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Antimicrobial Activity of Flavone Analogues

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Abstract

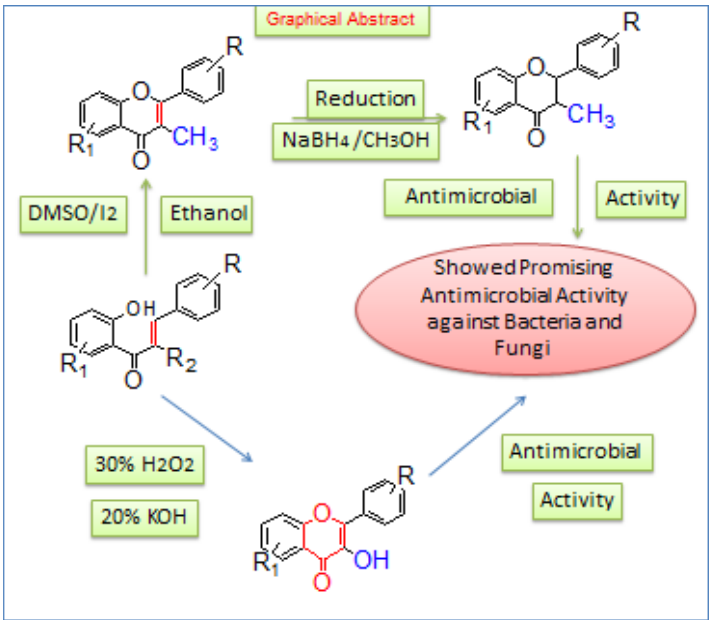
Background: Most of the available antimicrobial drugs have developed resistance; some of them suffer from severe toxicity, side effects. So, there is a need to discover novel compound(s) which should not only be potent, but also less toxic and cost effective.

Objectives: The aim of the study is to develop new synthetic antimicrobial agents (Anti-bacterial and anti-fungal) such as 3-substituted flavone/flavanone derivatives, which should be significantly potent with low toxicity.

Method: An attempt was made to synthesize a newer series of 3-methyl flavanone derivatives together with the synthesis of a series of 3-hydroxyl flavone analogues. The structures of the test compounds were elucidated and established by UV, IR, H-NMR[1], C-NMR[13] and mass spectrometry. The synthesized compounds were subjected for *in vitro* antimicrobial screening using cup plate methods, followed by the determination of zone of inhibitions.

Results: Two series (each 10) of 3-methyl flavanone and 3-hydroxy flavone derivatives were synthesized. The structures of the test compounds were characterized and established by various spectroscopic methods. The synthesized compounds were screened for *in vitro* antibacterial and antifungal activity against different strains (3-Gram positive, 3-Gram negative and 2-fungal strains).

Conclusion: Some of the 3-hydroxyl flavones derivatives (1b, 3b, 4b, and 5b) and 3-methyl flavanone derivatives (3a, 1a, 2a and 4a) were found to elicit potent antimicrobial activity. The study revealed that 3-hydroxy flavone derivatives were found to be most active against Gram negative, while 3-methyl flavanone derivatives were active against Gram positive bacteria.



Keywords: Antibacterial; Antifungal; 3-Methyl flavanone; 3-Hydroxy flavone; 2'-Hdroxypropiophenones; 2'-Hydroxyacetophenone

Introduction

Flavonoids are a group of natural compounds having a benzo-pyrone ring, and over 4,000 flavonoid compounds have been characterized and classified according to chemical structure [1]. Available reports tend to show that secondary metabolites of phenolic nature, including flavonoids are responsible for the variety of pharmacological activities [2-4]. Their activities are structure dependent. The chemical nature of flavonoids

