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SYNTHESIS, CHARACTERIZATION AND BIOLOGICAL EVALUATION OF IMIDAZOLO-CHALCONE DERIVATIVES

***Hemalatha Sattu and Perla Swathi**

Pharmaceutical Chemistry Department, Affiliation: Osmania University, Institution: Sarojini Naidu Vanitha Pharmacy Maha Vidhyalaya, Tarnaka, Secunderabad, India.

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***Corresponding Author**
Hemalatha Sattu
Pharmaceutical Chemistry Department, Affiliation: Osmania University, Institution: Sarojini Naidu Vanitha Pharmacy Maha Vidhyalaya, Tarnaka, Secunderabad, India.

ABSTRACT

A series of novel heterocyclic derivatives were prepared by acetylation of Imidazole (1) and Acetyl chloride (2) to give respective N-acetyl imidazole (3),which was further reacted with different substituted aromatic aldehydes (4) in the presence of (Aldol Condensation) Ethanol and NaOH used as base to give Imidazolo Chalcone derivatives (5). All the synthesized compounds are confirmed by physicochemical data by using various Softwares like Molinspiration, Molsoft, OSIRIS and spectral analysis of ^{1}H NMR, IR and MASS spectra. All the compounds are screened for antibacterial, antifungal and antioxidant activity. The antibacterial activity (**Oflaxacin** 100µg/ml) against ***B.Subtilis*** and The antifungal activity (**Greseofulvin** 100µg/ml) against ***pencillinium chrysogenum*** were determined by cup plate method. Anti oxidant activity is determined by stable free radical method, **ascorbic acid** is used as the standard. All the compounds showed good pharmacokinetic and pharmacodynamic properties. Among all the compounds 5a,5b (10 and 30 µg/ml) and 5c (200µg/ml) showed potent antibacterial and antifungal activity, All the synthesized compounds showed potent antioxidant activity.

KEYWORDS: Acetylation, Aromatic aldehydes, Aldol condensation and Imidazolo Chalcone derivatives.

INTRODUCTION

Chalcones are substructures in various natural products belonging to the flavonoid family.[1] They have attracted increasing attention due to numerous pharmacological applications such as antimicrobial, anti-inflammatory, anticancer and antitubercular activities.[1-7]

Chalcones undergoes The Claisen Schmidt condensation reaction is a valuable C–C bond-forming reaction.[2] Chalcones are natural biocides and are well known intermediates for synthesizing various heterocyclic compounds such as benzothiazepine, pyrazolines, pyrimidines,1,4-diketones and flavones.[3] Antimicrobial activity of these chalcones is attributed to the presence of a reactive α,β-unsaturated keto function that can be altered depending on the type and position of substituent on the aromatic rings.[4] Chalcones react with the side chain groups of bovine serum albumin and results in its precipitation.[5] Chalcone [1,3-diphenyl-2-propene-1-one] and related compounds "chalconoids" are those in which two aromatic rings are linked by a reactive keto ethylenic group (–CO–CH=CH–) that forms the central core for a variety of important biological compounds, and known collectively as chalcones.[6]

Imidazole and Pyrazole nuclei are important structures present in numerous natural and Synthetic Compounds, they have various application in medicinal chemistry.[7] Chalcones the bichrom-ophoric molecules separated by a keto-vinyl chain, constitute an important class of naturally occurring flavanoids exhibiting a wide spectrum of biological activities.[8] The present study aimed to synthesize and evaluate the Antimicrobial and antioxidant activity of Imidazolo-Chalcone derivatives (synthesized compounds) by using Claisen-Schmidth condensation method.

MATERIALS AND METHODS

INSTRUMENTATION

All the chemicals and reagents were purchased from Aldrich. All the solvents were dried and distilled before use. The melting points of the derivatives were determined by capillary tubes using melting point apparatus and are uncorrected. The synthesized compounds were purified by Column chromatography using Hexane**:** Ethyl acetoacetate (7:3) is as solvent system. Reactions were monitored by T.L.C. The visualization was achieved by Staining with I_2 or U.V light.IR spectrum of derivatives were recorded on FT-IR(Model:schimadzu) using potassium bromide. The ^{1}H NMR were recorded in $CDCl_3$ or DMSO 400MHZ BRUKER ADVANCE ^{1}HNMR. Chemical shift are reported by using Tetramethylsilane (TMS) as an

internal standard. Mass spectum is recorded on VG Micro Mass-7070h (Esi and Ei) were given Mass unit (M/Z).

