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SYNTHESIS AND ANTIMICROBIAL ACTIVITY OF N-{4-[(6-CHLORO-4-OXO-4*H*-CHROMEN-3-YLMETHYLENE) IMINO] PHENYL}-2-(SUBSTITUTED PHENOXY ACETAMIDE) DERIVATIVES

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6-chloro-4-oxo-4H-chromene-3-carboxaldehyde, Substituted phenols, Antibacterial activity, Antifungal activity

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ABSTRACT

Some N-{4-[(6-chloro-4-oxo-4*H*-chromen-3-ylmethylene) imino] phenyl}-2-(substituted phenoxy) acetamide derivatives **(3)** were synthesized by reacting N-{4-[(6-chloro-4-oxo-4*H*-chromen-3-ylmethylene) imino] phenyl}-2-chloroacetamide **(2)** with some substituted phenol in dry acetone in the presence of K_2CO_3 and catalytic amount of KI. The chemical structures of the compounds were elucidated by IR, ^{1}H-NMR and elemental analysis. Their antibacterial activity against gram positive bacterial strains (*S. aureus* and *B. subtilis*) and gram negative bacterial strains (*E. coli* and *P. aeruginosa*) were investigated by disc diffusion method. The antifungal activity of these compounds was also tested against *A. niger* and *A. flavipes.* The results showed that some of the compounds have strong antimicrobial activity.

INTRODUCTION: The synthesis of chromone derivatives is a research field of great interest and long history [1]. Compounds having chromone moiety are synthetically versatile molecules with a reactive carbonyl group. They have considerable significance for their biological activities and for their reactivity towards nucleophiles, which allow the synthesis of a wide variety of heterocycles.

4-oxo-4*H*-chromene derivatives possess various pharmacological activities like antimicrobial, [2, 3, 4] antiviral, [5] anti-inflammatory, antitumor etc.[6] The main aim of this work was the synthesis of pharmacologically more potent N-{4-[(6-chloro-4-oxo-4*H*-chromen-3-ylmethylene)imino] phenyl}-2-(substituted phenoxy) acetamide derivatives. Reaction of N-{4-[(6-chloro-4-oxo-4*H*-chromen-3-ylmethylene) imino] phenyl}-2-chloroacetamide with some substituted phenol were achieved. The progress of reaction was monitored by TLC. After completion of reaction, these newly prepared compounds were tested for their *in vitro* antimicrobial activities against different Gram-positive, Gram-negative bacteria and the fungal strains in comparison with reference standard drugs.