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depends on their structural class, degree of hydroxylation, reduction, other substitutions, conjugations, and degree of polymerization [5]. Flavonoids are widely present in the plant kingdom exhibiting a broad range of biological activities, including antibacterial, antifungal, antiviral, anti-allergic, anti-inflammatory, and anti-proliferative and antioxidant activities [6-9]. It has been reported that the intensity of the antimicrobial activity of a flavonoid strongly depends on its chemical structure, which is particularly influenced by the number and position of various functional groups such as, hydroxyl, methoxy, halogens, nitro, methyl, cyano groups attached to the two aromatic rings (A and B) [10-13]. The third ring C is linked through a three carbon chain, mostly organized as an oxygenated heterocyclic ring. A very few reports are available to the substitution pattern in ring C at 3-position. However 3-hydroxy flavones and 3-methyl flavones have been synthesized by many researchers [5,14], but their further reductions at 2,3-position in ring C are rare and yet to be explored. Substitution pattern at 3-position of ring C mainly regulates bioavailability and metabolism [15,16]. Whereas substitution at ring A and B influence biological activity. Flavonoids are well known as antibacterial agents against a wide range of pathogenic microorganism. Due to growing public concern regarding the negative effects of antimicrobial drugs on human health and the environment, there is a demand for novel antimicrobials. Flavonoids, synthesized from different substituted aromatic ketones and aromatic aldehyde have a potential value as antimicrobial agents. The antimicrobial activity of flavonoids has been suggested to be related to their chemical structure, especially at the 3-position by different substitutes besides the number and positions of methoxyl and hydroxyl groups [17,18] at ring A and B. Therefore, the structure–activity relationship of flavonoids is an important area of study coherently related with antimicrobial activity [19-22]. With increasing prevalence of untreatable infections induced by antibiotic resistant bacteria and fungi, flavonoids have attracted much interest because of the potential to be substitutes for antibiotics [23,24]. To further elucidate the structural requirements and SARs of flavonoids in relation to improve antimicrobial activity and to provide new experimental data, the present study probably helps in the utilization of flavonoids as potential antimicrobial agents.

Material and Methods

Chemicals

The chemicals used were of AR grade and LR grade, purchased from Loba Chemicals, Qualigens, NR Chemicals, Lancaster, Sigma, Reachem, S.D Fine Chemicals Ltd., Merck and Hi-Media**.**

Experimental

^{1}H-NMR and ^{13}C-NMR were recorded using TMS as internal standard. In DMSO or $CDCl_3$ with a BRUKER AVNCE II 400 NMR, Spectrometer SAIF, Panjab University, and Chandigarh. The mass spectra were recorded on waters Q-T OF MICROMASS (LC-MS) TOF MS/ES+. Melting points (uncorrected) were determined on Buchi 535 melting point apparatus. Separation of the compounds were done by column chromatography was carried out with Silica gel (60-120 mesh ASTM, E. Merck). Reactions were monitored on aluminum coated thin-layer chromatography (TLC) with UV light (256 nm), iodine, vanillin-sulphuric acid as developing agents. Chemical shifts have been expressed in δ values downfield from TMS. Multiplicity of NMR signals is designated as s (singlet), d (doublet), dd (double doublet), t (triplet), q (quartet), m (multiplet).

General procedure of synthesis of chalcone derivatives

To a solution of 0.01 mole of substituted 2'-Hydroxyacetophenones /2'-Hydroxypropiophenone in 10 ml of 40% KOH and 20 ml of ethyl alcohol, 0.01 mole of substituted benzaldehyde was added and mixture was stirred for 48-72 h. Completion of the reaction was monitored on TLC (20% ethyl acetate in toluene). The coloured solution was poured into crushed ice and acidified with 1N HCl at 24-26°C. The precipitate so obtained was washed with cold water, filtered, dried and recrystallized with absolute alcohol [25].

Synthesis of flavone derivatives

To a suspension of 0.01 ml of chalcone in 50 ml of ethanol was added l0 ml of 20% aqueous sodium hydroxide with stirring, followed by the careful addition of 15 ml of 30% hydrogen peroxide over a period of ½-1 h. The reaction mixture was stirred for 3-5 h at 30°C and completion of the reaction was monitored on TLC (20% Ethyl acetate in toluene) was poured into crushed ice containing 1NHCl. The precipitate was filtered, washed, dried and recrystallized from ethyl acetate [26].

Synthesis of 3-methyl flavone derivatives

To a solution of 0.01 moles of chalcone in 50 ml of dimethyl sulphoxide (DMSO) taken in 100 ml round bottom flask, fitted with reflux condenser was added of 15-20 granules of iodine. The reaction mixture was reflux for 3-4 h and kept for overnight. The precipitate was neutralized with sodium thiosulphate to remove unreacted I_2 washed with water, fitted, dried and recrystallized with absolute alcohol [26,27].

