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SYNTHESIS AND PHARMACOLOGICAL EVALUATION OF SUBSTITUTED N-(3-FORMYL-4-OXO-4H-CHROMEN-2-YL)-N- PHENYLBENZENESULFONAMIDE AND ITS DERIVATIVES

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ABSTRACT: Modification of a drug molecule of a series having optimal activity is widely used and continues to be an important factor necessary for new drug discovery. Infectious diseases which increase dramatically by resistant and multi resistant microbes are now a days the second major cause of death worldwide and the third leading cause of death in the developed countries. Although, the search for new lead structures for the development of antimicrobial agent is an increasingly important problem in medicinal chemistry. The treatment of infectious diseases still remains an important and challenging area of research due to multidrug resistance by microbes. The increasing incident of drug resistance in treatment of microbial diseases emphasizes worldwide need for newer antimicrobial agents. To treat these infectious diseases, a route is established to synthesize the pharmacological active novel chromone based sulfonamide derivatives *i.e.* substituted N- (3 –formyl -4-oxo -4H –chromen -2-yl) -N-phenyl benzene sulfonamide having antibacterial and antifungal activities. The objectives of the present work are: 1) to synthesize various derivatives of substituted N-(3-formyl-4-oxo-4H-chromen-2-yl)-N-phenyl benzene sulfonamides. 2) To analyses all synthesized derivatives by their respective spectral data. 3) To evaluate the antibacterial and antifungal activities.

INTRODUCTION: Chromones (1) represent the most common heterocyclic system in natural compounds of plant origin and serve as the basis of flavonoid structures [1]. Chromone (1), moiety forms the important component of pharmacophores of a number of biologically active molecules having synthetic or natural origin and many of them have useful medicinal applications.

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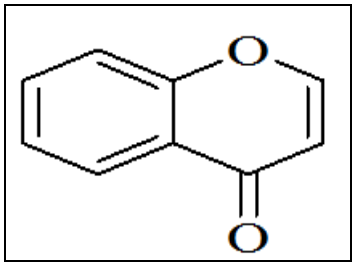
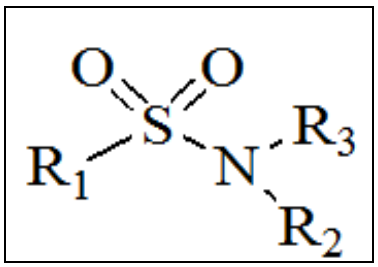
Chromones (1) are a group of naturally occurring oxygen containing heterocyclic compounds with a benzoannelated –γ-pyrone ring [2].



CHROMONES (1)

Chromone derivatives have a number of biological activities *viz.* tyrosine and protein kinase inhibition, telomerase inhibitors, antifungal, antiviral, anti-

hypertensive [3] and anticancer activities [4-7], mono-amine oxidase inhibitors [8]. Sulphonamides (2) are an important class of heterocyclic compounds which possess wide spectrum of biological properties [9].

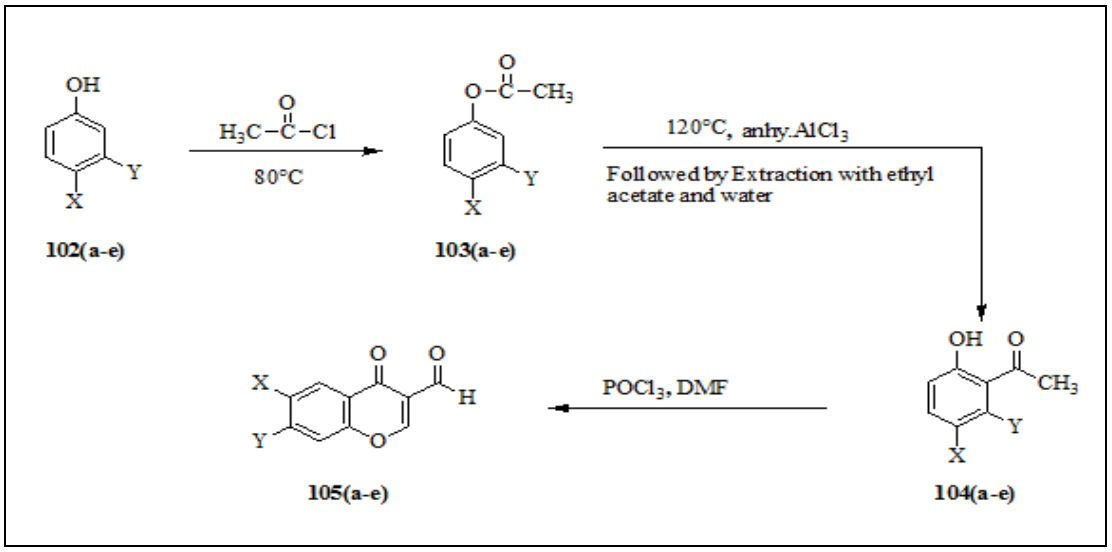


SULPHONAMIDE (2)

Sulfonamide or sulphonamide (2) is the basis of several groups of drugs. The original antibacterial sulfonamides (sometimes called sulfa drugs or sulpha drugs are synthetic antimicrobial agents that contain the sulfonamide group [10]. They are first used as antibacterial/antibiotic agents, but their applications have been extended to treat other diseases since. They possess various types of pharmacological activites such as antibacterial [11], antithyroid [12], anti-inflammatory [13], antidepressant [14], diuretic [15], protease inhibitors [16].