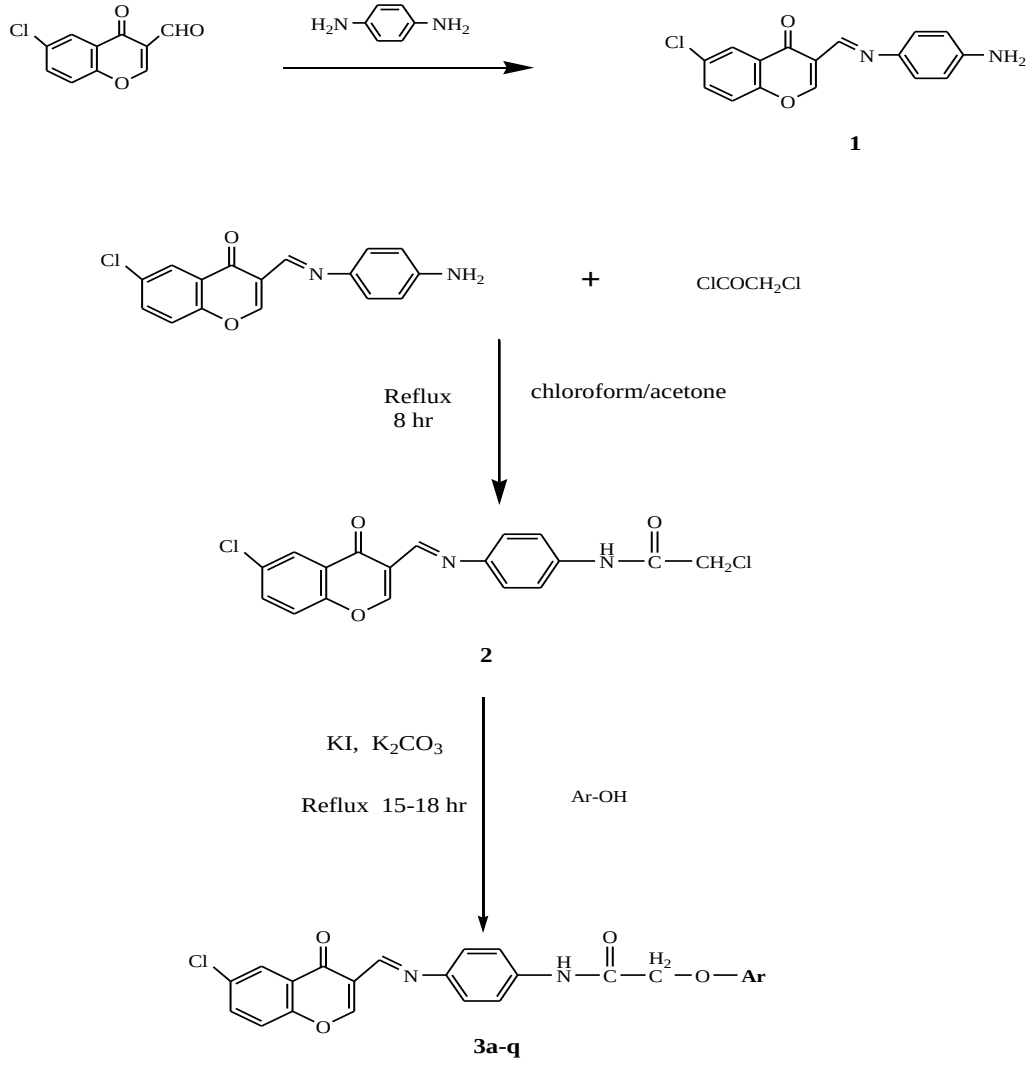
MATERIAL AND METHODS: Melting points were determined in open capillaries on Thomas Hoover apparatus and are uncorrected. IR spectra were recorded on a Shimadzu IR-435 spectrophotometer and ^{1}H-NMR spectra were recorded on a Bruker 250 MHz spectrometer instrument using tetramethylsilane (TMS) as an internal standard and DMSO-d6 as a solvent. Chemical shifts are given in parts per million (ppm). Elemental analyses were recorded on Perkin Elmer EAL 240 spectrometer. Purity of the compounds was checked by TLC (Thin Layer Chromatography) on silica gel plates and spot were visualized by exposure

to iodine vapor. The antibacterial and antifungal screening is carried out at microbiology laboratory of College of Pharmacy IFTM, Moradabad. The different microbial strains were procured from NCL Pune.

Synthesis of 3-[(4-aminophenylimino) methyl]-6-chloro-4-oxo-4H-chromene (1): A mixture of 6-chloro-4-oxo-4*H*-chromene-3-carboxaldehydes (0.005mol) and 1,4-phenylenediamine (0.005mol) in dry benzene (50 ml) containing 4-toluenesulfonic acid (0.01 g) was refluxed for 5 h. The obtained solid was filtered off and crystallized to give **1** [7].

N-{4-[(6-chloro-4-oxo-4H-chromen-3-ylmethylene) imino] phenyl}-2-cloroacetamide (2): Equimolar amounts of **1** (0.1 mol) and chloroacetyl chloride (0.1 mol) in chloroform (30 ml) was refluxed in the presence of K_2CO_3 (0.005 mol) for about 10 h. Excess of solvent was removed in vacuum and the residue was stirred with water (50 ml), filtered, washed with 2% $NaHCO_3$ (30 ml) and subsequently with water (30 ml). The crude product was crystallized from methanol [8].

General procedure for the synthesis of N-{4-[(6-chloro-4-oxo-4H-chromen-3-ylmethylene) imino] phenyl}-2-(substituted phenoxy acetamide) derivatives (3a-q): Equimolar quantities of N-{4-[(6-chloro-4-oxo-4H-chromen-3-ylmethylene) imino] phenyl}-2-cloroacetamide (0.05 mol) and different substituted phenols (0.01 mol) in presence of anhydrous potassium carbonate (0.01 mol), and catalytic amount of potassium iodide in dry acetone were refluxed for 15-18 h. The compound was then filtered and washed thoroughly with water and crystallized from ethanol. The synthetic route of compounds is outlined in **Scheme 1** and the substituents of the compounds are given in **Table 1**.