Synthesis of 2,3-dihydro-3-methyl flavanone derivatives

To 0.01 moles of 3-methyl flavone in 100 ml round bottom, the equimolar amount of $NaBH_4$ and 10-15 ml of methanol in the presence of $AlCl_3$ added and the mixture was refluxed for 2-3 h. The resulting solution was cooled to room temperature followed by the addition of ice cold water. The solid separated was filtered, washed with cold water and recrystallized from ethanol. The experiments suggest that the present reductive system initially reduces the conjugated double bond (Figures 1 and 2; Table 1) [28,29].

Biological Activity

Antimicrobial screening by agar diffusion assay

The antibacterial and antifungal activity was screened by agar diffusion method [30,31]. Initially, commercial samples of Ciprofloxacin for bacteria and Griseofulvin for fungi were selected as standards. The synthesized compounds were screened for their antibacterial (3-Gram positive, 3-Gram negative) and antifungal (two fungi strain) activity, both collectively and individually by agar cup-plate method in nutrient agar and Sabouraud Dextrose Agar (SDA) medium respectively. Petri dishes were filled to a depth of 4-5 mm with a nutrient agar and SDA medium that had previously been inoculated with a suitable inoculum of suitable test organisms were taken consisted of a suspension of organisms (Bacteria and Fungi). The temperature of the nutrient agar and SDA medium did not exceed 48-50°C. When it was inoculated and the dishes were kept at a temperature of 37°C. The petri dishes were specially selected with flat bottom and were placed on a level surface so as to ensure that the layer of medium is in uniform thickness. The Petri dishes were allowed to be sterilized at 160-170°C for 30 min before use. Small sterile borer of uniform size was placed approximately having an internal diameter 6-8 mm made of aluminum or stainless steel, four cylindrical cavities were made in the medium with the help of sterile borer. Three cavities for synthesized compounds of different concentrations and one cavity for positive control, i.e., standard drug (Ciprofloxacin) for bacteria and Griseofulvin for fungi)