MATERIAL AND METHODS:

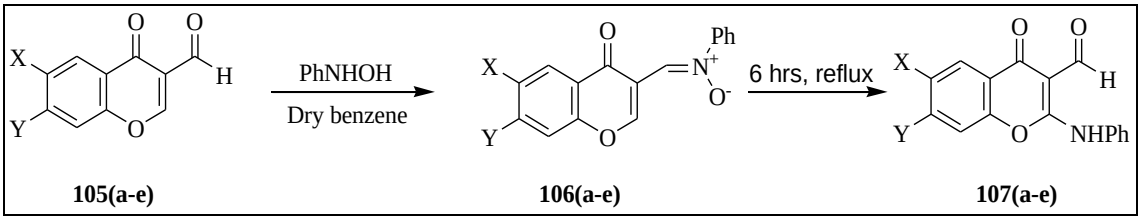
Synthesis of Substituded 3-Formyl Chromones 105(a-e), Starting from Phenols 101(a-e): During the course of present work, the starting compounds 105(a-e) were synthesized by starting from substituted phenols 102 (a-e). These compounds were obtained by acetylation of various phenols treating with acetyl chloride at 75 - 80 °C. Then, addition of anhydrous aluminium chloride has led to the formation of corresponding acetophenones at 120 °C - 125 °C. Then, these acetophenones were treated with $POCl_3$ and DMF to synthesize corresponding substituted-3-Formyl chromones 105(a-e).



SCHEME: 1

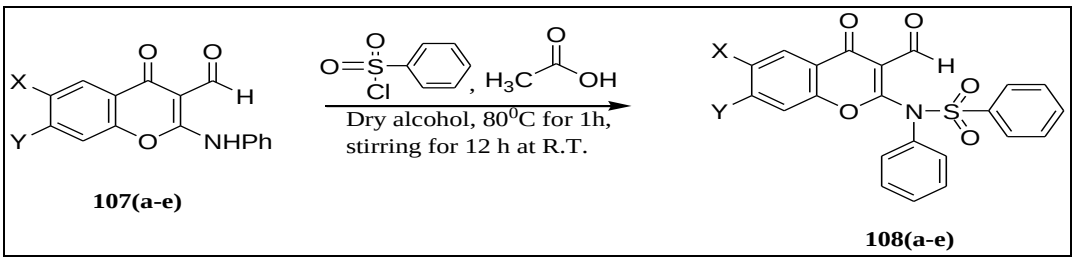
Compounds	X	Y
A	H	H
B	Br	H
C	H	Cl
D	NO_2	H
E	Cl	E

Synthesis of Substituted 4- Oxo- 2- (phenyl-amino)- 4H-chromene- 3- carbaldehyde 107(a-e) from Substituted 3-Formyl Chromones 105(a-e): These compounds were synthesized by starting with substituted 3-Formyl chromones 105(a-e). Substituted 3-Formyl chromones 105(a-e) and phenyl hydroxyl amine both were dissolved in dry benzene. Then, these were kept at room temperture for 1-1.5 hrs and solid nitrones were formed. The reactant mixture was refluxed with continuous stirring for 6 hrs followed by the addition of glacial acetic acid at 800 °C leading to formation of compounds 107(a-e).



SCHEME: 2

Synthesis of substituted N-(3-formyl- 4- oxo- 4H-chromen-2-yl)- N- phenylbenzene sulfonamide 108(a-e) from substituted 4- Oxo- 2- (phenyl amino)-4*H*-chromene-3-carbaldehyde 107 (a-e): The compounds 107(a-e) were refluxed with continuous stirring in dry ethanol and Benzene sulphonyl chloride at 80 °C. After 10 minutes, 1ml glacial acetic acid was added and continuous stirring for 1 hr was done with refluxing. Then, continuous stirring was carried out at room temperature for 12 hrs. The solid formed was filtered and recrystallised with alcohol and the final compounds 108 (a-e) were obtained.



SCHEME: 3

Compounds	X	Y
A	H	H
B	Br	H
C	H	Cl
D	NO_2	H
E	Cl	F

The investigations have provided an access to design novel chromone based sulfonamide moiety and are anticipated to display useful biological activities particularly antibacterial and antifungal activities. The results of investigations indicate that in most of the experimental observations maximum yield was obtained when chromone nucleus bears an electron withdrawing group at C-6 and C-7 position with more electronegativity.

TABLE 1: SOLVENTS TRIED FOR ABOVE REACTION

Solvents tried (Dry Solvents)	Results
Acetonitrile	No reaction
Pyridine	No reaction
Acetone	No reaction
Ethanol	Reaction occur

TABLE 2: THE %AGE YIELD, REACTION CONDITIONS ARE SUMMARIZED

S. no.	Compound No.	X	Y	Solvent (Dry)	Reaction Condition	Product (%Yield)
1	108 (a)	H	H	Ethanol	Reflux, 80 °C, 1 h, Stirr, R.T., (12h)	80%
2	108 (b)	Br	H	Ethanol	Reflux, 80 °C, 1 h, Stirr, R.T., (12h)	85%
3	108 (c)	H	Cl	Ethanol	Reflux, 80 °C, 1 h, Stirr, R.T., (12h)	94%
4	108 (d)	NO_2	H	Ethanol	Reflux, 80 °C, 1 h, Stirr, R.T., (12h)	82%
5	108 (e)	Cl	F	Ethanol	Reflux, 80 °C, 1 h, Stirr, R.T., (12h)	90%

Experimental Studies: The identification and characterization of compounds synthesized were carried by the following techniques to ascertain that all prepared compounds reported conform to data given:

- Melting Point
- Solubility
- Thin Layer Chromatography
- Infrared Spectroscopy
- 1H-Nuclear Magnetic Resonance Spectroscopy
- Mass Spectroscopy.

Solvents, starting materials and reagents were purchased from commercial suppliers and used after purification. All the solvents were purified by the standard procedure prior to use. All melting points were measured on a liquid paraffin bath in open glass capillary tubes using Digital Melting point apparatus.

The reaction progress and product purity was checked by thin layer chromatography using silica gel-G coated glass plates (TLC plates) which were visualized by exposure to iodine vapour as visualizing agent. IR spectrum was recorded on Perkin Elmer 882 model spectrometer. Frequencies were recorded in wave number.