SCHEME 1

TABLE 1: SUBSTITUENTS OF COMPOUNDS 3a-q

Compound	Ar
3-a	4-$NO_2C_6H_4$
3-b	3-$NO_2C_6H_4$
3-c	C_6H_5
3-d	4-$CH_3C_6H_4$
3-e	2-$CH_3C_6H_5$
3-f	3-$CH_3$4-ClC_6H_3
3-g	4-Cl 3,5-CH_3 C_6H_2
3-h	4-C_6H_4-C-$(CH_3)_3$
3-i	4-ClC_6H_4
3-j	4-BrC_6H_4
3-k	4-C_6H_4-CH-$(CH_3)_2$
3-l	2-$0CH_3$,3-$CH_3C_6H_3$
3-m	3,5-$OCH_3C_6H_3$
3-n	2-ClC_6H_4
3-o	2-Cl,4-$NO_2C_6H_3$
3-p	3,4-$OCH_3C_6H_3$
3-q	2-$NO_2C_6H_4$

N-{4-[(6-chloro-4-oxo-4H-chromen-3-ylmethylene) imino]phenyl}-2-(4-nitrophenoxy) acetamide (3a): Yield 48%, mp 170 - 171°C. IR (KBr, cm^{-1}): 3240 (NH), 3045 (CH_{arom}), 2928 (CH_{aliph}), 1659 ($C=O_{amide}$), 1618 ($C=O_{pyrone}$), 1606 (C=N), 1230 and 1026 (-C-O-C-), 1598 (C=C in aromatic ring). ^{1}H-NMRδ: 4.30 (2H, s, CH_2), 6.92-7.90 (13H, m, Ar-H, CH=N and H-2), 9.98 (1H, s, NH); Anal. Cal. for $C_{24}H_{16}ClN_3O_6$: C, 60.32; H, 3.37; N, 8.79. Found: C, 60.24; H, 3.34; N, 8.72.

N-{4-[(6-chloro-4-oxo-4H-chromen-3-ylmethylene) imino]phenyl}-2-(3-nitrophenoxy) acetamide (3b): Yield 47%, mp 165 - 166°C. IR (KBr, cm^{-1}): 3238 (NH), 3046 (CH_{arom}), 2926 (CH_{aliph}), 1662 ($C=O_{amide}$), 1617 ($C=O_{pyrone}$), 1604 (C=N), 1231 and 1030 (-C-O-C-), 1596 (C=C in aromatic ring). ^{1}H-NMRδ: 4.30 (2H, s, CH_2), 6.80-7.82 (13H, m, Ar-H, CH=N and H-2), 9.97 (1H, s, NH); Anal. Cal. for $C_{24}H_{16}ClN_3O_6$: C, 60.32; H, 3.37; N, 8.79. Found: C, 60.24; H, 3.40; N, 8.70.

N-{4-[(6-chloro-4-oxo-4H-chromen-3-ylmethylene) imino]phenyl}-2-phenoxy acetamide (3c): Yield 38%, mp 150 - 151°C. IR (KBr, cm^{-1}): 3216(NH), 3050(CH_{arom}), 2929(CH_{aliph}), 1657($C=O_{amide}$), 1618($C=O_{pyrone}$), 1604(C=N), 1240 and 1035 (-C-O-C-), 1598 (C=C in aromatic ring). ^{1}H-NMRδ, 4.28(2H, s, CH_2), 6.58-7.50(13H, m, Ar-H, CH=N and H-2), 9.90(1H, s, NH); Anal. Cal. for $C_{24}H_{17}ClN_2O_4$: C, 66.59; H, 3.96; N, 6.47 Found: C, 66.60; H, 3.96; N, 6.44.

