was conforimed by using TLC using suitable solvent system. 4-acetyl-2- carboxyethyl-3,5-dimethyl pyrrole derivatives and 2-chloro-3- quinolinyl aldehyde undergo claisen-schmidit condensation with ketones to corresponding chalcones Were prepared steps as stated below.

STEP-I The synthesis of aryl substituted chalcones of 4-acety-2-carbxyethyl-3,5-dimethylpyrrole.

The solution of 2,4-dimethyl-3-acetyl-5-carbethoxypyrrole (0.01M) and aldehyde (0.01M) in ethanol at room temp. was add sodium hydroxide (0.01M) with constant stirring. The reaction mixture was stirred further until a precipitate was formed. The reaction mixture was diluted with ice water and neutralized by using (0.01M) diluted hydrochloric acid. The product was filtered washed with water and recrystallized from ethanol.

STEP-II The synthesis of aryl substituted chalcones of 2-Cl-3- quinolinyl aldehyde.

The solution of 2-chloroquinolinyl-3-aldehyde(0.01M) and substituted ketone (0.01M) in ethanol (10ML) at room temperature was added solution hydroxide (0.01M) with constant stirring. The reaction mixture was stirred further until a precipitate was formed. The reaction mixtyre was diluted with ice water and neuterlized by using (0.01M) dilute Hcl. The product was filtered. Washed with water and recrystallised from ethanol. To get the respective chalcone derivatives.

STEP-III The synthesis of aryl substituted chalcones of 3-phenyl-5-Cl-2-furfural.

The solution of 3-phenyl-5-Cl-2-furfur (0.01M) and substituted aromatic ketone (0.01M) in ethanol at room temperature was added sodium hydroxide (0.01M) with constant stirring . The reaction mixture was stirred further until a precipitate was formed. The reaction mixture until a precipitate was formed. The reaction mixture was diluted with ice water and neutralized by using (0.01M) dilute hydrochloric acid, The product was filtered washed with water and recrystallised from ethanol to get the respective chalcone derivatives.

Anti-inflammatory activity[1]

The Anti-inflammatory activity of all the synthesized compounds were studied in –vivo for their percent inhibition of edema in the carrageenan modelof inflammation in rats using the method illustrated by winter et al. All the tested compound revealeted that anti-inflammatory activity standard anti-inflammatory drug Indomethacin. The result are shown in table No- 3.

Anti-bacterial activity[8]

Anti-bacterial activity of all synthesized compound wasdetermined by the disc diffusion method against the gram +ve organism.

Bacillus subtills and Bacillus pumilis and gram –ve organisms E-coli, pseudomonas aeruginosa at 100mg/mL concentration. The bacteria's were sub cultured in nutrient agar medium. The petri dishes were incubated at 37^0C for 24hours. Standard antibacterial drug ampicillin at 100mg/ml concentration was also increased under similar conditions. The results are shown in table No.

RESULTS AND DISCUSSION

Anti-inflammatory activity

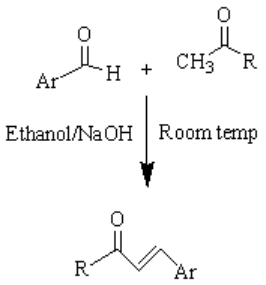
The synthesized 7 compound were selected for the screened for the Anti-inflammatory activity were studied in- vivo for their precent inhibition of edema in the carrageenan model of inflammation in rats, were was comparable to standard Indomethacin B_3, B_4 and B_6 exhibiting highest inhibition.

Animals- Sprague-Dawley rats (140-200gm) of both sexes. Group of six each and fasted for 12 hrs before the experiment paw edema induced by carrageenan. The carrageenan (0.1ml, 1%) administered in to the planter surface of the right hind paw. Negative control group (0.5%CMC) (1hrs prior). Positive controle group (20mg/Kg Indomethacin. Before injection- the average volume (v_o) of the right hind paw of each rat. After injection- the paw volume (v_t) was measured after 3 hrs with plethysmoeter. The percentage inhibition of acute edema was obtaind as follows,

% Inhibition= (1-(V experimenta l/ V control)) = +100 , where $V= V_t - V_o$ = Mean paw volume.

Table no-1 Physical characterization data of compounds (B_1-B_7)

S.no	Compounds	R	Ar	M.P	Mol.Formula	Mol.Wieght
1	B_1	2,4dimethyl-3-acetyl-5-carbethoxy pyrrole	Phenol	165^{oC}	$C_{18}H_{19}O_3N$	297
2	B_2	2,4dimethyl-3-acetyl-5-carbethoxy pyrrole	4-Cl-phenol	210^{oC}	$C_{18}H_{18}O_3NCl$	331
3	B_3	2,4dimethyl-3-acetyl-5-carbethoxy pyrrole	4-methoxy phenol	165^{oC}	$C_{19}H_{21}O_4N$	327
4	B_4	4-Cl-phenol	2-Cl quinolin-3-yl	135^{oC}	$C_{18}H_{11}ONCl_2$	328
5	B_5	4-Br-phenol	2-Cl quinolin-3-yl	185^{oC}	$C_{18}H_{11}ONClBr$	371
6	B_6	4-Br-phenol	3-phenyl-5-Cl-2-furfuryl	120^{oC}	$C_{19}H_{12}O2ClBr$	386
7	B_7	4-Br-phenol	3-phenyl-5-Cl-2-furfuryl	120^{oC}	$C_{19}H_{12}O2ClBr$	353



