Synthesis, Characterization and Biological Evaluation of Chalcones and its derivatives for Antibacterial and Anti inflammatory Activity.

Abstract:

Medicinal chemistry or pharmaceutical chemistry is a discipline at the intersection of chemistry and pharmacology involved with designing, synthesizing and developing pharmaceutical drugs.Chalcones is a generic term given to compounds bearing the 1,3- diarylprop2-en-1-one, which can be functionlized in the propane chain by the presence of olefinic, keto and/or hydroxyl group. Chalcones belongs to the flavonoid family. Chalcones are an important class of natural products and are considered as the precursors of flavonoids and isoflavonoids. Chemically, chalcones are 1,3-diaryl-2-propen-1-ones in which two aromatic rings are joined by a three carbon bridge having a carbonyl moiety and α, β unsaturation. The compounds with the backbone of chalcones have been reported to possess various biological activities such as antimicrobial, anti-inflammatory, analgesic, anti platelet, anti- ulcerative, anti malarial, anticancer, antiviral, anti leishmanial, antioxidant, antitubercular, anti-hyperglycemic, immunomodulatory, inhibition of chemical mediators release, inhibition of leukotriene B4, inhibition of tyrosinase and inhibition of aldose reductase activities. This paper mainly focuses on chalcones synthesized by Claisen Schmidt condensation which involves the condensation between an aromatic aldehyde or ketone with an aliphatic ketone or aldehyde catalysed by the presence of dilute alkali or acid to form alpha beta unsaturated compound. through reviewing different biological significance of chalcones and their derivatives have been reported along with their chemistry and of synthesis.

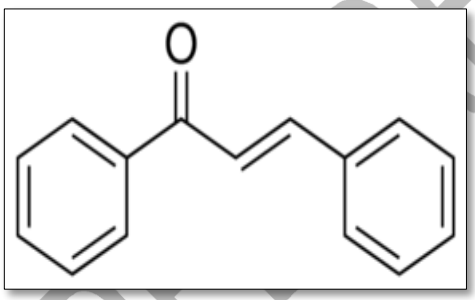
Key Words:- Chalcone, Aldol condensation, Claisen Schmidt condensation, Pharmacological / Biological activity.

Introduction :

Chalcones are a major class of natural products belonging to the flavonoid family. They are considered as the precursors of flavonoids and isoflavonoids .[1] Chalcone (and related compounds "chalconoids") is an aromatic ketone that forms the central core for a variety of important

biological compounds, which are known collectively as chalcones. They are also the precursors of a number of biologically important heterocyclic compounds [2]. Chalcones have been used as intermediates for the preparation of compounds having therapeutic value.[3,4] They are widely distributed in fruits, vegetables, tea, spices, soy based foods and other plant products. Chemically, chalcones are 1,3-diaryl-2-propen-1-ones in which twoaromatic rings or substituted aromatic rings are joined together by a three carbon atom α,β unsaturated carbonyl system. Pharmacological properties of chalcones are due to the presence of both a,ß-unsaturation and an aromatic ring. Chalcones considered as precursors of flavonoids and isoflavonoids are abundant in plants (Ni *et al.* 2004; Nowakowska, 2007; Dimmock *et al.* 1999).

Fig 1 : They have the following general structure and formula



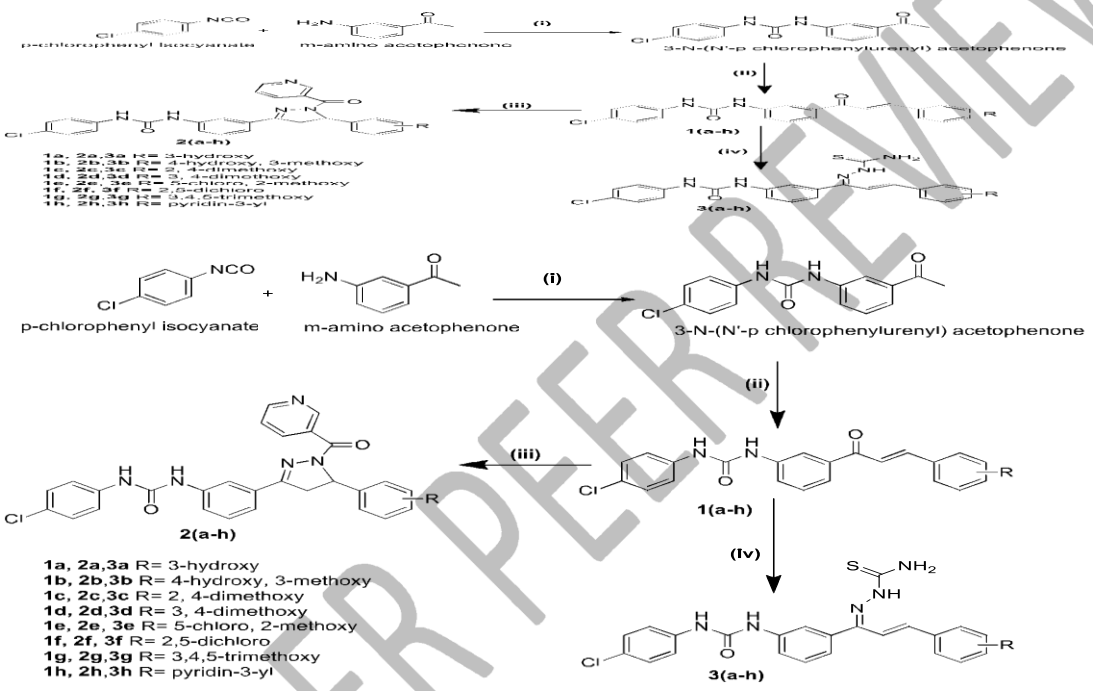
Material and Methods:

The following methods for synthesizing an Chalcones and chalcones derivatives. All the chemicals used were obtained from Sigma-Aldrich, Spectrochem and High Media.The melting point is determined by using an open capillary and are uncorrected .TLc were performed on silica sel G plates with observation in under UV or iodine chamber . IR spectra were recorded on a FT-IR Shimadzu DZU 8400S spectrophotometer in KBr disks and Elemental analysis were done on a Perkin-Elmer 2400C, H, N analyzer and values were found to be within the acceptable limits of the calculated values. The ^{1}H-NMR spectra of the synthesized compounds in $CDCl_3$/DMSO were recorded at 400 MHz by Bruker Advance II 400 NMR spectrometer. Chemical shift values are given in scale using tetramethylsilane (TMS) as an internal standard. Significant ^{1}H-NMR data are written in order: number of protons, multiplicity (b, broad; s, singlet; d, doublet; dd, double doublet; t, triplet; m, multiplet), coupling constants in Hertz,

assignment. The FAB mass spectra (at room temperature) were recorded on TOF MS-ES$^+$ mass spectrometer.

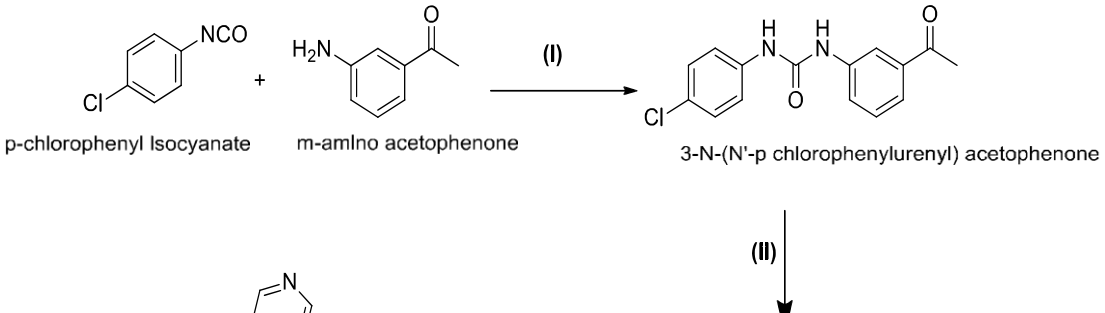
Synthesis of Chalcones

Chalcones are synthesized by Claisen-Schmidt condensation (Furniss *et al.*, 1989; Kumar *et al.*, 2010) of aldehyde and ketone by base catalyzed or acid catalyzed followed by dehydration to yield chalcones (Figure 4.5).