GENERAL METHODS

1. Synthesis of N-Acetyl Imidazole

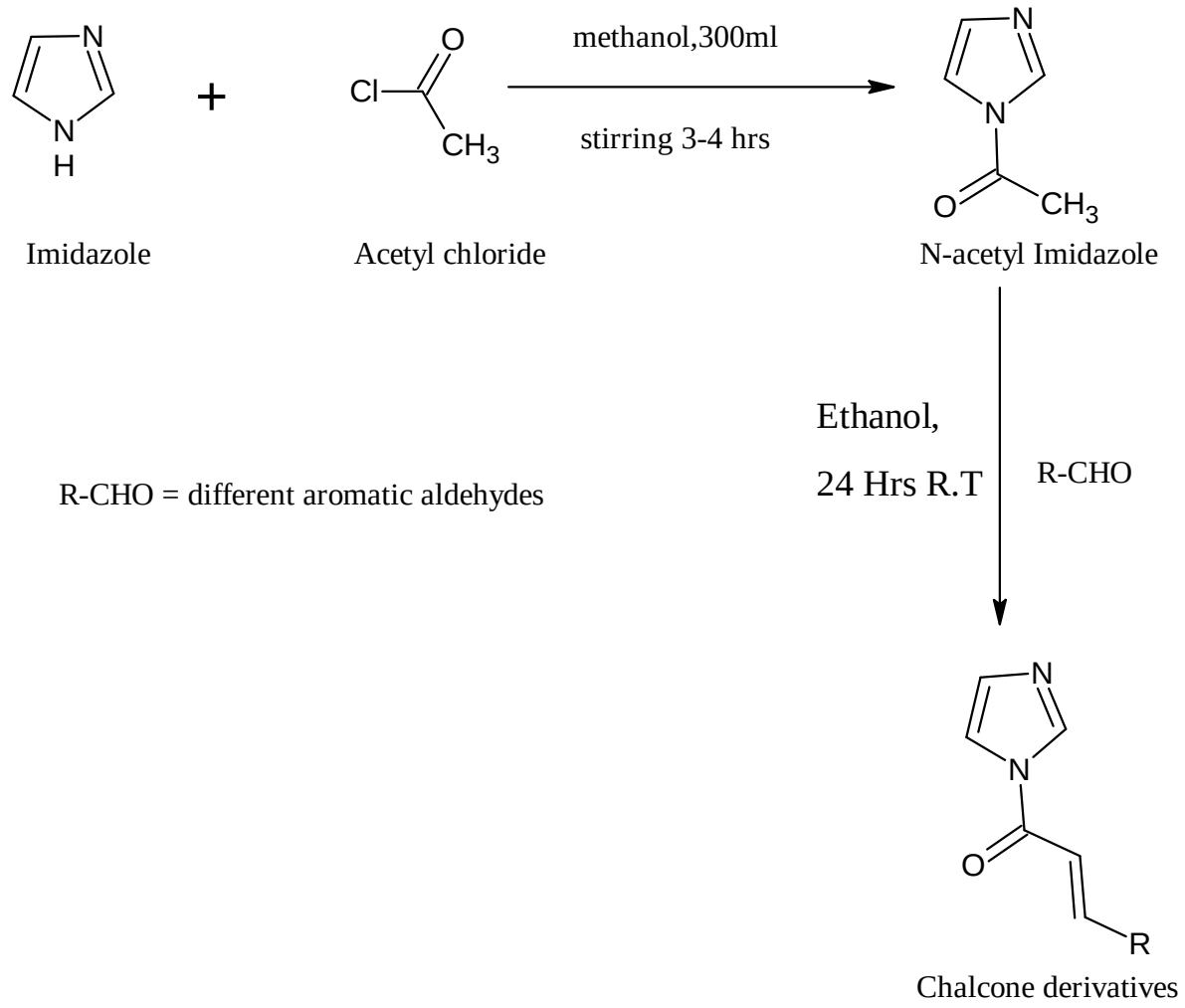
Imidazole derivatives are very interesting class of Nitrogen containing 5-membered heterocyclic compounds. Equimolar quantities of imidazole 0.01 mole (1.1g) and 0.01 mole (0.79g) of acetyl chloride were added, mixed and stirred for 4 hrs. concentrated ammonia was added and the product obtained was recrystallized from 20% aqueous ethanol.