Proton NMR spectroscopy was performed using Bruker Advance II (300 MHz) NMR spectrometer for solution in CDCl3/DMSO-d6 using tetra-methylsilane (TMS) as internal reference. All chemical shift were reported in parts per million (ppm). Chemical shifts were reported in ppm (δ) and coupling constant (J) values in Hertz. The mass spectra were recorded on Q-TOF Micromass (LC-MS) instrument. The m/e values were obtained.

N-[3-Formyl-4-oxo-4H-chromene-2-yl)-N-phenyl benzenesulfonamide 108 (a): Reaction of 4-Oxo-2-(phenylamino)- 4H- chromene- 3- carbaldehyde 107(a), (1.0g) with Benzene sulphonyl chloride (0.57ml) according to the procedure described above offered 108(a) pale yellow crystals with (0.80g, 80%) yield, melting point 199 °C, $C_{22}H_{15}NO_5S$, molecular weight 405g, solubility in DMSO.

IR (KBr): V_{max} cm^{-1}: 3024 (-C-H, Ar, s), 1715.13 (-C=O), 1677 (H-C=O), 1258.63 (-C-O-C, s), 1184(-C-N, m), 1315 (S=O), 1535 (-C==C, Ar).

^{1}H-NMR: δ_{ppm} (DMSO; 300 MHz): 9.2 (s, 1H, 3CHO), 6.8-6.6 (m, 5H, N-phenyl), 7.9-7.4 (m, 5H, phenyl along with SO_2), 7.6 (dd, 1H, C_5-H), 7.4-7.1 (m, Ar, 3Hs).

Mass: m/e: 428(M^++Na).

N-(6-Bromo-3- formyl-4-oxo- 4H-chromen-2-yl)-N- phenyl benzene sulfonamide 108 (b): Reaction of 6-Bromo-4-oxo-2- (phenylamino)- 4H-chromene-3-carbaldehyde 107(b), (1.0g) with Benzene sulphonyl chloride (0.44ml) according to the procedure described above offered 108(b) pale yellow crystals with (0.850g, 85%) yield, melting point 213 °C, $C_{22}H_{14}$ $BrNO_5S$, molecular weight 485g, solubility in DMSO.

IR (KBr) V_{max} cm^{-1}: 561.12 (C-Br, s), 2924 (-C-H, s), 1735 (-C=O), 1690.48 (H-C=O), 1253 (-C-O-C, s), 1173.14 (-C-N, m), 1318.29 (S=O), 1491 (-C=C, Ar).

^{1}H-NMR: δ_{ppm} (DMSO; 300 MHz): 9.4 (s, 1H, 3CHO), 6.3-6.0 (m, 5H, N-phenyl), 8.6-8.3 (m, 5H, Phenyl along with SO_2), 7.6 (d, 1H, C_5-H), 7.5-7.3 (m, Ar, 3Hs).

Mass: m/e: 485(M^+).

N-(7-Chloro-3-formyl-4-oxo-4H-chromen- 2- yl)-N-phenylbenzenesulphonamide 108 (c): Reaction of 7-Chloro-4-oxo-2-(phenylamino)-4H-chromene-3-carbaldehyde 107(c), (1.0g) with benzene sulphonyl chloride (0.50ml) according to the procedure described above offered 108(c) pale yellow crystals with (0.94g, 94%) yield, melting point 232 °C, $C_{22}H_{14}ClNO_5S$, molecular weight 439g, solubility in DMSO.

IR (KBr) V_{max} cm^{-1}: 715.21 (C-Cl, s), 3053 (-C-H, s), 1728.21 (-C=O), 1712.18 (H-C=O), 1255 (-C-O-C, s), 1180 (-C-N, m), 1175 (S=O), 1549 (-C=C, Ar).

^{1}H-NMR: δ_{ppm} (DMSO; 300MHz): 10.0 (s, 1H, 3CHO), 7.0-6.9 (m, 5H, N-phenyl), 8.1-7.8 (m, 5H, Phenyl along with SO_2), 7.1 (d, 1H, C_5-H), 7.6-7.4 (m, Ar, 3Hs).

Mass: m/e: 439(M^+).

N- (6-Nitro- 3-formyl-4-oxo- 4H-chromene-2-yl)-N-phenylbenzenesulfonamide 08 (d): Reaction of 6-Nitro-4-oxo-2-(phenylamino) - 4 *H*- chromene-3-carbaldehyde 107(d), (1.0g) with Benzene sulphonyl

chloride (0.49ml) according to the procedure described above offered 108(d) pale yellow crystals with (0.82g, 82%), melting point 223 °C, $C_{22}H_{14}N_2O_7S$, molecular weight 450g, solubility in DMSO.

IR (KBr) V_{max} cm^{-1}: 1470.09 (NO_2-Ar, s), 1720 (-C=O), 1738 (H-C=O), 1179 (-C-O-C, s), 1158 (-C-N, m), 1297.81(S=O), 1552 (-C=C, Ar).

^{1}H-NMR: δ_{ppm} (DMSO; 300MHz): 9.6 (s, 1H, CHO), 7.1-6.9 (m, 5H, N-phenyl), 8.4-7.8 (m, 5H, Phenyl along with SO_2), 7.9 (d, 1H, C_5-H), 7.7-7.4 (m, Ar, 3Hs).

Mass: m/e: 450.2(M^+).

N- (7- Chloro- 6- fluoro- 3- formyl- 4- oxo- 4H- chromen-2-yl)-N-phenylbenzene sulphonamide 108 (e): Reaction of 7-Chloro-6-flouro-4-oxo-2-(phenylamino)- 4H- chromene- 3- carbaldehyde 107(e), (1.0g) with Benzene sulphonyl chloride (0.48ml) according to the procedure described above offered 108(e) pale yellow crystals with (0.90g, 90%), melting point 223 °C, $C_{22}H_{13}ClFNO_5S$, molecular weight 457g, solubility in DMSO.