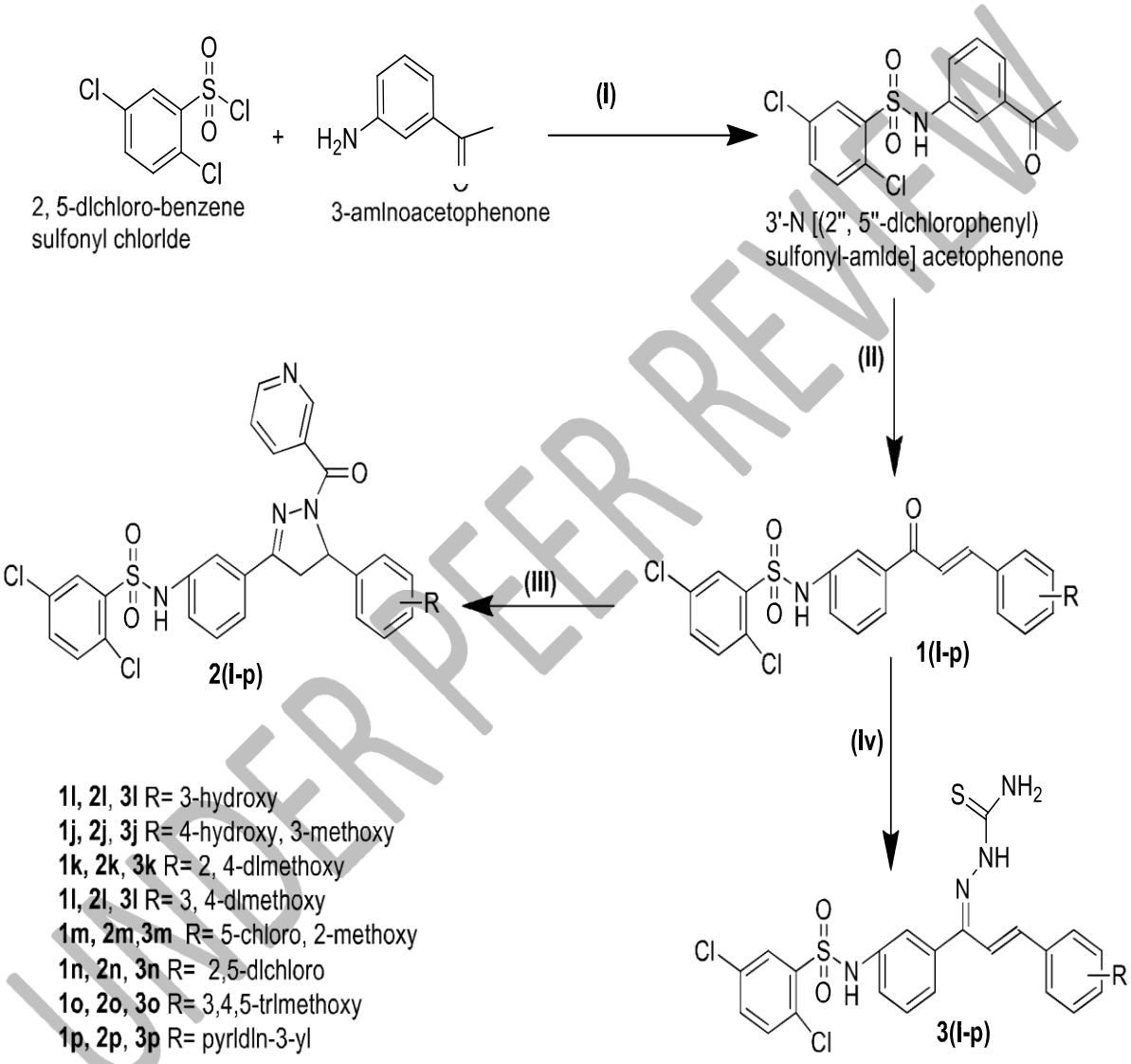


Mechanism of reaction for synthesis of chalcone derivatives (1a-1p)

The synthesis of the designed compounds 1a-1h, 2a-2h, 3a-3h (i) Me_2CO, rt, 6 hr (ii) substituted benzaldehyde, methanolic NaOH, stirred at room temperature, 24 hr (iii) *n*-butanol, reflux (iv) thiosemicarbazide, EtOH, AcOH, reflux



The synthesis of the designed compounds 1i-1p, 2i-2p, 3i-3p (i) $CHCl_3$, rt, 3-6 hrs (ii) substituted benzaldehyde, methanolic NaOH, stirred at room temperature, 24 hr (iii) *n*-butanol, reflux (iv) thiosemicarbazide, EtOH, AcOH, reflux.

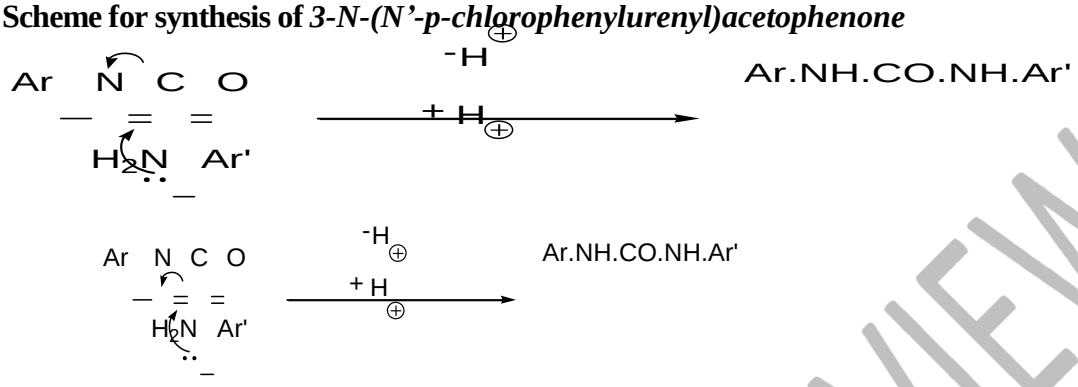


Synthesis 3-N-(N'-p-chlorophenylurenyl)acetophenone

Synthesis of methyl ketone derivative was carried out by making *m*-amino acetophenone react with the *p*-chlorophenyl isocyanate. A mixture of the *m*-aminoacetophenone (2.7 g, 20 mmol) and *p*-chlorophenyl isocyanate (3 g, 20 mmol) was

dissolved in dry acetone (100 mL). The mixture was stirred for 6-7 hrs at room temperature, filtered, and the crude compound urenylacetophenone was recrystallized using ethanol (Sonmez *et al.*, 2011).

Scheme for synthesis of *3-N-(N'-p-chlorophenylurenyl)acetophenone*

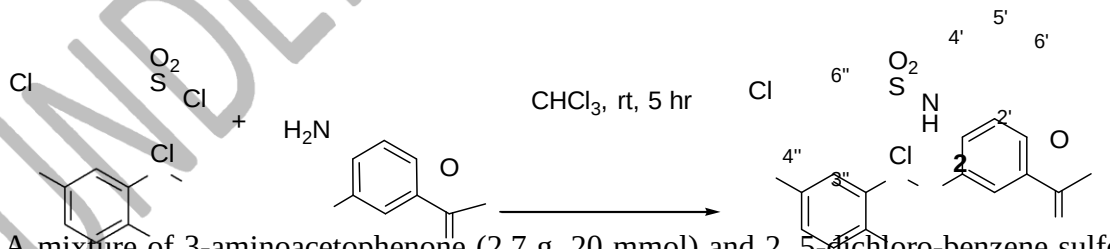


Yield 3.3 g, 58%, White solid; mp 272-274 ^{o}C; IR(KBr) $_{max}$ /cm^{-1} 3372 (N-H), 3056 (ArC-H), 2962 2872 (C-H), 1711 ($COCH_3$), 1645 (C=O), 1614, 1534, 1461 (Ar C=C), 1515, 1290, 1185 (ArC-N), 1147 (Ar-Cl) 756, 687 (Ar); ^{1}H-NMR (DMSO-d_6, 400 MHz): $_{H}$ 9.12 (br s, 1H, NH), 8.91 (br s, 1H, NH); 8.18 (1H, s, H-2), 7.78 (1H, d, *J* 5.9, H-6), 7.53 (3H, m, H-4, 2', 6'), 7.30 (1H, t, *J* 6.30, H-5), 7.21 (2H, d, *J* 6.65, H-3', 5'), 2.53 (s, 3H, 3-$COCH_3$).