2. General Procedure for the Synthesis of Imidazolo-Chalcone Derivatives

Equimolar amount of acetylated imidazole and different aromatic aldehydes were dissolved in alcohol and taken in 100 ml RB flask. To this mixture NaOH solution (40%) was added drop wise and stirred for 1 hr. The Progresses of reaction were monitored by TLC. After completion of the reaction, the mixtures were poured into crushed ice and acidify with conc. HCl. Solid thus obtained were separated by filtration and recrystallized with 50% aq. Ethanol from proper solvent to get imidazolo- chalcones.[15]

Chemistry

N-acetyl imidazole was prepared by the acetylation of imidazole with acetyl chloride,which further condensed (Claisen-Schmidt condensation) with different substituted aromatic aldehydes (a-h) in the presence of sodium hydroxide in methanol at room temperature produced new chalcone derivatives(5a-5h). The synthetic strategy of title compounds (5a-5h) is represented in scheme 1 and 2. All the synthesized compounds were characterized by IR, ^{1}H NMR and Mass spectra. The ^{1}H NMR spectrum of chalcone derivatives (5a) indicated the following signals: the singlet at 3.96ppm indicated the presence of methoxy group. All other aromatic protons were observed at expected regions.



Scheme 1: Synthesis of Imidazolo-Chalcone derivatives(5a-5h).

Experimental conditions

1) Methanol, stirring 3-4hr 2) NaoH, Room temperature 24 hrs, Ethanol 3) Different substituted aldehydes (a-h).

RESULTS AND DISCUSSION

The Claisen-Schmidt condensation is an important C-C bond formation for the synthesis of Chalcones. It is generally carried out by the using strong bases such as NaOH or KOH in polar solvents (MeOH or DMF). The purity of the compounds was checked by thin layer chromatography and structures of the synthesized products were confirmed by their spectral analysis.

N-Acetyl Imidazole (2)

Pale yellow solid,yield 76%,M.P. 100-104^{0}C.

IR (KBr):3250,2956,2890,1750,1510,1420,1390,1320,1290.

^{1}HNMR(400MHZ,$CDCl_3$): δ 8.28(S,1H),8.0(D,J=15.21H),7.26(D,J=7.2Hz,1H),2.1(S,3H).

EIS-MS:M/Z 111g $(M+1)^+$.

(2Z)-3-(3,4-dimethoxyphenyl)-1-(1H-imidazol-1-yl)prop-2-en-1-one(5a)

Pale yellow solid,yield,69%,M.P.94-96^{0}C

IR (KBr): 3362, 2916, 1648, 1589, 1253.

^{1}HNMR(400MHZ, $CDCl_3$): δ7.76(D,J=7.8 Hz,H),7.48(S,1H),6.94(D,1H,J=8.4 Hz), 6.7(M,3H), 3.96(S,1H).

EIS-MS: M/Z 259g $(M+1)^+$.

(2Z)-3-(2-chloro-5-nitrophenyl)-1-(1H-imidazol-1-yl) prop -2-en-1-one(5b)

Pale yellow solid, yield,65%,M.P.96-98^{0}C.

IR (KBr): 1714, 1538, 1518, 1351, 1103,787.

^{1}HNMR(400MHZ,$CDCl_3$): δ 8.2(D,J=15.6Hz 1H),7.7(D,J=15.6Hz,1H),7.6(S,1H),7.3(M,3H), 6.93(D,J=8Hz,1H),6.89(D,J= 8Hz,1H).

EIS-MS:M/Z 259g.

(2E)-1-(1H-imidazol-1-yl)-3-(1-methyl-1H-pyrrol-2-yl) prop-2-en-1-one(5c)

Pale yellow solid,yield,66%,M.P.102-104^{0}C.

IR(KBr):2339,1678,1598,1518,1350.

^{1}HNMR(400MHZ,$CDCl_3$):δ7.71(D,J=15.8Hz,H),7.65(S,H),7.3(M,J=15.6Hz,3H),6.96(D,J=6. 8Hz,H),6.84(D,J=7.4HzH), 6.54(D,J=5.8Hz,1H),3.57(S,3H).

EIS-MS M/Z**:** 201g$(M-1)^+$.

(2E)-1-(1H-imidazol-1-yl)-3-(3,4,5-trimethoxyphenyl)pro p-2-en-1-one(5d)

Pale yellow solid,yield,72%,M.P114-116-^{0}C.

IR(KBr):2959,1686,1587,1518,1326, 1225.

^{1}HNMR(400MHZ,$CDCl_3$):δ7.78(D,J=15.6Hz,H),7.6(S,H),7.4(D,H),6.97(D,J=8.4Hz,H),6.7 (M,3H),6.84(D,J=8.4Hz,H),3.94(S,6H),3.7(S,J=4.8Hz,3H).

EIS-MS**:** M/Z 289g.

(2E)-3-(furan-2-yl)-1-(1H-imidazol-1-yl)prop-2-en-1-one (5e)

Pale yellow solid, yield, 66%, M.P104-106-^{0}C.

IR(KBr): 2969, 1685, 1587, 1518, 1326, 1225.