(1-7 Compound)
SCHEME

Antibacterial Activity

The synthesized 7 compounds were screened for the Antibacterial activity studies at 50µg/mL and 100µg/mL using DMSO as a control against staphylococcus aureus, Bacillus pumilis, Bacillus subtilis, Escherichisa coli and Pseudomonas aeruginosa by disk-diffusion method on nutrient agar media, Ampicillin was used as standard drug for the comparison at the concentration 50µg/mL and 100µg/mL against Gram-positive and Gram-negative bacteria used for the study.

Data in the Table.No-4. Clearly indicates that none of the compound exhibits antibacterial activity. The zone of inhibition of the entire synthesized compounds was between 7-10 mm at 50µg/mL concentration and 11-13 mm at 100µg/mL concentration.

Whereas the zone of inhibition of standard drug Ampicillin was 21-24 mm at 50µg/mL concentration and 32-35 mm 100µg/mL concentration, many studies have revealed that Chalcone derivatives, are having good antibacterial activity, but in the present study none of the synthesized compound exhibits such anti-bacterial activity. Which may be leads to the rigidity of the compounds and this may hinders the cleavage of molecules in physiological pH, which is a basic requirement for the activity of Chalcone derivatives.

Table no-2 Spectral data of Synthesis of Heteroaryl Chalcone derivatives: IR and NMR Spectra

	IR	NMR
1-3	IR(KBR):1690cm-1 (C=O),3285cm-1(NH),815cm-1(Ar-Cl):	1NMR(DMSO):S1.38(t,3H,OCH2CH3),2.62(S,3H,CH3),7.15(d,2H,3,5,H)7.35(d,2H,4,6,H)7.50(d,1H,CH=CH),7.53(d,1H,CH=CH),9.13(S,1H,NH),2.17(S,2H,H2O).
4-5	IR(KBR):1715cm-1 (C=O),1555cm-1(CH=CH),2919cm-1(C-H), 745cm-1(Ar-Cl):	1NMR(DMSO):S7.28(S,1H,4H Quinolin-3-yl),7.98(S,1H,5HqUINOLIN-3-yl),7,61(t,1H,6HQuinolin-3-yl), 7.78(t,1H,7HQuinolin-3-yl),8.54(S,1h,8hQuinolin-3-yl), 7.90(d,1H,(CH=CH),8.24(d,1H,(CH=CH),7.41(d,2H,3,5,H),7.5(d,2H,4,6,),2.17(S,2H,H2O).
6-7	IR(KBR):1667cm-1 (C=O),1555cm-1(CH=CH),3298cm-1(NH,str), 763cm-1(Ar-Cl):	1NMR(DMSO):S7.65-7.80(m,5H, aromatic)7.50(d,1H,ch=ch),7.53(d,1h,(CH=CH),7.857.95(m,5H, aromatic),2.17(S,2H, H2O)

Table No3 In Vivo anti-inflammatory activities of aryl and Heteroaryl chalcone derivatives.

Compounds	Vt - Vo (mean+ -SEM)	% Inhibition of edema at the end of three hrs.
B1	0.0086 + - 0.016	70.12*
B2	0.0088 + - 0.017	72.00*
B3	0.126 + - 0.020	81.01*
B4	0.090 + - 0.012	82.12*
B5	0.0073 + - 0.004	79.00*
B6	0.075 + - 0.004	85.00*
B7	0.065 + - 0.021	71.00*
Indomethacin	0.09 + - 0.010	90.00*

Value expressed as Mean +- SEM, n = 6 in each group. *P< 0.01 Compound with control .

Table No4 Antibacterial activity of newly synthesized aryl and Hetroaryl chalcon derivatives.

Sample code	Inhibition zone diameter in nm							
	B.subtills		B.pumills		E.coli		P.aureaginosa	
	50µg	100 µg	50µg	100 µg	50µg	100 µg	50µg	100 µg
B1	9	13	9	12	9	13	8	13
B2	8	12	8	13	8	11	8	12
B3	9	12	9	12	9	12	9	12
B4	8	13	8	11	8	13	9	11
B5	6	11	7	8	7	10	8	11
B6	6	10	7	10	7	9	7	9
Ampicillin	22	34	21	32	22	35	24	34
DMSO	-	-	-	-	-	-	-	-

*Average of triplicate ± standard deviation

Note:- " _" denotes no activity, 7-9 mm better activity,10-13 mm good activity.

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