IR (KBr) V_{max} cm^{-1}: 1470.09 (C-Cl, s), 1413.59 (C-F, s), 1169 (-C=O), 1731 (H-C=O), 1256 (-C-O-C, s), 1074 (-C-N, m), 1299 (S=O), 1492 (-C=C).

^{1}H-NMR: δ_{ppm} (DMSO; 300MHz): 10.0 (s, 1H, CHO), 7.3-6.9 (m, 5H, N-phenyl), 8.2-7.6 (m, 5H, Phenyl along with SO_2), 7.3 (d, 1H, C_5-H), 7.0 (d, 1H, C_8-H).

Mass: m/e: 457.6(M^+).

Antimicrobial Activity: An antimicrobial agent is a substance that kills or inhibits the growth of microorganism such as bacteria, fungi, or protozoans. Disinfectants are antimicrobial substances used on non-living objects or outside the body. On the basis of their primary activity, they are more specifically called antibacterial, antifungal, antiprotozoal, antiparasitic or antiviral agents etc [17].

Microorganisms Tested: The antimicrobial activities were tested against one Gram positive bacterial strain (*Staphylococcus aureus*), and one Gram negative bacterial strain (*Escherichia coli*) and two fungal strains (*Aspergillus niger* and *Candida albicans*).

TABLE 3: LIST AND CONDITIONS FOR THE GROWTH OF MICROORGANISMS

MTCC No.	Microorganisms	Growth Condition	Incubation time	Temperature
3160	*Staphylococcus aureus*	Aerobic	24 hrs	37 °C
1678	*Escherichia coli*	Aerobic	24 hrs	30 °C
183	*Candida albicans*	Aerobic	48 hrs	30 °C
281	*Aspergillus niger*	Aerobic	7 days	30 °C

Revival of Cultures: The bacterial and fungal strains used were obtained from freeze dried ampoules that were collected from Microbial Type Collection and Gene Bank, Institute of Microbial Technology, Chandigarh. The upper top of the ampoules were disinfected with alcohol, marked the ampoule near the middle of the cotton wool with a sharp knife, disinfect the surface around the mark with alcohol, and ampoule was broken at the marked area. The cotton plug was removed from the ampoule, freeze dried power was suspended in water for injection and suspension taken from ampoules and swabbing was done on sterile nutrient broth medium and incubated at 370 °C for 48 hrs.

Antibacterial Activity: An antibacterial is an agent that inhibits bacterial growth or kills bacteria [17]. The antibacterial activity is determined by two methods that are mentioned below.

Preparation of Broth Medium: The nutrient broth medium for bacterial strains were prepared according to following compositions and was autoclaved at 1210 °C under a 15 psi atmosphere pressure for 15 min.

Composition of Broth Medium for Bacterial Strains:

TABLE 4: *STAPHYLOCOCCUS AUREUS* (GRAM POSITIVE STRAIN)

Ingredient	Standard Quantity	Quantity Used
Beef extract	1.0g	500mg
Yeast extract	2.0g	1.0g
Peptone	5.0g	2.5g
NaCl	5.0g	2.5g
Agar (for solid media only)	15g	7.5g
Distilled water	Upto 1.0L	Upto 500ml

Antimicrobial Assay or Sensitivity of Microorganisms to Different Samples: There are two methods to determine sensitivity of microbes:

- Zone of inhibition method (Kirby-Bauer disc diffusion method) [18-19].
- Turbidity method (Tube dilution method) [20].

TABLE 5: *ESCHERICHIA COLI* (GRAM NEGATIVE STRAIN)

Ingredient	Standard Quantity	Quantity Used
Yeast extract	5 gm	2.5g
Triptone	10 gm	5.0g
NaCl	10 gm	5.0g
Agar (for solid media only)	15g	7.5g
Distilled water	Upto1.0L	Upto500ml

Sensitivity of different bacterial strains to samples was measured in terms of Minimum Inhibitory Concentration (MIC) by using Turbidity method and Zone of inhibition method. MIC is the minimum inhibitory concentration of the substance that inhibits growth of microbial strains after 18-24 hrs [21].

Generally, Turbidity Method is used for non turbid solutions and Zone of inhibition is used for both turbid and less-turbid solutions [22]. Our solutions are transparent in nature but we use both methods for this assay. The synthesized novel chromone based sulfonamide derivatives were screened for antibacterial activity against *Escherichia coli* (Gram-negative bacteria) and *Staphylococcus aureus* (Gram-positive bacteria) by using modified Kirby-Bauer disc diffusion method and Tube dilution method.

Zone of Inhibition Method (Agar Well Diffusion Assay or Kirby-Bauer Disc Diffusion Method): Minimum inhibitory concentration was determined by using agar well diffusion assay in terms of zone of inhibition. The nutrient agar media was sterilized and poured into sterilized petri plates. Put it aside for some times for solidification. After solidify-cation, it was swabbed with inoculum over the entire surface of medium. The inoculated petri plates were incubated for 24 hrs at 37 °C for sufficient growth of microbes. After 24 hours, petri plates were taken out from incubator. Then, the wells were bored using a sterilized stainless steel borer at equidistance into the seeded agar plates. Separately, Stock solution of samples were prepared and then, diluted to form different concentrations (300, 200, 100, 50, 30 µg/mL).

Then, the test samples (different concentration), control and standard drug were loaded in respective wells with a 0.1mL volume into seeded petri plates. All the petri plates were again incubated at 37 °C for 24 hrs and resultant zone of inhibition was measured. For each sample, this procedure was performed in three replicate plates for each organism. During replication of plates, tests were also performed by using filter paper disc impregnated with sample and standard drugs. DMSO was used as control and standard drug Ciprofloxacin was taken as antibacterial standard.