^{1}HNMR(400MHZ,$CDCl_3$): δ 8.05(S,J=16.2Hz,1H),7.78(D,J=16.2Hz,1H), 7.52(D,J=15.2Hz,1H), 7.26(D,J=7.2Hz,1H), 6.96(D,J=8.4Hz,1H), 6.6(D,J=5.8Hz,1H), 6.3(M,H).

EIS-MS M/Z189g(M+1).

(2E)-4-[(1E)-3-hydroxy-3-(1H-imidazol-1-yl)prop-1-en-1-yl]phenol(5f)

Pale yellow solid,yield,67%, M.P98-100^{0}C.

IR(KBr): 3398, 2377, 2310, 1690, 1660, 1385.

^{1}HNMR(400MHZ,$CDCl_3$): δ 7.76(D,J=7.6Hz,1H),7.6(D,J=7.6Hz,1H), 7.3(M,7H),6.96(D, J=8.4Hz,H).

EIS-MS M/Z 215g$(M+1)^+$.

(2E)-1-(1H-imidazol-1-yl)-3-(4-methoxyphenyl)prop-2-en-1-one(5g)

Pale yellow solid,yield,68%,M.P 100-102^{0}C.

IR (KBr): 1680, 1590, 1253, 1224.

^{1}HNMR(400MHZ,$CDCl_3$):δ7.78(D,J=7.8Hz,1H),7.6(S,H),7.35(M,J=8.4Hz,H),6.96(D,J=8.4 Hz,H),6.54(D,J=5.8Hz,H),6.2 (S,H),3.84(S,3H).

EIS-MS M/Z 229g $(M+1)^+$.

(2E)-3-(2-hydroxyphenyl)-1-(1H-imidazol-1-yl)prop-2-en-1-one(5h)

Pale yellow solid,yield,68%,M.P.118-120^{0}C.

IR (KBr): cm^{-1} 3398, 2377, 2310, 1690, 1660, 1518,1320.

^{1}HNMR(400MHZ,$CDCl_3$): δ 7.76(D,J=15.6Hz,1H),7.6(S,H),7.3(M,7H), 6.9(D,J=7.4Hz,H).

EIS-MS M/Z 215g $(M+1)^+$.

ANTIMICROBIAL AND ANTIOXIDANT SCREENING

The synthesized compounds were evaluated for antibacterial activity ***Bacillus subtilis(+ve), Escherichia coli(-ve),***[4] antifungal activity ***Pencillium chrysogenum***[12] by cup plate method and antioxidant activity by DPPH method. The bacterial(24h) and fungal(48h) cultures from the slants were diluted sterile water mixed thoroughly to prepare a clear homogenous suspension. These suspension were spread on solidified agar, nutrient agar for bacteria medium and potato dextrose agar for fungi. The filter paper disks prepared by only methanol with solution of 50 µg/L concentration of test compounds (5a-5h) as well as standard compounds (Ofloxacin and Griseofulvine) were incubated at 37^{0}C for 24 hr for bacteria and at 28-30^{0}C for 48 hr for fungi. After the incubation period, the plants were examined for the

the zone of inhibition. All determinations were made in triplicate for the compounds, average values were taken.

All the title compounds were screened for antioxidant activity using DPPH method. All the compounds were evaluated for antioxidant activity against the standard ascorbic acid. For The evaluation of antioxidant activity, we have used stable free radical α,α di phenyl-β- picryl hydrazyl(DPPH), at the concentration of 0.2 mM in ethanol.

Molecular Property Prediction

Molecular property is a complex balance of various structural features which determine whether a particular molecule is similar to the known drugs. These properties mainly hydrophobicity, molecular size, flexibility and presence of various pharmacophoric features influence the behavior of molecules in a living organism, including oral bioavailability. Molecular properties are calculated using software's like Molinspiration, Molsoft and OSIRIS to evaluate the drug likeness and toxicity of the synthesized compounds.