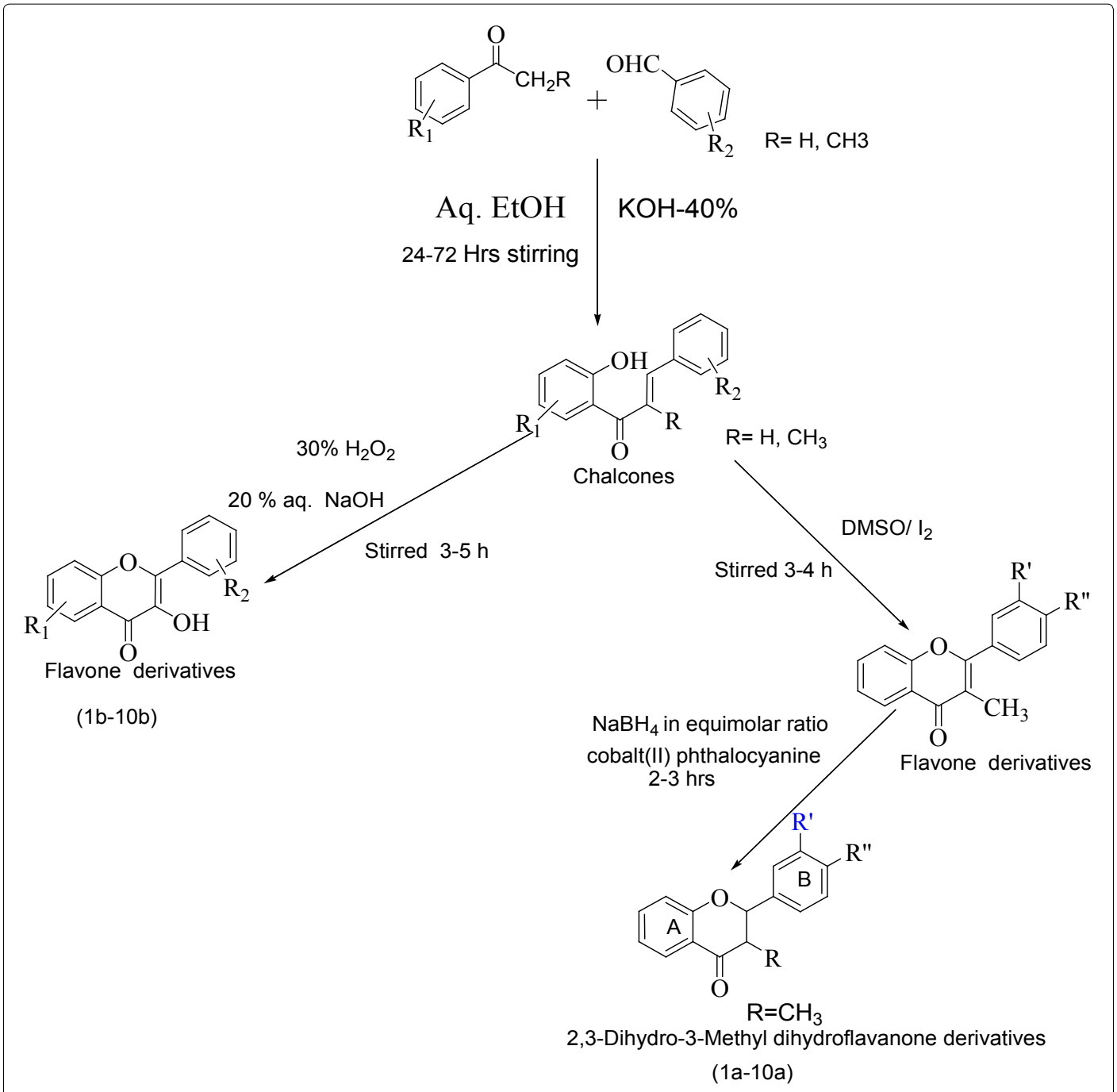

Figure 1: General scheme of synthesis of flavone and 2,3-dihydroflavanone derivatives.

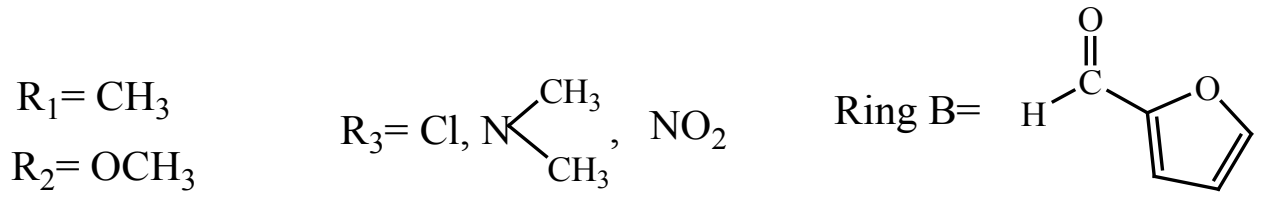

Figure 2: Different substitutions on ring A & B (1b-10b).

Compounds	R'	R"
1a	H	F
2a	H	Cl
3a	H	OH
4a	H	OCH_3
5a	Methylene dioxide	R_2 & R_3
6a	Cl	H
7a	H	CH_3
8a	H	Br
9a	OCH_3	H
10a	H	H

Different substitution pattern on ring B

Table 1: Substitution on ring B of (1a-1b).

were taken. The solutions were incorporated in the cavity or holes by means of a 1 ml syringes delivery. A uniform amount of 0.1 ml of the test (100 µg/ml) and standard solution was added to cavity of the cup. The plates were incubated in Biochemical Oxygen Demand (BOD) incubators at 37°C for 24 h (bacteria); 28°C for 48 h (fungi). The zone of inhibition obtained by different test compounds was compared with that of standard drugs.

Results

Chemistry

The chalcones are generally synthesized by Claisen-Schmidt condensation having aldehyde with no α hydrogen atom and ketone should be having at least one α-hydrogen atom. The chalcones though strongly hydrogen bonded are still having free rotation to yield number of conformers with the result that the activity is reduced. To make it rigid, *Trans* elimination of water molecule leads to the synthesis of different stable 2'-hydroxy chalcone analogues. The Algar-Flynn-Oyamada reaction is a chemical reaction where by a chalcone undergoes an oxidative cyclization to form a flavonols [26,27]. It chosen as our primary method to synthesizes, 3-methyl flavanone and 3-hydroxy flavones, because it is a modular synthetic method using commercially available starting material, which make it an ideal method for combinatorial synthesis. So, aldol-condensation between 2'-hydroxy propiophenone and acetophenone derivative and different aldehyde to give chalcone products. Chalcones were converted to 3-hydroxy flavones by treating with hydrogen peroxide and base in ethanol. Whereas, 3-methylflavones were synthesized in the presence of DMSO/I_2, Further, the 3-methyl flavone was subjected to reduction in the presence of $NaBH_4$/CH_3OH yielded a series of novel 3-methyl flavanone derivatives.