TABLE 6: ZOI STUDIED FOR *STAPHYLOCOCCUS AUREUS* BY KIRBY-BAUER DISC DIFFUSION METHOD

Synthesized Compounds	*Staphylococcus aureus* Zone of inhibition (mm)				
	30 µg/mL	50 µg/mL	100 µg/mL	200µg/mL	300µg/mL
108(a)	2.3	2.7	2.9	3.1	3.5
108(b)	2.1	2.2	2.5	3.3	5.0
108(c)	-	2.1	2.5	2.7	2.9
108(d)	1.8	2.0	2.1	2.3	2.6
108(e)	-	2.6	2.8	3.1	3.4
Ciprofloxacin(Std)	3.9				

TABLE 7: ZOI STUDIED FOR *ESHCHERICHIA COLI* KIRBY-BAUER DISC DIFFUSION METHOD

Synthesized Compounds	*Eshcherichia coli* Zone of inhibition (mm)				
	30 µg/mL	50 µg/mL	100µg/mL	200µg/mL	300µg/mL
108(a)	-	1.9	2.0	2.2	2.3
108(b)	-	1.5	1.6	1.8	1.9
108(c)	2.3	2.5	2.7	2.9	3.0
108(d)	-	2.0	2.4	2.7	2.9
108(e)	-	2.6	2.8	3.1	3.3
Ciprofloxacin (Std)	3.3				

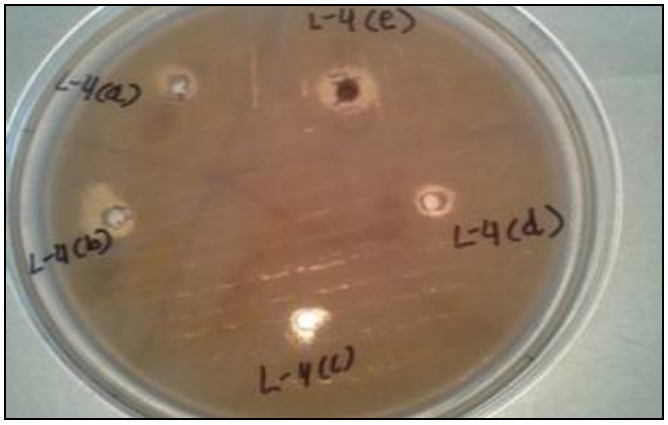


FIG. 1: ZOI AGAINST *S. AUREUS* 108(A-E)

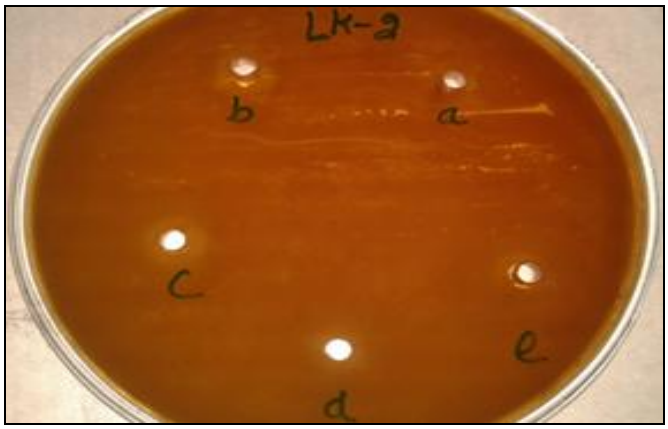


FIG. 2: ZOI AGAINST *E. COLI* 108(A-E)

FIG. 3: MIC AGAINST *S. AUREUS* 108 (A-E)

FIG. 4: MIC AGAINST *E. COLI* 108(A-E)

Tube Dilution Method (Turbidity Method): The Minimum Inhibitory Concentration was also determined by using Tube dilution method. The 2mL of sterilized liquid nutrient broth media was poured in to the sterilized test tubes. The standard inoculum of the microbes were taken and transferred in to those test tubes. The test tubes was covered with aluminium strip and incubated for 24 hrs at 37 °C for growth of microbes. The turbidity of the solution indicated the growth of the microorganisms. Separately, Stock solution of samples were prepared which was then diluted to form different concentrations (300, 200, 100, 50, 20 µg/mL). Now, 0.5ml of different sample concentrations was added to test tubes containing nutrient broth.

TABLE 8: ZOI STUDIED FOR S. *AUREUS* AND *E.COLI* BY TUBE DILUTION METHOD

Synthesized Compounds	MIC (µg/mL)	
	S. aureus	*E. coli*
108(a)	30	50
108(b)	30	50
108(c)	50	30
108(d)	30	50
1008(e)	50	50
Ciprofloxacin(Std)	30	30

All the test tubes were again incubated at 37 °C for 24 hrs. After incubation period check the turbidity in the test tubes starts disappearing which is called Minimum inhibitory concentration (MIC). DMSO was used as control and standard drug Ciprofloxacin was taken as antibacterial standards.

Antifungal Activity: An antifungal agent that kills or inhibits the growth of fungal infections. An antifungal medication is a pharmaceutical fungicide that used to treat mycoses and serious systemic infections such as cryptococcal meningitis [17]. The antifungal activity can be also determined by two methods that are mentioned below.