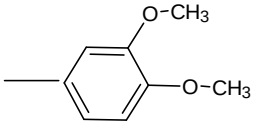
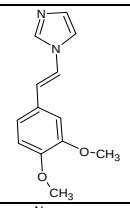
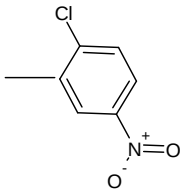
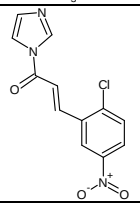
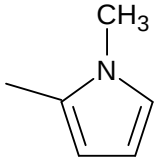
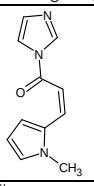
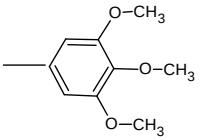
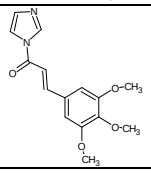
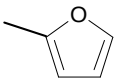
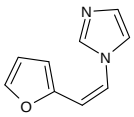
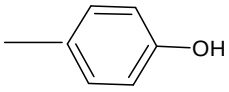
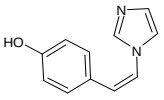
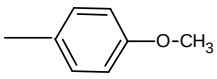
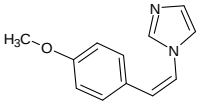
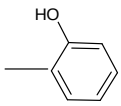
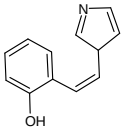
Table 1: Physico chemical parameters of the synthesized compounds. Chalcone derivatives(5a-5h).

S. No	Com. code	Molecular formulae	Molecular weight (gms)	% yield	Melting point (^{o}C)
1	(3)	$C_5H_6N_2O$	110g	76	100-104
2	5a	$C_{14}H_{14}N_2O_3$	258g	69	94-96
3	5b	$C_{12}H_8N_3O_3$ Cl	259g	65	96-98
4	5c	$C_{11}H_{12}N_3O$	202g	66	102-104
5	5d	$C_{12}H_{16}N_5O_4$	288g	72	114-116
6	5e	$C_{10}H_8N_2O_5$	188g	66	104-106
7	5f	$C_{12}H_{10}N_2O_5$	214g	67	98-100
8	5g	$C_{13}H_{12}N_2O_2$	228g	68	100-102
9	5h	$C_{12}H_{10}N_2O_2$	214g	68	118-120

In The Table 1 consists of eight derivatives. Compound (3) indicating that it is a starting material molecular formulae is $C_5H_6N_2O$, molecular weight is 110g, Melting point is measured by melting point apparatus. The percentage yield of N-Acetyl Imidazole (3) was found to be 76 %, melting point was found to be 100-104^{0}C.The compound (3) is prepared by the acetylation of imidazole(1) with acetyl chloride(2) further condensed (Claisen-Schmidt condensation) with different substituted aromatic aldehydes (4a-4h) in presence of sodium hydroxide in methanol at room temperature produced new chalcone derivatives(5a-5h).

These molecular formulaes are (5a) $C_{14}H_{14}N_2O_3$, (5b) $C_{12}H_8N_3O_3Cl$, (5c) $C_{11}H_{12}N_3O$,(5d) $C_{15}H_{16}N_2O_4$,(5e) $C_{10}H_8N_2O_2$, (5f) $C_{12}H_{10}N_2O_2$, (5g) $C_{13}H_{12}N_2O_2$ and (5h) $C_{12}H_{10}N_2O_2$. Melting points are 94-96^{0}C, 96-98^{0}C, 102-104^{0}C,114-116^{0}C, 104-106^{0}C, 98-100^{0}C, 100-102^{0}C and 118-120^{0}C. The percentage yield of the derivatives were found to be 69%, 65%, 66%, 72%, 66%, 67%, 68% and 68% . Molecular weights of derivatives are (5a) 258g, (5b) 259g, (5c) 202g, (5d) 288g, (5e) 188g, (5f) 214g, (5g) 228g and (5h) 214g.

Table 2: Scheme details.

	R- aromatic aldehydes (4a-4h)	Chalcone derivatives (5a-5h)
a.		
b.		
c.		
d.		
e.		
f.		
g.		
h.		

N-acetyl imidazole was prepared by the acetylation of imidazole with acetyl chloride,which further condensed (Claisen-Schmidt condensation) with different substituted aromatic

aldehydes (a-h) in the presence of sodium hydroxide in methanol at room temperature produced new Chalcone derivatives(5a-5h).

In This Table (2) R-is aromatic aldehydes these are (4a) 3,4 Dimethoxy benzaldehyde, (4b) 2-Chloro, 5-Nitrobenzaldehyde, (4c) N- methyl pyrrole carboxaldehyde,(4d) 3,4,5 Trimethoxybenzaldehyde,(4e) furfural, (4f) 4Hydroxy benzaldehyde, (4g) 4- Methoxy benzaldehyde, (4h)2- Hdroxy benzaldehyde.