Characterization

The synthesized molecules (20) were characterized by various spectroscopic techniques, such as UV, IR, ^{1}H-NMR, ^{13}C-NMR and Mass spectrometry.

2-(4-fluorophenyl)-2,3-dihydro-3-methylchromen-4-one (1a)

Pale yellow solid, physical data summarized in Table 2.

IR spectra (KBr cm^{-1}): 3041(ArC-H), 2762 (C–H), 1707 (C=O), 1514 (aromatic C=C), 1156 (C-F). ^{1}H-NMR (400MHz, $CDCl_3$ δ, TMS=0): 8.2(1H, d, *J*=7.72 Hz, 5-H), 7.66 (1H, dd, *J*=2.76 Hz, *J*=7.88 Hz, 7-H), 7.65 (2H, m,2'6,'-H), 7.46 (1H, d, *J*=7.84 Hz, 6-H),7.40(1H,d,J=7.32Hz, 8-H), 7.05 (2H, m, 5',3'-H), 4.50 (1H, d, 3-H J=7.01 Hz), 5.12 (1H, d, 2-H *J*=12.36Hz), 2.19(3H, s, 3-CH_3)., ^{13}C NMR (400 MHz, δ, $CDCl_3$, TMS=0): Aromatic Ring-A (156.19, 135.24, 131. 07, 130.03, 125.94, 118.76,) 182.88 (C=O), 125.36 (2-C), 109.78 (3-C), Aromatic Ring B (159.47, 128.45, 128.03, 116.68, 115.50,) 76.58 (5-C), 42.45(4-C), 25-3CH_3, TOF MS ES+ m/z) 257.

2-(4-chlorophenyl)-2,3-dihydro-3-methylchromen-4-one (2a)

Light yellow solid, the physical data summarized in Table 2.

IR Spectra (KBr cm^{-1}): 3052 (ArC-H), 2951 (C–H), 1700 (C=O), 1495 (aromatic C=C), 758 (C-Cl). ^{1}H-NMR (400MHz, $CDCl_3$δ, TMS=0): 8.26(1H, d, *J*=8.62 Hz, 5-H), 8.23 (1H, d, *J*=8.62 Hz,7-H), 7.74 (2H, m,2',6'-H), 7.60 (1H, dd, *J*=8.52 Hz, 6-H), 7.52(1H, d,J=8.44 Hz, 8-H), 7.54 (2H, m, 5',3'-H), 4.55 (1H, d, 3-H J=7.01 Hz), 5.23 (1H, d, 2-H *J*=12.36Hz), 2.1(3H, s, 2-CH_3), ^{13}C NMR (400 MHz, δ, $CDCl_3$, TMS=0): Aromatic Ring-A (157.19, 135.04, 132. 07, 129.03, 123.94, 116.16,) 181.88 (C=O), 126.36 (2-C), 113.78 (3-C), Aromatic Ring B (139.47, 128.45, 128.03, 127.13, 126.68, 125.50,) 20-3CH_3, TOF MS ES+ m/z) 272.5.

2,3-dihydro-2-(4-hydroxypenyl)-3-methylchromen-4-one (3a)

Dark brown solid, physical data is summarized in Table 2.

IR Spectra (KBr cm^{-1}): 3570 (Ar-OH), 3060 (ArC-H), 2870 (C–H), 1715 (C=O), 1512 (aromatic C=C), ^{1}H-NMR (400MHz, $CDCl_3$, δ, TMS=0): 8.12(1H, d, *J*=7.75 Hz, 5-H), 7.60 (1H, d, *J*=7.52 Hz, 7-H), 7.50 (2H, m, 6',2'-H), 7.21 (1H, dd, *J*=7.90 Hz, 6-H), 6.99 (2H, m, 5',3'-H), 6.8 0(1H, d, J=7.75 Hz, 8-H), 4.87 (1H, d, 3-H J=7.67 Hz), 5.45 (1H, d, 2-H *J*=12.36Hz), 1.9 (3H, s, 2-CH_3). ^{13}C NMR (400 MHz, δ, $CDCl_3$, TMS=0): Aromatic Ring-A (156.19, 135.24, 131. 24, 130.03, 122.94, 115.06,) 183.88 (C=O), 125.36 (2-C), 115.78 (3-C), Aromatic Ring B (152.47, 126.45, 125.03, 123.34, 117.13, 116.68,) 10-3CH_3, TOF MS ES+ m/z) 255.5.