Composition of Nutrient Broth Medium for Growth of Fungal Strains:

TABLE 9: *CANDIDA ALBICANS*

Ingredients	Standard Quantity	Quantity used
Yeast extract	3.0g	1.5g
Malt extract	3.0g	1.5g
Peptone	5.0g	2.5g
Glucose	10.0g	5.0g
Agar (for solidification)	15g	7.5g
Distilled Water	Upto 1.0L	Upto 500ml

TABLE 10: *ASPERGILLUS NIGER*

Ingredients	Standard Quantity	Quantity used
*Czapek concentrate	10ml	5ml
K_2HPO_4	1.0g	0.5g
Yeast extract	5.0g	2.5g
Sucrose	30.0g	15.0g
Agar (for solidification)	15g	7.5g
Distilled water	Upto 1.0L	Upto 500ml

TABLE 11: *CZAPEK CONCENTRATE

Ingredients	Standard Quantity	Quantity used
$NaNO_3$	30.0g	0.30g
KCl	5.0g	0.05g
$MgSO_4.7H_2O$	5.0g	0.05g
$FeSO_4.7H_2O$	0.1g	0.001g
Distilled Water	Upto 1.0L	Upto 10ml

TABLE 12: ZOI STUDIED FOR *ASPERGILLEUS NIGER* BY KIRBY-BAUER DISC DIFFUSION METHOD

	Aspergilleus niger				
	Zone of inhibition (mm)				
Synthesized compounds	30µg/ mL	50µg/ mL	100µg/ mL	200µg/ mL	300µg/ mL
108(a)	1.2	1.3	1.5	1.7	1.9
108(b)	1.0	1.0	1.3	1.6	2.0
108(c)	-	1.5	1.7	1.9	2.1
108(d)	0.5	0.6	0.8	0.9	0.9
108(e)	-	1.2	1.5	1.7	2.3
Fluconazole (Std)	2.0				

TABLE 13: ZOI STUDIED FOR *CANDIDA ALBICANS* BY KIRBY-BAUER DISC DIFFUSION METHOD

	Candida albicans				
	Zone of inhibition (mm)				
Synthesized compounds	30 µg/mL	50 µg/mL	100 µg/mL	200 µg/mL	300 µg/mL
108(a)	-	-	0.7	0.9	0.9
108(b)	1.0	1.3	1.5	1.8	2.0
108(c)	0.8	0.9	1.0	1.2	1.3
108(d)	1.3	1.8	2.0	2.3	2.6
108(e)	1.1	1.1	1.2	1.3	1.6
Fluconazole (Std)	2.0				

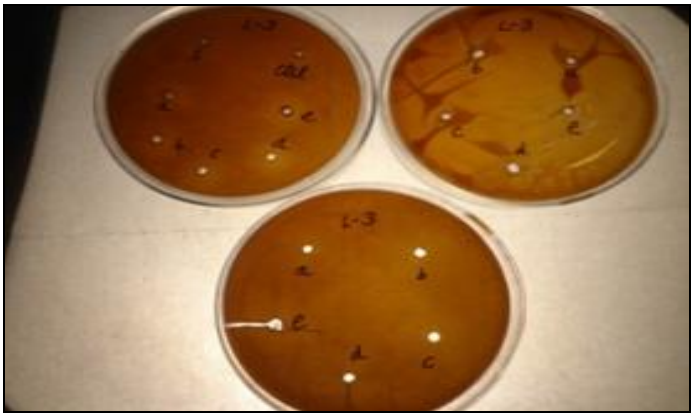


FIG. 5: ZOI AGAINST *A. NIGER* 108 (A-E)

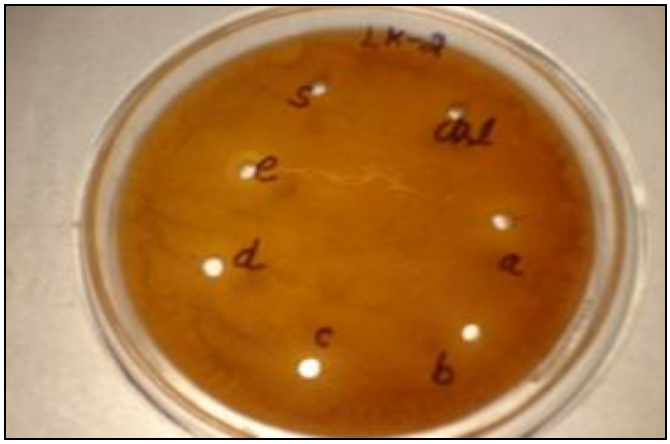


FIG. 6: ZOI AGAINST *C. ALBICANS* 108 (A-E)

TABLE 14: ZOI STUDIED FOR *A. NIGER* AND *C. ALBICANS* BY TUBE DILUTION METHOD

Synthesized Compounds	MIC (µg/mL)	
	A .niger	*C. albicans*
108(a)	30	50
108(b)	30	30
108(c)	50	30
108(d)	30	30
108(e)	30	30
Fluconazole (Std)	30	30