The derivatives are (5a) 3-(3,4-Dimethoxyphenyl)-1-(1*H*-Imidazol-1-Yl)Prop-2-En-1-One, (5b) 3-(2-Chloro-5-Nitrophenyl)-1-(1H-Imidazol-1Yl)Prop2-En-1-One,(5c)1-(1H-imidazol-1-yl)-3-(1-methyl-1H-pyrrol-2- yl)prop-2-en-1-one, (5d) 1-(1H-Imidazol-1-Yl)- 3- (3,4,5-Trimethoxyphenyl) Prop2-En-1-One, (5e) 3-(Furan-2-Yl)-1-(1H-Imidazol-1-Yl)Prop-2-En-1One,(5f) 4-[(1E)-3-Hydroxy-3-(1H-Imidazol-1-Yl)Prop-1en-1-Yl] Phenol,(5g) (2E)-1-(1H-Imidazol-1-Yl)-3-(4methoxyphenyl)Prop-2-En-1-One, (5h) (2E)-3-(2-Hydroxyphenyl)-1-(1H-Imidazol-1Yl)Prop-2-En-1-One.

Table 3: Results of Antibacterial activity of the compounds.

Compound code	Zone of inhibition in mm							
	Bacillus Subtilis (µg/ml)				E.Coli (µg/ml)			
	10	20	30	40	10	20	30	40
5a	…..	…..	…..	…..	9	11	15	17
5b	6	8	10	12	…..	…..	…..	…..
5c	…..	…..	…..	…..	4	6	8	10
5d	…..	…..	…..	…..	…..	…..	…..	…..
5e	…..	…..	…..	…..	…..	…..	…..	…..
5f	…..	…..	…..	…..	…..	…..	…..	…..
5g	…..	…..	…..	…..	…..	…..	…..	…..
5h	…..	…..	…..	…..	…..	…..	…..	…..
Ofloxacin	8	8	6	11	10	12	15	20

Results of Antibacterial activity

All the synthesised compounds were evaluated for anti-bacterial activity against grampositive and gram negative bacteria by agar cup plate method. The zone of inhibition (in mm) value was taken as a parameter for activity. The zone of inhibition of the test compounds were compared to that of standard drug i.e, Ofloxacin for anti bacterial activity.

All the compounds were screened for antibacterial activity against B.subtilis among the series of the compound (5a) 3,4 di methoxy benzaldehyde derivative showed equipotent activity i.e (15 mm at 30µg/ml) as compared to standard drug (15 mm at 30µg/ml). The compound (5b)

2-chloro 5- nitro benzaldehyde derivative and (5c) N-methyl 2-pyrrole carboxaldehyde derivative showed moderate activity against the gram negative bacteria Escherichea coli when compared to standard Ofloxacin which is shown in Table 3.

Method of testing

Nutrient agar was dissolved and distributed in 25ml quantities in 100ml conical flasks and were sterilized in an autoclave at 121^0C (15lbs/sq.in) for 20 minutes.The sterilized was cooled to 45^0c with gentle shaking to bring about to uniform cooling and then inoculated with 18 to 24 hours old culture under aseptic conditions, mixed well by gentle shaking. All the Petri dishes were transferred to laminar air flow unit then the discs which were previously prepared. This was poured into sterile Petri dishes and allowed the medium to solidify. In the petri dishes four cups of 10mm diameter at equal distances were made. The test and standard solutions i.e 50,100,150 and 200µg/ml, were added and these plates were subsequently incubated at 20-25^0C for 24 h. These Petri dishes were kept as it is for 1hr for diffusion at room temperature and then incubation at 37^0c for 24hr in an incubator. The extent diameter of inhibition after 24 hours was measured as the zone of inhibition in mm.

Table 4: Results of antifungal activity of the compounds.

S. No	***Pencillium chrysogenum***				
Zone of inhibition(mm)					
Conc. (µg/ml)					
	Compound code	50	75	100	150
1	5a	6	8	12	13
2	5b	…..	…..	…..	…..
3	5c	12	9	13	15
4	5d	…..	…..	…..	…..
5	5e	…..	…..	…..	…..
6	5f	…..	…..	…..	…..
7	5g	…..	…..	…..	…..
8	5h	…..	…..	…..	…..
Standard	Greseofulvin	12	12	15	17

All the title compounds were screened for antifungal activity against *Pencillium chrysogenum* using Saubaurd agar medium. The zone of inhibition (in mm) value was taken as a parameter for activity. The zone of inhibition of the test compounds were compared to that of standard drug i.e Griseofulvin.

All the title compounds were screened for antifungal activity against *Pencillium chrysogenum.*

Among the series of compounds (5c) 3,4,5 tri methoxy benzaldehyde showed equipotent activity i.e (12mm at 50µg/ml) compare to standard drug Griseofulvin i.e (12mm at 50µg/ml). The compound (5a) showed moderate activity when compared to **standard Griseofulvin.**

Table 5: Results of antioxidant activity of the compounds.