N-{4-[(6-chloro-4-oxo-4H-chromen-3-ylmethylene) imino]phenyl}-2-(p-tolyloxy) acetamide (3d): Yield 40%, mp 190 - 191°C. IR (KBr, cm^{-1}): 3225(NH), 3048(CH_{arom}), 2930(CH_{aliph}), 1655($C=O_{amide}$), 1615 ($C=O_{pyrone}$), 1606(C=N), 1236 and 1035 (-C-O-C-), 1600 (C=C in aromatic ring), 2992(CH in CH_3). ^{1}H-NMRδ: 2.20(3H, s, CH_3), 4.29(2H, s, CH_2), 6.35-7.42(13H, m, Ar-H, CH=N and H-2), 9.91(1H, s, NH); Anal. Cal. for $C_{25}H_{19}ClN_2O_4$: C, 67.19; H, 4.29; N, 6.27. Found: C, 67.25; H, 4.26; N, 6.24.

N-{4-[(6-chloro-4-oxo-4H-chromen-3-ylmethylene) imino]phenyl}-2-(4-chloro-3-methylphenoxy) acetamide (3f): Yield 59%, mp 195 - 196°C. IR (KBr, cm^{-1}): 3237(NH), 3048(CH_{arom}), 2926(CH_{aliph}), 1657($C=O_{amide}$), 1615($C=O_{pyrone}$), 1604(C=N), 1236 and 1033 (-C-O-C-), 1597 (C=C in aromatic ring), 2987(CH in CH_3). ^{1}H-NMRδ: 2.20(3H, s, CH_3), 4.30(2H, s, CH_2), 6.38-7.60(13H, m, Ar-H, CH=N and H-2), 9.94(1H, s, NH);Anal. Cal. for $C_{25}H_{18}C_{l2}N_2O_4$: C, 62.38; H, 3.77; N, 5.82;. Found: C, 62.40; H, 3.79; N, 5.79.

N-{4-[(6-chloro-4-oxo-4H-chromen-3-ylmethylene) imino]phenyl}-2-(4-chloro-3,5-dimethylphenoxy) acetamide (3g): Yield 57%, mp 175 - 176°C. IR (KBr, cm^{-1}): 3240(NH), 3052(CH_{arom}), 2930(CH_{aliph}), 1654($C=O_{amide}$), 1616($C=O_{pyrone}$), 1604(C=N), 1238 and 1031 (-C-O-C-), 1599 (C=C in aromatic ring), 2987(CH in CH_3). ^{1}H-NMRδ: 2.30(3H, s, CH_3), 4.30(2H, s, CH_2), 6.30-7.24(13H, m, Ar-H, CH=N and H-2), 9.92(1H, s, NH);Anal. Cal. for $C_{26}H_{20}C_{l2}N_2O_4$: C, 63.04; H, 4.07; N, 5.66. Found: C, 63.10; H, 4.09; N, 5.61.

N-{4-[(6-chloro-4-oxo-4H-chromen-3-ylmethylene) imino]phenyl}-2-(4-tert-butylphenoxy) acetamide (3h): Yield 39%, mp 201 - 202°C. IR (KBr, cm^{-1}): 3218(NH), 3048(CH_{arom}), 2929(CH_{aliph}), 1652($C=O_{amide}$), 1617($C=O_{pyrone}$), 1605(C=N), 1230 and 1023 (-C-O-C-), 1599 (C=C in aromatic ring), 2980(CH in CH_3). ^{1}H-NMRδ, 1.22(9H,s, CH_3), 4.29(2H, s, CH_2), 6.32-7.80(13H, m, Ar-H, CH=N and H-2), 9.90(1H, s, NH);Anal. Cal. for $C_{28}H_{25}ClN_2O_4$: C, 68.78; H, 5.15; N, 5.73. Found: C, 68.70; H, 5.27; N, 5.70.

N-{4-[(6-chloro-4-oxo-4H-chromen-3-ylmethylene) imino]phenyl}-2-(4-chlorophenoxy) acetamide (3i): Yield 54%, mp 210 - 211°C. IR (KBr, cm^{-1}): 3236(NH), 3050(CH_{arom}), 2928(CH_{aliph}), 1657($C=O_{amide}$), 1615($C=O_{pyrone}$), 1604(C=N), 1233 and 1022 (-C-O-C-), 1598 (C=C in aromatic ring); ^{1}H-NMRδ: 4.30(2H, s, CH_2), 6.42-7.76(13H, m, Ar-H, CH=N and H-2), 9.97(1H, s, NH);Anal. Cal. for $C_{24}H_{16}C_{l2}N_2O_4$: C, 61.69; H, 3.45; N, 5.99. Found: C, 61.81; H, 3.26; N, 5.95.