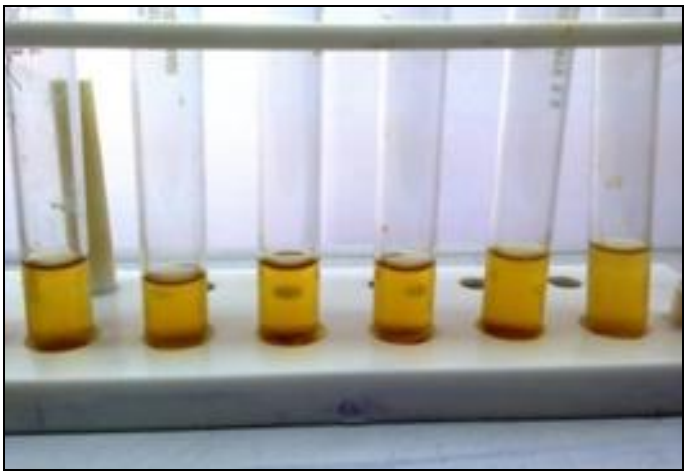
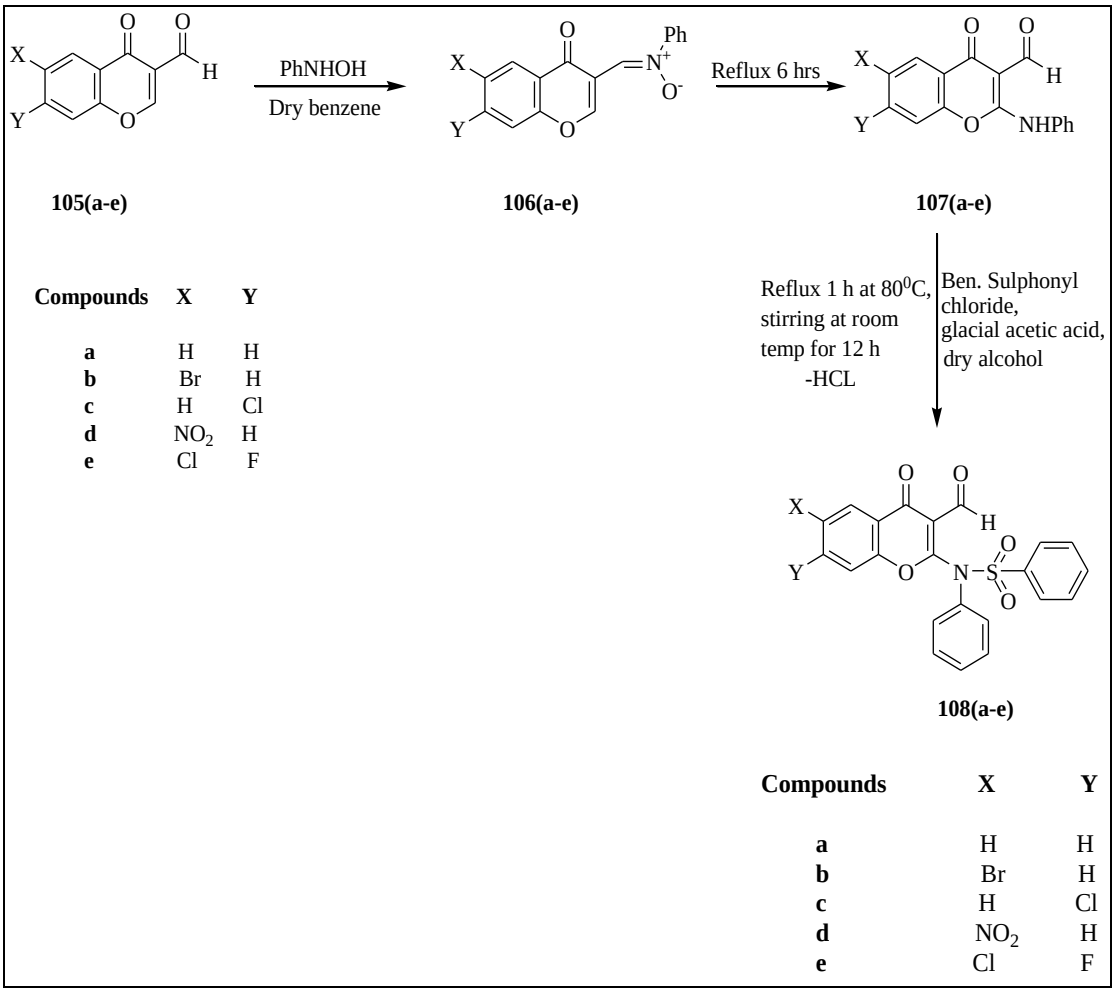


FIG. 7: MIC AGAINST *A. NIGER* 108 (A-E)

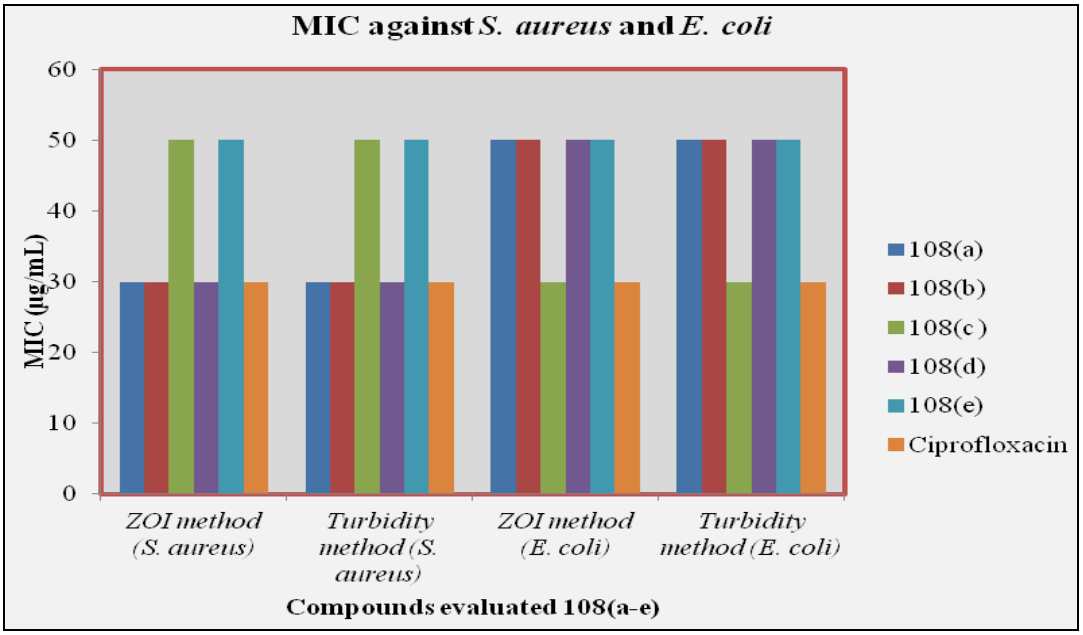
FIG. 8: MIC AGAINST *C. ALBICANS* 108 (A-E)

CONCLUSION AND SUMMARY:

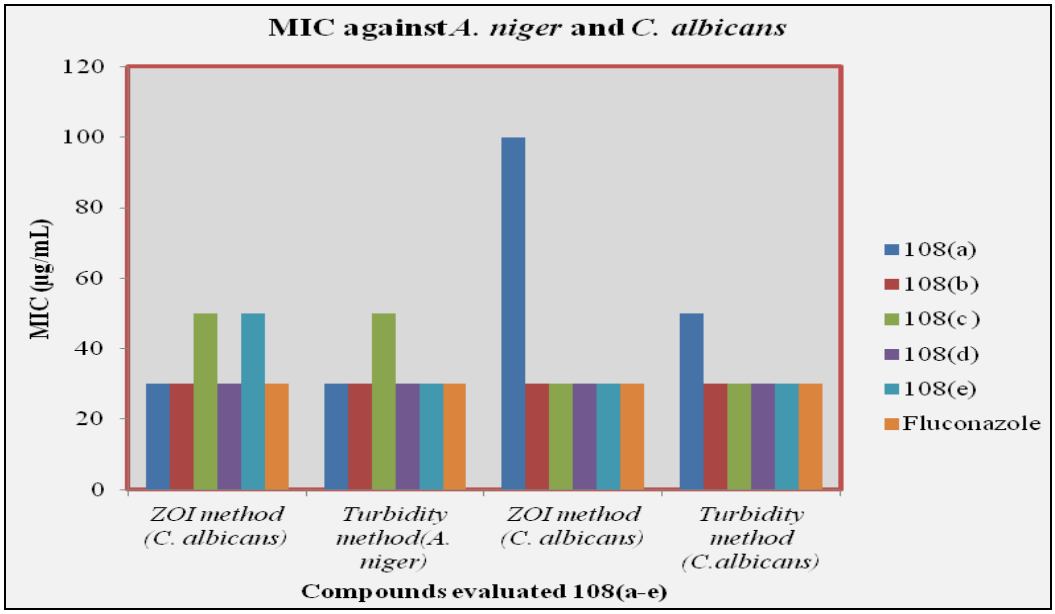


Compounds	X	Y
a	H	H
b	Br	H
c	H	Cl
d	NO_2	H
e	Cl	F

SCHEME: 4



GRAPH 1: COMPARISON OF MIC (µg/ml) OF SYNTHESIZED COMPOUNDS 108 (A-E) WITH CIPROFLOXACIN AGAINST *S. AUREUS* AND *E. COLI* BY USING KIRBY-BAUER DISC DIFFUSION METHOD AND TUBE DILUTION METHOD



GRAPH 2: COMPARISON OF MIC (µG/ML) OF SYNTHESIZED COMPOUNDS 108 (A-E) WITH FLUCONAZOLE AGAINST *A. NIGER* AND *C. ALBICANS* BY USING KIRBY-BAUER DISC DIFFUSION METHOD AND TUBE DILUTION METHOD

From the data of **Table 7**, we observed that the novel chromone based sulfonamide nucleus gives the maximum yield, when electron withdrawing groups with more electronegativity were attached at C-6 and C-7 position.

TABLE 15: The %AGE YIELD, REACTION CONDITIONS ARE SUMMARIZED

	Antibacterial activity (µg/mL) Ciprofloxacin as Std. (30 µg/mL)		Antifungal activity (µg/mL) Fluconazole as Std. (30µg/mL)	
Compounds	***S. aureus***	***E. coli***	***A. niger***	***C. albicans***
108 (a)	30	50	30	50
108 (b)	30	50	30	30
108 (c)	50	30	50	30
108 (d)	30	50	30	30
108 (e)	50	50	30	30

From the above graph, we concluded that compounds 108(a), 108(b) and 108(d) 30 µg/mL may be most potent against *S. aureus* (Gram Positive bacteria) and compound 108(c) 30 µg/mL may be most potent against *E. coli* (Gram Negative bacteria) when compared with standard drug Ciprofloxacin 30 µg/mL. From the above graph, we concluded that the compounds 108(a), 108(b), 108(d), 108(e) 30µg/mL may be most potent against *Aspergillus niger* and and compounds 108(b), 108(c), 108(d), 108(e) 30µg/mL may be most potent against *Candida albicans* when compared with standard drug Fluconazole 30µg/mL. From the above results, it may concluded that the Compounds 108 (a-e) possess moderate to potent antibacterial and antifungal activity when compared to standard, Ciprofloxacin and Fluconazole respectively.

There is an unending quest for new effective and safe drugs. Efforts are also being made to improve the existing drugs by increasing their potency, duration of action, decreasing side effects. Synthetic chemistry along with drug design by molecular manipulation is efficient source of new drugs. Chemical modification of a drug molecule of a series having optimal activity is widely used and continues to be an important factor necessary for new drug discovery.

The literature review has also been shown that Chromone nucleus has antimicrobial, anti-platelet, anti HIV, antiviral and anti cancer activities and sulfonamide nuclei have also exhibited a wide variety of pharmacological activities such as antimicrobial, antimalarial, anti HIV, high ceiling diuretic, antithyroid, antitumor, insulin releasing

antidiabetic. Hence, in present study, the Chromone is taken as a lead molecule to synthesize "Substituted N-(3-Formyl-4-Oxo-4H-Chromen-2-yl)-N-Phenylbenzenesul Fonamide and its derivatives" and to evaluate their *in vitro* antimicrobial activity by testing them on various microbial strains. The compounds 108 (a-e) have been shown anti-bacterial activity against *S. aureus* (Gram Positive bacteria) and *E. coli* (Gram Negative bacteria) and antifungal activity against *Aspergillus niger* and *Candida albicans* when compared with standard drugs, Ciprofloxacin as antibacterial and Fluconazole as antifungal respectively by Kirby-Bauer disc diffusion assay method and Tube dilution method.

All compounds exhibited moderate to potent antibacterial as well antifungal activity against all the microbes tested. Pharma-cological results indicate that the new novel chromone based sulfonamide derivatives *i.e.* Substituted N-(3-Formyl-4-OXO- 4H - Chromen-2-yl) - N Phenyl benzenesulfonamide and its deriva tives show greater biological significance. Hence, these compounds 108 (a-e) might be promising new antibacterial agent and antifungal agent.

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CONFLICTS OF INTEREST: Nil

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