S. No	Compound code	IC_{50}(µM/L)
1	5a	2.50
2	5b	2.50
3	5c	2.49
4	5d	2.50
5	5e	2.52
6	5f	2.50
7	5g	2.52
8	5h	2.50
Standard	Ascorbic acid	3.41

Results of Antioxidant activity

All the compounds were evaluated for antioxidant activity against the standard ascorbic acid. All compounds IC_{50} values are less than the standard that is 3.41. All the compounds were tabulated in table 5.The synthesized compounds showed potent compared to standard. Among all the derivatives (5c) showed good activity and IC_{50} value is 2.49 (µM/L).

Table 6: Molinspiration Calculation of derivatives.

Comp. code	Log p	TPSA	n. of atoms	M. wt	Non	NOH	V
5a	1.6	53.36	19	258.2	5	0	234.1
5b	2.60	80.72	19	277.6	6	0	219.9
5c	1.26	39.83	15	201.2	4	0	184.9
5d	1.85	62.59	21	288.3	6	0	259.7
5e	1.30	48.03	14	188.1	4	0	164.6
5f	1.74	55.12	16	214.2	4	1	191.1
5g	2.28	44.13	17	228.2	4	0	228.6
5h	1.98	55.12	16	214.2	4	1	191.1
Ofloxcacin.	-0.62	75.01	25	347.3	7	1	294.5
Greseofulvin.	0.65	61.84	24	356.8	5	0	320.1

Mw- Molecular Weight,

Tpsa- Total Polar Surface Area,

N On- No. of Hydrogen Acceptors,

N OH- No. of Hydrogen Donors,

V- Volume

Ofloxc- Ofloxacin

Greseo- Greseofulvine

Results of Molecular property prediction studies

Molinspiration: All the chalcone derivatives were predicted by using molecular property prediction. Molinspiration calculate the molecular properties like (log P, molecular polar surface area, molecular volume, molecular weight, rule of 5 properties, number of rotatable bonds and bioactivity) when log P altered hydrophobicity is also altered. Hydrophobicity effets the drug absorption , Bioavailability and activity of the compounds.

All the compounds obey the lipinski rule of 5. The rule state, that most "drug-like"molecule have log P <=5,molecular weight<=5, number of hydrogen bond acceptors <=10 and number of hydrogen bond donors<=5.In the below table 6,among all the synthesized compounds the compound (5b) compound showed excellent activity when compared to standard ofloxacin and griseofulvin. because it have log P value (2.609), higher TPSA(80.72) ,higher hydrogen bond acceptors (6). So There is no violating one of these rules.

Table 7: Molsoft Calculation of derivatives.

Code	HBA	HBD	Log p	Log S	MPSA	M. V	S.C	DL
5a	4	0	1.95	-2.23	40.89	267.75	0	0.32
5b	4	0	2.21	-3.26	63.89	244.86	0	0.51
5c	2	0	0.78	-1.44	28.53	215.24	0	0.23
5d	5	0	1.92	-1.93	48.61	299.59	0	0.53
5e	3	0	1.11	-1.46	33.38	190.45	0	0.64
5f	3	1	1.63	-1.96	43.25	215.03	0	0.08
5g	3	0	1.98	-2.36	33.18	236.33	0	0.55
5h	3	1	1.51	-1.67	42.18	215.01	0	0.66
Ofl.	5	1	0.93	-2.38	59.25	350.29	0	0.78
Gri.	6	0	3.06	-1.56	56.45	429.69	0	0.52

HBA - Hydrogen bond acceptors

HBD - Hydrogen bond donors

MV - molecular volume,

M.P - mol Log P

SC - No. of stereo centers

M.S - mol Log S

DL - Drug likeness

Molsoft

Molsoft online tool calculate the chemical properties like molecular formula, molecular weight, number of hydrogen bond acceptors, number of hydrogen bond donors, mol log P, mol log S, polar surface area, volume, number of stereo centers and Drug likeness model

score. In the below table 7, all the compounds obey the Lipinski rule. Among the synthesized compounds (5b) compound showed potent activity and more bioavailability when compared to standard Ofloxacin and Griseofulvin. Because This compound have HBA value (4), log P(2.21), log S (-3.26) , PSA(63.89). higher the log P higher the bioavailability.

Table 8: OSIRIS Calculations of synthesized compounds.