Synthesis of 3'-N [(2'', 5''-dichlorophenyl) sulfonyl-amide] acetophenone

The intermediate compound 3'-N[(2'',5''-dichlorophenyl) sulfonyl-amide] acetophenone was synthesized adopting the procedure described by Leon *et al*. (2007) with some modifications (Figure 4.4).

Scheme for synthesis of 3'-N[(2'',5''-dichlorophenyl) sulfonyl-amide] acetophenone



A mixture of 3-aminoacetophenone (2.7 g, 20 mmol) and 2, 5-dichloro-benzene sulfonyl chloride (4.9 g, 20 mmol) in 5 mL of chloroform was stirred at room temperature (rt) for 3–6 hrs. The resulting precipitate was washed with acetone, filtered, and the crude material obtained was recrystallized in acetonitrile to give pure compound 3'-N[(2'',5''-dichlorophenyl) sulfonyl-amide] acetophenone. Yield 3.6 g, 52%, Brown crystals; mp 230–232 °C; IR 3216 (N-H); 1667 (C=O);

1715 ($COCH_3$), 1337, 1270 (SO_2), 1142 (Ar-Cl), 3060 (Ar-H), 2967 (C-H), 1584, 1461, 1357, 1297, 1273, 1166, 993, 852, 819, 795, 720 (Ar); ^{1}H-NMR: $_H$ 11.38 (s, 1H, NH), 7.94 (1H, s, H-6´´), 7.70 (1H, d, *J* 8.44, H-3´´), 7.25-7.44 (3H, m, H-2´, 5´, 6'), 7.71 (d, 1H, *J* 6.42, H-4´´), 6.94 (1H, d, *J* 8.91, H4'), 2.51 (s, 3H, CH_3CO).

General procedure for the synthesis of chalcone derivatives (1a-1p)

To a solution of substituted acetophenone (16 mmole) in 10 mL of methanol on an ice bath, freshly prepared 2 N methanolic NaOH solution (60 mL) was added and stirred for 10 min. To this, appropriate aldehyde (16 mmole) was added and stirred at room temperature for 12-24 hrs. The reaction mixture was cooled on an ice bath, neutralized with diluted HCl and the precipitate was washed three times with 50 mL distilled water to give the crude product. The product was recrystallized from methanol or ethanol/water.

The purity of the product was checked by TLC using ethylacetate and hexane (4:6) as mobile phase and iodine vapors as detecting agent.

[(E)-1-(4''-chlorophenyl)-3-(3-(3'-(3-hydroxyphenyl)acryloyl)phenyl)urea (1a)

(E)-1-(4''-chlorophenyl)-3-(3-(3'-(4-hydroxy-3-methoxyphenyl)acryloyl)phenyl)urea (1b) Synthesis of (E)-1-(4''-chlorophenyl)-3-(3-(3'-(2,4-dimethoxyphenyl)acryloyl) phenyl)urea (1c) Synthesis of (E)-1-(4''-chlorophenyl)-3-(3-(3'-(3,4-dimethoxyphenyl)acryloyl) phenyl)urea (1d) Synthesis of (E)-1-(3-(3-(5-chloro-2-methoxyphenyl)acryloyl)phenyl)-3-(4-chloro-phenyl)urea (1e) Synthesis of (E)-1-(4''-chlorophenyl)-3-(3'-(3-(2,5-dichlorophenyl)acryloyl) phenyl)urea (1f)

Synthesis of (E)-1-(4''-chlorophenyl)-3-(3'-(3-(3,4,5-trimethoxyphenyl) acryloyl) phenyl)urea (1g)

Synthesis of (E)-1-(4''-chlorophenyl)-3-(3'-(3-(pyridin-3-yl)acryloyl) phenyl) urea (1h)

Synthesis of (E)-2'',5''-dichloro-N-(3'-(3-(3-methoxyphenyl)acryloyl)phenyl)benzene sulfonamide (1i)

Synthesis of (E)-2'',5''-dichloro-N-(3'-(3-(3-hydroxy,4-methoxyphenyl)acryloyl)phenyl) benzenesulfonamide (1j)

Synthesis of (E)-2'',5''-dichloro-N-(3'-(3-(2,4-dimethoxyphenyl)acryloyl)phenyl) benzene sulfonamide (1k)

Synthesis of (E)-2'',5''-dichloro-N-(3'-(3-(3,4-dimethoxyphenyl)acryloyl) phenyl) benzene sulfonamide (1l)

Synthesis of (E)-2'',5''-dichloro-N-(3'-(3-(5-chloro-2-methoxyphenyl)acryloyl)phenyl) benzenesulfonamide (1m)