N-{4-[(6-chloro-4-oxo-4H-chromen-3-ylmethylene) imino]phenyl}-2-(4-bromophenoxy)acetamide (3j): Yield 50%, mp 216 - 217°C. IR (KBr, cm^{-1}): 3234(NH), 3051(CH_{arom}), 2927(CH_{aliph}), 1654($C=O_{amide}$), 1616($C=O_{pyrone}$), 1604(C=N), 1229 and 1022 (-C-O-C-), 1598 (C=C in aromatic ring); ^{1}H-NMRδ: 4.30(2H, s, CH_2), 6.44-7.79(13H, m, Ar-H, CH=N and H-2), 9.96(1H, s, NH); Anal. Cal. for $C_{24}H_{16}BrClN_2O_4$: C, 56.33; H, 3.15; N, 5.47. Found: C, 56.41; H, 3.16; N, 5.49.

N-{4-[(6-chloro-4-oxo-4H-chromen-3-ylmethylene) imino]phenyl}-2-(4-isopropylphenoxy)acetamide (3k): Yield 46%, mp 235 - 236°C. IR (KBr, cm^{-1}): 3218(NH), 3048(CH_{arom}), 2929(CH_{aliph}), 1652($C=O_{amide}$), 1617($C=O_{pyrone}$), 1605(C=N), 1229 and 1022 (-C-O-C-), 1599 (C=C in aromatic ring), 2980(CH in CH_3). ^{1}H-NMRδ, 1.19(6H,s, CH_3), 3.10(1H,s ,CH), 4.29(2H, s, CH_2), 6.50-7.42(13H, m, Ar-H, CH=N and H-2), 9.78(1H, s, NH). Anal. Cal. for $C_{27}H_{23}ClN_2O_4$ C, 68.28; H, 4.88; N, 5.90; Found: C, 68.26; H, 4.90; N, 5.92.

N-{4-[(6-chloro-4-oxo-4H-chromen-3-ylmethylene) imino]phenyl}-2-(2-methoxy-4- methyl phenoxy) acetamide (3l): Yield 42%, mp 220 - 221°C. IR (KBr, cm^{-1}): 3223(NH), 3040(CH_{arom}), 2927(CH_{aliph}), 1660($C=O_{amide}$), 1618($C=O_{pyrone}$), 1606(C=N), 1230 and 1026 (-C-O-C-), 1599 (C=C in aromatic ring). ^{1}H-NMRδ, 2.12(3H,s,CH3), 4.30(2H, s, CH_2), 6.67-7.52(12H, m, Ar-H, CH=N and H-2), 9.70(1H, s, NH). Anal. Cal. for $C_{26}H_{21}ClN_2O_5$ C, 65.48; H, 4.44; N, 5.87; Found: C, 65.48; H, 4.44; N, 5.87.

N-{4-[(6-chloro-4-oxo-4H-chromen-3-ylmethylene) imino]phenyl}-2-(3,5dimethoxy phenoxy) acetamide (3m): Yield 48%, mp 245 - 246°C. IR (KBr, cm^{-1}): 3230(NH), 3042(CH_{arom}), 2927(CH_{aliph}), 1660($C=O_{amide}$), 1618($C=O_{pyrone}$), 1606(C=N), 1230 and 1026 (-C-O-C-), 1599 (C=C in aromatic ring). ^{1}H-NMRδ, 3.42(6H, s, CH3), 4.31(2H, s, CH_2), 5.56-7.32(12H, m, Ar-H, CH=N and H-2), 9.76(1H, s, NH). Anal. Cal. For $C_{26}H_{21}ClN_2O_6$ C, 63.35; H, 4.29; N, 5.68; Found: C, 63.39; H, 4.30; N, 5.66.