Compound code	Toxicity Assessment				DS
	MUT	TUMO	IRR	REP	
5a					0.41
5b					0.30
5c					0.41
5d					-0.27
5e					0.34
5f					0.34
5g					0.31
5h					0.31
Ofloxacine					0.42
Griseofulvine					0.52

MUT - mutagenic,

TUMO - tumerogenic,

IRR - irritant,

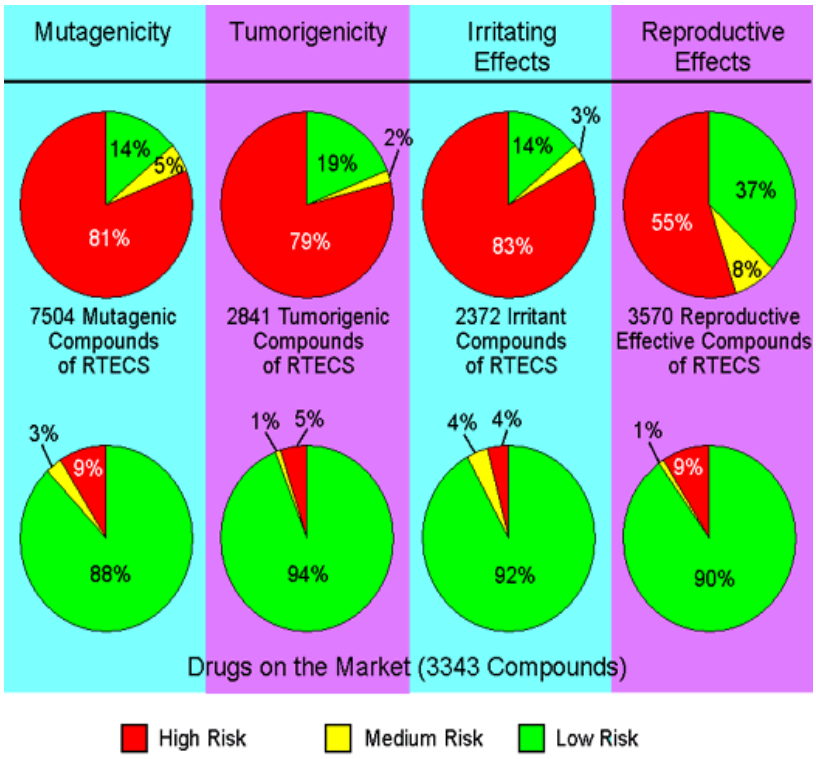
REP - reproductive effective,

D.S - Drug score

OSIRIS

OSIRIS soft ware allows a user to draw chemical structures and calculates on the fly various drug-relevant properties whenever a structure is valid. Molecular properties like (solubility, drug likeness and drug score) are predicted. Results are valued and colour coded. Properties with high risks of undesired effects like mutagenicity or a poor intestinal absorption are shown in red.Where as green colour indicates drug-conform behavior.In the below table 8, all the compounds showed green colour. Among all these compounds the compound (5c)

showed excellent activity when compared to standard Ofloxacin and Griseofulvin. Because this compound have the drug score value (0.41).



Toxicity Assessment of Chalcones

The prediction process relies on a pre computed set of structural fragment that give rise to toxicity alerts in case they are encountered in the structure currently drawn. These fragment lists were created by rigorously shreddering all compounds of the RTECS database known to be active in a certain toxicity class (e.g. mutagenicity). During the shreddering any molecule was first cut at every rotatable bonds leading to a set of core fragments. These in turn were used to reconstruct all possible bigger fragments being a substructure of the original molecule. Afterwards, a substructure search process determined the occurrence frequency of any fragment (core and constructed fragments) within all compounds of that toxicity class. It also determined these fragment's frequencies within the structures of more than 3000 traded drugs. Based on the assumption that traded drugs are largely free of toxic effects, any fragment was considered a risk factor if it occurred often as substructure of harmful compounds but never or rarely in traded drugs.

CONCLUSION

All the synthesized compounds were evaluated for antibacterial activity.The compound (5a) 3,4-di methoxy imidazolo chalcone showed equipotent activity i.e (15 mm at 30µg/ml) as compared to standard (Ofloxacin).

The antifungal activity is performed by cup plate method taking griseofulvin(100µg/ml) as standard, against two fungal organisms.The compound (5b) 3,4,5-tri methoxy imidazolyl chalcone showed equipotent antifungal activity (12mm at 50µg/ml) compared to standard griseofulvin. All the synthesized compounds showed moderate antioxidant activity when compared to standard Ascorbic acid.Various chalcone derivatives which containing electron donating methoxy group showed potent antibacterial activity and antifungal activity.

The unique structure of Chalcone nuclei is assoiciated with various biological activities.

Hetero cyclic Chalcone hybrids exhibited extensive activity against various types of anti microbial,antioxidant and cancer cells. Chalcone hybrids are found to exhibited considerable scientific interest because of its unique structural activity relationship and this research would be certainly useful in providing an approach to develop a new potent Chalcone hybrids for future research in the the field of drug discovery.

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