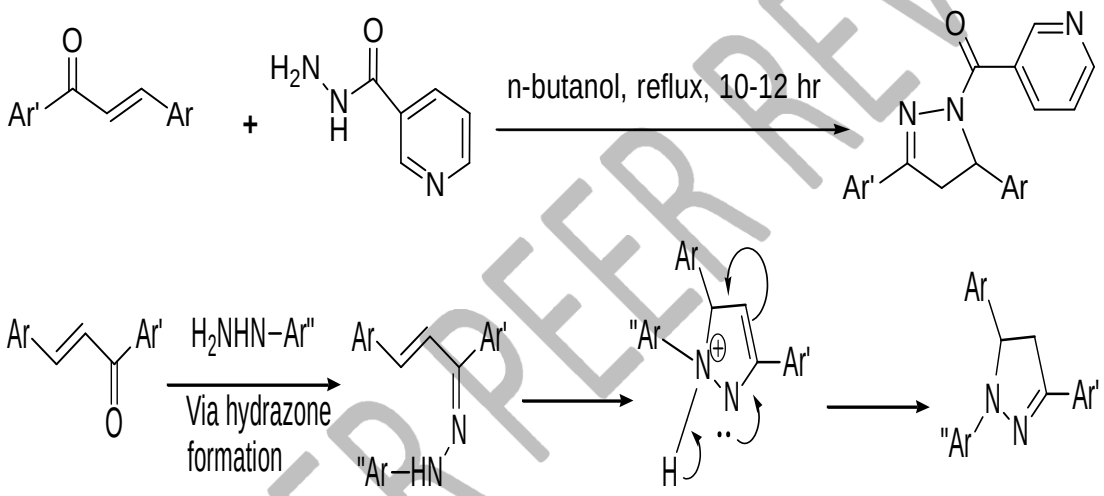
Synthesis of (E)-2'',5''-dichloro-N-(3'-(3-(2,5-dichlorophenyl)acryloyl)phenyl) benzenesulfonamide(1n)

Synthesis of (E)-2'',5''-dichloro-N-(3'-(3-(3,4,5-trimethoxyphenyl)acryloyl)phenyl)benzene sulfonamide (1o)

Synthesis of (E)-2'',5''-dichloro-N-(3'-(3-(pyridin-3-yl)acryloyl)phenyl) benzene sulfonamide (1p)**]**

General method for synthesis of 1, 3, 5-trisubstituted pyrazolines (2a-2p)

1,3,5-trisubstituted pyrazolines (**2a-2p**) were synthesized according to the scheme depicted in Figure 4.6 (Ozdemir *et al.*, 2008). In this method, chalcone and nicotinic acid hydrazide were refluxed in *n*-butanol in order to synthesize the desired product (Kini and Gandhi, 2008). Factors such as the structure and position of the substituents have profoundly influenced the rate of the reaction. The generally accepted interpretation of this reaction, involves the initial formation of an aryl hydrazone with subsequent nucleophilic attack of nitrogen upon the carbon-carbon double bond at □ position. Hence the electropositive nature of □ carbon may control the overall rate of the reaction. The electropositive nature of □ carbon is controlled by the aromatic ring directly connected to it. Halogens being electron withdrawing in nature significantly increase the positive character of □ carbon lead to faster reaction while electron donating alkyl and alkoxy groups contributed for slower reaction.



Scheme and mechanism of reaction for synthesis of compounds (2a-2p)

To the solution of the appropriate chalcone **1a-1p** (4 mmole) in 10 mL of *n*-butanol, (0.55 g, 4 mmole) of nicotinic acid hydrazide was added and the reaction mixture was refluxed for 8–10 hrs. The excess of solvent was removed under reduced pressure and the reaction mixture was cooled on an ice bath. The products precipitated out at low temperature were washed five times with 50 mL distilled water, reconstituted in minimum amount of methanol and dried under reduced pressure. This product was further purified by recrystallization from the ethanol-DMF mixture (1:1). Purity of the products was checked by TLC using mixture of acetone and petroleum ether (40:60 V/V) as mobile phase.

[a-(4”-chlorophenyl)-c-(3-(5''-(3'-hydroxyphenyl)-1-nicotinoyl-4,5-dihydro-1H-pyrazol-3-yl)phenyl)urea (2a)

a-(4”-chlorophenyl)-c-(3-(5''-(4’-hydroxy,3'-methoxyphenyl)-1-nicotinoyl-4,5-dihydro-1H-pyrazol-3-yl)phenyl)urea (2b)

a-(4”-chlorophenyl)-c-(3-(5-(2',4'-dimethoxyphenyl)-1-nicotinoyl-4,5-dihydro-1H-pyrazol-3-yl)phenyl)urea (2c)

a-(4”-chlorophenyl)-c-(3-(5-(2',4'-dimethoxyphenyl)-1-nicotinoyl-4,5-dihydro-1H-pyrazol-3-yl)phenyl)urea (2d)

a-(4”-chlorophenyl)-c-(3-(5-(3',4'-dimethoxyphenyl)-1-nicotinoyl-4,5-dihydro-1H-pyrazol-3-yl)phenyl)urea (2e)

a-(4”-chlorophenyl)-c-(3-(5-(2',5'-dichloroyphenyl)-1-nicotinoyl-4,5-dihydro-1H-pyrazol-3-yl)phenyl)urea (2f)

a-(4”-chlorophenyl)-c-(3-(5-(3',4’,5’-trimethoxyphenyl)-1-nicotinoyl-4,5-dihydro-1H-pyrazol-3-yl)phenyl)urea (2g)

a-(4”-chlorophenyl)-c-(3-(5-(pyridine-3’-yl)-1-nicotinoyl-4,5-dihydro-1H-pyrazol-3-yl)phenyl)urea (2h)

2”,5”-dichloro-N-(3-(5-(3'-hydroxyphenyl)-1-nicotinoyl-4,5-dihydro-1H-pyrazol-3-yl)phenyl)benzenesulphonamide (2i)