N-{4-[(6-chloro-4-oxo-4H-chromen-3-ylmethylene) imino]phenyl}-2-(2-chloro phenoxy) acetamide (3n): Yield 55%, mp 270 - 271°C. IR (KBr, cm^{-1}): 3235(NH), 3051(CH_{arom}), 2930(CH_{aliph}), 1657($C=O_{amide}$), 1614($C=O_{pyrone}$), 1604(C=N), 1230 and 1026 (-C-O-C-), 1600 (C=C in aromatic ring).^{1}H-NMRδ: 4.32(2H, s, CH_2), 6.58-7.48(13H, m, Ar-H, CH=N and H-2), 9.84(1H, s, NH). Anal. Cal. for $C_{24}H_{16}C_{l2}N_2O_4$ C, 61.69; H, 3.45; N, 5.99; Found: C, 61.71; H, 3.48; N, 5.97.

N-{4-[(6-chloro-4-oxo-4H-chromen-3-ylmethylene) imino]phenyl}-2-(2-chloro,4-nitrophenoxy) acetamide (3o): Yield 60%, mp 280 - 281°C. IR (KBr, cm^{-1}): 3240(NH), 3046(CH_{arom}), 2927(CH_{aliph}), 1660($C=O_{amide}$), 1618($C=O_{pyrone}$), 1606(C=N), 1230 and 1026 (-C-O-C-), 1599 (C=C in aromatic ring). 4.34(2H, s, CH_2), 6.78-8.00(12H, m, Ar-H, CH=N and H-2), 9.92(1H, s, NH). Anal. Cal. For $C_{24}H_{15}Cl_2N_3O_6$ C, 56.27; H, 2.95; N, 8.20; Found: C, 56.30; H, 2.98; N, 8.10.

N-{4-[(6-chloro-4-oxo-4H-chromen-3-ylmethylene) imino]phenyl}-2-(3, 4 dimethoxy phenoxy) acetamide (3p): Yield 35%, mp 258 - 259°C. IR (KBr, cm^{-1}): 3220(NH), 3040(CH_{arom}), 2927(CH_{aliph}), 1660($C=O_{amide}$), 1618($C=O_{pyrone}$), 1606(C=N), 1230 and 1026 (-C-O-C-), 1599 (C=C in aromatic ring). ^{1}H-NMRδ. 3.38 (6H,s, CH_3), 4.29(2H, s, CH_2), 6.10-7.56(12H, m, Ar-H, CH=N and H-2), 9.82(1H, s, NH). Anal. Cal. For $C_{26}H_{21}ClN_2O_6$ C, 63.35; H, 4.29; N, 5.68; Found: C, 63.48; H, 4.39; N, 5.59.

N-{4-[(6-chloro-4-oxo-4H-chromen-3-ylmethylene) imino]phenyl}-2-(2-nitrophenoxy) acetamide (3q): Yield 50%, mp 159 - 160°C. IR, 3240(NH), 3044(CH_{arom}), 2927(CH_{aliph}), 1660($C=O_{amide}$), 1618($C=O_{pyrone}$), 1606(C=N), 1230 and 1026 (-C-O-C-), 1599 (C=C in aromatic ring); ^{1}H-NMRδ, 4.31(2H, s, CH_2), 6.76-7.89(13H, m, Ar-H, CH=N and H-2), 9.40(1H, s, NH). Anal. Cal. For $C_{24}H_{16}ClN_3O_6$ C, 60.32; H, 3.37; N, 8.79; Found: C, 60.40; H, 3.31; N, 8.81.

Antibacterial activity: Antibacterial activity of the compounds, **3a-q** using the Hi-media agar medium was studied against *Staphylococcus aureus* (NCIM NO. 2654), *Bacillus subtilis* (NCIM NO. 2195), *Escherchia coli* (NCIM NO. 2341) and *Pseudomonas aeruginosa* (NCIM NO. 2914) by disc-diffusion method [9]. Agar media was taken in the pre-sterilized petri-dishes and the microorganisms were grown. Each test compounds were dissolved in dimethyl sulphoxide (DMSO) to get a concentration of 10 mg/ml. The disc (6 mm in diameter) was impregnated with 10µl and 5µl of each test solution to get 100 µg/disc and 50 µg/disc respectively, placed on the seeded agar medium and the petri-dishes were incubated at 37^{o}C for 24 hr. Zone of inhibition of each compound in mm was recorded, Ofloxacin (10 µg/disc) was used as standard drug.

Antifungal activity: The newly synthesized compounds (**3a-q**) were screened for their antifungal activities against *Aspergillus niger* (NCIM NO. 618*)* and *Aspergillus flavipes* (NCIM NO. 1209) by filter paper disc technique [9]. The antifungal activity was studied using Sabouraud dextrose agar (SDA) medium (Hi-media), Fluconazole (25µg/disc) was used as standard drug. The concentration of test compounds used was 50 µg/disc and 100 µg/disc. The petridishes were incubated at 22^{o}C for 48 hr and then the zone of inhibition produced by each compound is measured in mm.

RESULTS AND DISCUSSION: Condensation reaction of 6-chloro-4-oxo-4*H*-chromene-3-carboxaldehyde with *p*-phenylenediamine in dry benzene containing 3-4 drops glacial acetic acid gave 3-[(4- aminophenyl) imino) methyl]-6-chloro-4-oxo-4*H*-chromene (**1**). This compound, on condensation with chloroacetylchloride gave N- {4- [(6- chloro- 4- oxo- 4*H*- chromen- 3- ylm ethylene) amino] phenyl}- 2- chloroacetamide **(2).** Reaction of compound **(2)** with some substituted phenol gave desired derivatives **(3a-q).** The purity of the compounds was routinely checked by thin layer chromatography (TLC). Spectroscopic data were recorded by the following instruments. IR: Shimadzu IR-435 spectrophotometer; ^{1}H-NMR: Bruker 250 MHz spectrometer, the elemental analyses were performed using Perkin Elmer EAL 240 spectrometer and all values were within ± 0.4 % of the theoretical values.

The antibacterial activity of the compounds against gram positive bacteria (*S. aureus* and *B. subtilis*) and gram negative bacteria (*E. coli* and *P. aeruginosa*) revealed that the compounds **3-a, 3-d, 3-f, 3-i, 3-j** and **3-k** against *S. aureus*; compouns **3-e, 3-g, 3-k** and **3-o** against *B. subtilis*; compounds **3-a, 3-b, 3-d, 3-e, 3-f, 3-h, 3-i, 3-j, 3-l, 3-n, 3-o** and **3-q** against *E. coli*; and compounds **3-a, 3-b, 3-d, 3-e, 3-i, 3-j, 3-n, 3-o** and **3-q** are having more than 12 mm of zone of inhibition at both 50 and 100 µg/disc. Hence, compounds **3-a, 3-b, 3-d, 3-e, 3-i, 3-j, 3-n, 3-o** and **3-q** are more active against gram negative bacteria while compound **3-k** is most active against both the gram positive strains. Compound **3-p** is least active against gram positive and inactive against gram negative bacteria at the tested doses. Compound **3-m** is inactive against *S. aureus* and *P. aeruginosa* (**Table 2**).

Antifungal activity of the compounds against *A. niger* and *A. flavipes* showed that all the compounds are having antifungal activity against the tested microbes. Compound **3-a**is most active and compound **3-o** is least active against both the strains (**Table 3**).

TABLE 2: ANTIBACTERIAL ACTIVITY OF COMPOUNDS 3a-q

Compounds (µg/disc)		*Zone of inhibition (in mm)			
		Gram positive bacteria		Gram negative bacteria	
		S. aureus	*B. subtilis*	*E. coli*	*P. aeruginosa*
3-a	50	12.67±0.33	9.67±1.20	14.67±0.88	16.33±0.67
	100	18.33±0.33	13.67±0.33	19.33±0.67	22.67±0.33
3-b	50	-	-	13.67±0.33	12.0±0.57
	100	11.33±0.88	9.67±0.33	19.67±1.20	18.33±0.33
3-c	50	-	12.33±0.88	10.33±0.67	-
	100	10.33±0.88	14.33±0.33	11.0±1.15	10.67±0.88
3-d	50	14.67±0.67	11.33±.33	16.33±0.88	14.67±0.33
	100	16.33±0.33	15.67±1.45	22.67±0.88	20.33±1.20