2”,5”-dichloro-N-(3-(5-(4’-hydroxy,3'-methoxyphenyl)-1-nicotinoyl-4,5-dihydro-1H-pyrazol-3-yl)phenyl)benzenesulphonamide (2j)

2”,5”-dichloro-N-(3-(5-(2',4'-dimethoxyphenyl)-1-nicotinoyl-4,5-dihydro-1H-pyrazol-3-yl)phenyl)benzenesulphonamide (2k)

2”,5”-dichloro-N-(3-(5-(3',4'-dimethoxyphenyl)-1-nicotinoyl-4,5-dihydro-1H-pyrazol-3-yl)phenyl)benzenesulphonamide (2l)

2”,5”-dichloro-N-(3-(5-(5’-chloro,2'methoxyphenyl)-1-nicotinoyl-4,5-dihydro-1H-pyrazol-3-yl)phenyl)benzenesulphonamide (2m)

2”,5”-dichloro-N-(3-(5-(2’,5’-dichlorophenyl)-1-nicotinoyl-4,5-dihydro-1H-pyrazol-3-yl)phenyl)benzenesulphonamide (2n)

2”,5”-dichloro-N-(3-(5-(3',4’,5’-trimethoxyphenyl)-1-nicotinoyl-4,5-dihydro-1H-pyrazol-3-yl)phenyl)benzenesulphonamide (2o)

2”,5”-dichloro-N-(3-(5-(pyridine-3’-yl)-1-nicotinoyl-4,5-dihydro-1H-pyrazol-3-yl)phenyl)benzenesulphonamide (2p)**]**

General procedure for synthesis of thiosemicarbazide derivatives (3a-3p)

A mixture of chalcones (**1a–3p**) (0.5 mmol) and thiosemicarbazide (0.5 mmol) in hot ethanol (50 mL) had a few drops of concentrated hydrochloric acid added. The reaction mixture was stirred at

reflux temperature for 2–6 hrs, and monitored by TLC using hexane:ethyl acetate (8:2) as the eluent. Afterwards, the precipitate was filtered off and the crude product purified by recrystallization from ethanol, resulting in the target compounds (**3a–3p**).

[(Z)-2-((E)-1-(3-(3-(4-chlorophenyl)ureido)phenyl)-3-(3hydroxyphenyl)allylidene) hydrazine carbothioamide (3a)

(Z)-2-((E)-1-(3-(3-(4-chlorophenyl)ureido)phenyl)-3-(4-hydroxy-3-methoxyphenyl) allylidene)hydrazine carbothioamide (3b)

(Z)-2-((E)-1-(3-(3-(4-chlorophenyl)ureido)phenyl)-3-(2,4-dimethoxyphenyl)allylidene) hydrazinecarbothioamide (3c)

(Z)-2-((E)-1-(3-(3-(4-chlorophenyl)ureido)phenyl)-3-(3,4-dimethoxyphenyl)allylidene) hydrazinecarbothioamide (3d)

(Z)-2-((E)-3-(5-chloro-2-methoxyphenyl)-1-(3-(3-(4-chlorophenyl)ureido)phenyl) allylidene)hydrazinecarbothioamide (3e)

(Z)-2-((E)-1-(3-(3-(4-chlorophenyl)ureido)phenyl)-3-(2,5-dichlorophenyl)allylidene) hydrazinecarbothioamide (3f)

(Z)-2-((E)-1-(3-(3-(4-chlorophenyl)ureido)phenyl)-3-(3,4,5-trimethoxyphenyl) allylidene)hydrazinecarbothioamide (3g)

(Z)-2-((E)-1-(3-(3-(4-chlorophenyl)ureido)phenyl)-3-(pyridin-3-yl)allylidene)hydrazine carbothioamide (3h)(Z)-2-((E)-1-(3-(2,5-dichlorophenylsulfonamido)phenyl)-3-(3-hydroxyphenyl) allylidene)hydrazinecarbothioamide (3i)

(Z)-2-((E)-1-(3-(2,5-dichlorophenylsulfonamido)phenyl)-3-(4-hydroxy-3methoxy phenyl) allylidene)hydrazinecarbothioamide (3j)

(Z)-2-((E)-1-(3-(2,5-dichlorophenylsulfonamido)phenyl)-3-(2,4-dimethoxyphenyl) allylidene)hydrazinecarbothioamide (3k)

(Z)-2-((E)-1-(3-(2,5-dichlorophenylsulfonamido)phenyl)-3-(2,4-dimethoxyphenyl) allylidene)hydrazinecarbothioamide (3l)

(Z)-2-((E)-3-(5-chloro-2-methoxyphenyl)-1-(3-(2,5-dichlorophenylsulfonamido) phenyl)allylidene)hydrazinecarbothioamide (3m)

(Z)-2-((E)-3-(2,5-dichlorophenyl)-1-(3-(2,5-dichlorophenylsulfonamido)phenyl) allylidene) Hydrazine carbothioamide (3n)

(Z)-2-((E)-1-(3-(2,5-dichlorophenylsulfonamido)phenyl)-3-(3,4,5-trimethoxyphenyl) allylidene)hydrazinecarbothioamide (3o)

*(Z)-2-((E)-1-(3-(2,5-dichlorophenylsulfonamido)phenyl)-3-(pyridin-3-yl)allylidene) hydrazine carbothioamide (3p)***]**

Pharmacological Evolutions

Antibacterial activity:

All the synthesized compounds (**1a-1p, 2a-2p, 3a-3p)** have been evaluated for their antibacterial activity against, *Bacillus pumilis*, *Bacillus subtilis* (gram-positive) and *Escherichia coli*, *Proteus vulgaris* (gram-negative). The results of this evaluation have been viewed by taking chloramphenicol (1000 pg/mL), a broad spectrum antibiotic as the standard. The antibacterial activity data of synthesized compounds (**2a-2p, 3a-3p**) is presented in Table 5.1. It could be observed from the table that all the compounds have a noticeable degree of inhibition, especially against *B. pumilis*, *B. subtilis* and *E. coli*. Compounds **2f, 2g, 2h, 2i, 2j, 2k, 2l, 2m, 2n, 2o, 2p, 3o and 3p** only showed mild inhibitory action on *P. vulgaris*. Compounds **2g, 2h, 2j, 2k, 2l, 2m, 2n, 2o, 2p, 3o** and **3p** have shown significant activity on *B. pumilis*, *B. subtilis*, *P. vulgaris* and *E. coli*. However, chloramphenicol is not having any activity against *B. pumilis*.

Table 1:Antibacterial activity of synthesized compounds (2a-2p, 3a-3p)

Compounds	**Zone of inhibition (in mm)**							
	B.pumilis		***B.subtilis***		***E.coli***		***P.vulgaris***	
	0.05 ml	**0.1 ml**	**0.05 ml**	**0.1 ml**	**0.05 ml**	**0.1 ml**	**0.05 ml**	**0.1 ml**
2a	8	9	6	7	6	7	-	-
2b	9	8	8	9	9	8	-	-
2c	7	9	8	10	8	9	-	-
2d	6	8	7	9	8	10	-	-
2e	8	10	7	8	7	9	-	-
2f	7	9	8	11	9	12	9	11
2g	12	15	13	15	12	16	12	16
2h	14	18	12	17	15	18	15	17
2i	8	10	10	14	13	16	11	13
2j	10	15	8	9	11	11	10	12
2k	11	12	9	11	7	10	8	11
2l	13	13	10	12	9	10	8	10
2m	11	13	10	13	10	12	9	11

2o	15	18	13	16	14	18	14	16
2p	11	15	11	15	10	12	9	12
3a	10	12	12	15	10	13	-	-
3b	8	11	9	10	11	11	-	-
3c	7	8	9	9	10	12	-	-
3d	9	10	8	9	7	9	-	-
3e	9	11	7	9	8	10	-	-
3f	8	10	8	10	8	11	-	-
3g	9	12	9	11	7	9	-	-
3h	7	10	8	10	9	12	-	-
3i	10	11	10	15	11	11	-	-
3j	8	9	10	10	8	11	-	-
3k	7	10	8	10	8	12	-	-
3l	8	9	7	10	9	11	-	-
3m	8	10	9	12	10	11	-	-
3o	13	15	14	15	15	18	12	14
3p	11	14	12	15	11	13	13	14
Chloramphenicol	-	-	17	-*	13	-*	12	-*

Concentration of the test compound: 100 pg/cup; Chloramphenicol: 200 pg/mL.

(-) indicates no zone of inhibition; (-*) indicates inhibition not done.

Anti-inflammatory activity:

The anti-inflammatory activity of the sixteen chalcones (**2a-2p**) has been evaluated by using carrageenan-induced rat paw oedema method.

Calculation:

It was calculated according to following formula,

$$\text{Percentage increase in paw thickness } = \frac{\text{Yt} - \text{Yo}}{\text{Yo}} \times 100$$

where Yt = paw thickness at the time 't' hours (After injection)

Y_0 = paw thickness at the time '0' hours (Before injection)

The percent increase in paw thickness during 6 hrs was determined. The percent inhibition ofpaw oedema thickness is calculated using the formula,

$$\text{Percentage inhibition} = [1 - \frac{Y_t}{Y_0}] \times 100$$

where Yt == Average increase in paw thickness in groups tested with test compounds

Yc = Average increase in paw thickness in control

Table 2:Anti-inflammatory activity of synthesized compounds (2a-2p)

	Percent inhibition ± SEM **at various time intervals**				
Compound	**1 hr**	**2 hr**	**3 hr**	**4 hr**	**6 hr**
2a	48.36 ± 1.54	40.38±1.45	55.73 ± 5.34	54.43 ± 1.73	42.83 ± 5.83
2b	51.43± 1.45	45.47 ±1.48	58.31 ± 2.81	56.83 ± 2.93	44.73 ± 5.93
2c	59.67 ±1.69	50.54 ± 2.56	53.62 ± 5.75	60.84 ± 1.28	56.38 ± 5.28
2d	50.39 ± 1.48	52.43 ± 4.94	45.85 ± 4.83	41.83 ± 2.45	50.83 ± 5.84
2e	58.49 ± 2.28	60.83 ± 2.57	54.98 ± 2.91	51.93 ± 1.56	58.93 ± 2.90
2f	70.12 ± 5.65	71.43 ± 2.63	57.92 ± 4.01	69.73 ± 2.36	62.94 ± 5.47
2g	72.54 ± 1.98	75.76 ± 2.76	75.30 ± 5.57	70.83 ± 5.51	66.83 ± 5.38
2h	54.48 ± 2.48	56.76 ± 4.56	59.09 ± 2.83	65.83 ± 5.36	51.93 ± 2.57
2i	58.34 ± 2.40	61.59 ± 2.54	63.30 ± 2.91	60.63 ± 1.36	56.83 ± 2.62
2j	39.43 ± 2.65	51.43 ± 4.23	55.92 ± 5.77	50.83 ± 5.93	38.29 ± 1.27
2k	41.45± 2.74	66.83 ± 2.13	69.83 ± 2.92	65.93 ± 5.93	51.93 ± 2.95
2l	49.41 ± 5.54	55.73 ± 2.71	60.82 ± 2.28	58.93 ± 2.83	42.94 ± 2.49
2m	59.40 ± 2.10	51.32 ± 4.26	65.59 ± 2.93	62.93 ± 2.67	55.83 ± 5.72
2o	74.43 ± 2.65	78.52 ± 4.92	80.73 ± 5.83	75.83 ± 2.56	71.81 ± 2.16
2p	72.21 ± 5.56	77.83 ± 1.72	78.35 ± 5.16	75.72 ± 2.93	72.83 ± 1.38
Indomethacin	79.28 ± 4.94	85.45 ± 5.41	92.54 ± 2.74	81.45 ± 5.83	86.45 ± 5.83