3-e	50	-	12.67±0.33	13.0±0.57	13.67±0.88
	100	11.33±1.20	14.0±1.0	16.33±0.67	15.33±.33
3-f	50	13.67±0.67	9.0±0.57	13.0±0.67	11.67±0.88
	100	18.0±0.57	12.33±0.33	16.67±0.33	16.0±0.57
3-g	50	11.33±1.20	12.0±1.15	11.0±1.0	11.0±0.57
	100	14.33±0.88	15.67±0.33	17.0±1.15	15.67±0.33
3-h	50	11.67±0.33	11.67±0.33	12.33±0.67	-
	100	13.0±0.57	12.67±1.45	15.33±1.45	12.67±0.33
3-i	50	14.67±0.33	10.0±1.15	16.33±1.20	13.33±0.88
	100	18.33±0.88	12.67±0.88	22.23±0.33	19.67±0.88
3-j	50	12.67±0.33	9.67±0.88	14.33±0.33	12.67±0.33
	100	16.33±0.33	14.0±1.15	20.33±0.33	17.0±1.0
3-k	50	13.0±1.0	12.0±0.57	11.33±0.67	10.67±1.33
	100	17.33±0.88	15.0±0.57	15.0±0.00	15.33±0.88
3-l	50	-	10.0±1.0	13.67±0.33	-
	100	9.33±0.33	13.67±0.33	15.67±0.33	10.67±0.33
3-m	50	-	9.67±0.33	-	-
	100	-	11.67±0.88	9.67±0.67	-
3-n	50	11.0±0.57	10.0±1.0	16.0±0.57	12.67±0.33
	100	16.33±0.67	12.0±0.57	21.0±1.15	16.0±0.57
3-o	50	9.67±0.67	15.33±0.67	16.0±0.57	13.33±0.67
	100	11.0±1.0	20.67±0.88	22.33±0.88	18.67±0.33
3-p	50	-	-	-	-
	100	9.33±1.33	9.67±0.33	-	-
3-q	50	-	11.66±0.33	13.33±0.67	13.67±1.20
	100	9.67±0.33	14.0±1.0	17.67±0.33	15.67±0.33
Ofloxacin	10	25.33±0.33	23.0±0.0	24.33±0.33	26.00±0.0

*****Values are mean ± SEM of three readings

TABLE 3: ANTIFUNGAL ACTIVITY OF COMPOUNDS 3a-q

Compounds (µg/disc)		*Zone of inhibition (in mm)	
		Fungal strains	
		A. flavipes	*A. niger*
3-a	50	20.67±0.33	25.67±0.33
	100	30.67±0.33	32.67±0.33
3-b	50	17.33±0.33	20.33±0.67
	100	25.33±0.33	27.33±0.33
3-c	50	12.67±0.88	13.67±1.20
	100	15.33±0.67	18.33±0.67
3-d	50	13.67±0.88	12.67±0.33
	100	23.67±0.88	20.00±1.00
3-e	50	13.33±0.88	19.33±0.67
	100	18.0±1.0	29.67±0.88
3-f	50	10.33±0.88	16.0±0.57
	100	15.67±0.33	27.0±1.00
3-g	50	11.33±0.67	12.57±0.33
	100	12.33±0.33	14.67±0.33
3-h	50	13.33±0.33	14.00±0.57
	100	15.67±0.33	24.0±1.00
3-i	50	-	13.67±0.88
	100	18.0±1.0	20.33±0.67
3-j	50	17.67±1.20	13.33±0.88
	100	25.0±1.0	22.33±0.33
3-k	50	16.67±0.33	14.67±0.33
	100	24.33±1.20	21.33±0.88
3-l	50	15.67±0.33	11.33±0.67
	100	21.33±0.67	18.0±0.57
3-m	50	10.33±0.33	11.33±1.20
	100	10.33±0.67	16.33±1.20
3-n	50	14.33±0.88	12.0±0.57
	100	16.33±0.33	16.0±1.0
3-o	50	-	-
	100	8.33±0.88	9.33±0.88
3-p	50	15.0±0.57	15.33±0.33
	100	21.0±0.57	20.67±0.67
3-q	50	15.0±0.57	13.67±1.20
	100	20.67±0.67	21.67±0.88
Fuconazole	10	33.33±0.33	35.33±0.33

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