Dose: Standard and sample solution is 100 mg/kg body weight. Values are expressed as mean ± SEM (n=6).

*p< 0.05; ** p < 0.01; *** p < 0.001 compared to control. Student's t-test

The results of the evaluation have been viewed by taking Indomethacin as the standard drug. Compound **2o** has shown highest percent inhibition of 80.73 at 3rd hour. This has been followed by compounds **2p, 2g, 2k** and **2m** with highest percent inhibition of 78.35, 75.30, 69.83, and 65.59 respectively.

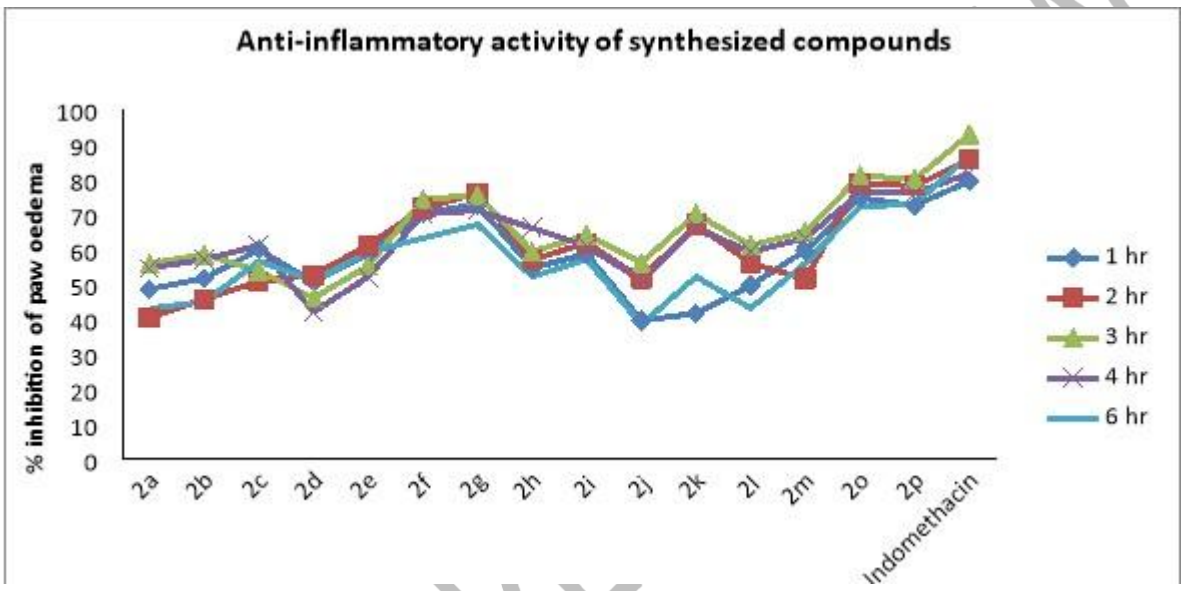


Fig. 2. Anti-inflammatory activity of synthesized compounds (2a-2p)

CONCLUSION

All the synthesized compounds (**2a-2p, 3a-3p)** have been evaluated for their antibacterial activity against, *Bacillus pumilis, Bacillus subtilis* (gram-positive) and *Escherichia coli, Proteus vulgaris* (gram-negative). It could be observed from the table 1 that all the compounds have a noticeable degree of inhibition, especially against *B. pumilis, B. subtilis* and *E. coli.* Compounds **2f, 2g, 2h, 2i, 2j, 2k, 2l, 2m, 2n, 2o, 2p, 3o and 3p** only showed mild inhibitory action on *P. vulgaris.* Compounds **2g, 2h, 2j, 2k, 2l, 2m, 2n, 2o, 2p, 3o** and **3p** have shown significant activity on *B. pumilis, B. subtilis, P. vulgaris* and *E. coli.* It is also observed from the Table1 that all the compounds exhibited considerable inhibitory action specially against *A. niger* and *R. oryzae.* However, their action has been found to be very weak against *A. flavus.* Compounds **2m, 2o, 2p, 3i** and **3p** have shown high potency specially against *A. niger, R. oryzae* and *A. flavus.*

The anti-inflammatory activity of the sixteen chalcones (**2a-2p**) has been evaluated by using carrageenan-induced rat paw oedema method (Table 2 and Fig 1). Compound **2o** has shown highest percent inhibition of 80.73 at 3rd hour. This has been followed by compounds **2p, 2g, 2k** and **2m** with highest percent inhibition of 78.35, 75.30, 69.83, and 65.59 respectively.

COMPETING INTERESTS DISCLAIMER:

Authors have declared that no competing interests exist. The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

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