2,3-dihydro-2-(3-hydroxy-4-methoxypenyl)-3-methylchromen-4-one (4a)

Yellow solid, physical data summarized in Table 2.

IR spectra (KBr cm^{-1}): 3074(ArC-H), 2851 (C-H), 1685 (C=O), 1514 (aromatic C=C), 1182 (C-O).^{1}H-NMR (400MHz, $CDCl_3$ δ, TMS=0): 7.94(1H, d, *J*=9.56 Hz, 5-H), 7.51 (1H, dd, J=8.64Hz, 2.8Hz,7-H), 7.47(1H, dd, J=7.45Hz,J=2.8Hz, 6-H), 7.07 (1H,d, J=8.2Hz, 8-H), 7.02 (1H, d,J=8.45Hz, 6' -H), 6.98(1H,d, J=1.96Hz, 2'-H), 6.91(1H,d, J=7.88Hz, 5'H), 5.02(1H, s, 3'-OH) Exchangeable with D_2O, 4.30 (1H, d, 3-H J=7.67 Hz), 5.56 (1H, d, 2-H *J*=12.36Hz), 3.92(3H, s, 4'-OCH_3), 2.19(3H, s, 3-CH_3). ^{13}C NMR (400 MHz, δ, $CDCl_3$, TMS=0): Aromatic Ring-A (156.29, 135.24, 132.24, 129.03, 123.94, 116.06,) 182.88 (C=O), 145.36 (2-C), 112.78 (3-C), Aromatic Ring B (155.47, 128.45, 128.03, 124.34, 115.13, 116.68,), 60.5 – OCH3, (10.09 -3 CH_3), TOF MS ES+ m/z) 287.5.

2-(benzo[d][1,3]dioxal-6-yl)-2,3-dihydro-3-methylchromene-4-one (5a)

Yellow solid, physical data summarized in Table 2.

IR Spectra (KBr cm^{-1}): 3074 (ArC-H), 2887 (C-H), 1682 (C=O), 1490 (aromatic C=C), 1249 (C-O). ^{1}H-NMR (400MHz, $CDCl_3$, δ, TMS=0): 8.23(1H, d, *J*=8.32 Hz, 5-H), 7.69(1H, d, *J*=7.08 Hz, 7-H), 7.56(1H, dd, *J*=8.4 Hz, *J*=8.53 Hz, 6-H), 7.42 (1H, d, J=6.89 Hz. 8-H), 7.38 (1H,d, J=7.00 Hz.2'-H), 6.96 (1H, d, *J*=8.24Hz, 5'-H), 6.71(1H,d, J=7.56Hz,6'-H), 6.0(2H, s, 4"-CH2). 4.40 (1H, d, 3-H J=7.80 Hz), 5.60 (1H, d, 2-H *J*=12.56Hz), 1.8 (3H, s, 3-CH_3). ^{13}C NMR (400 MHz, δ, $CDCl_3$, TMS=0): Aromatic Ring-A (157.29, 133.24, 132.24, 128.03, 122.94, 115.06,) 183.88 (C=O), 155.36 (2-C), 110.78 (3-C), Aromatic Ring B (149.47, 148.45, 126.03, 120.34, 116.13, 112.68, 107,23), (9.09 -3

Code	Molecular Formula	Molecular Weight	(%) Yield	Melting Point (°C)	λ_{max} nm	R_f Value	Elemental Analysis Calculated (%)				
							C	H	O	N	Cl/F
1a	$C_{16}H_{13}FO_2$	256.02	73	95-100	341	0.73	77.20	5.27	13.06		7.90
2a	$C_{16}H_{13}ClO_2$	272.71	80	170-175	351	0.62	69.67	4.93	12.60	-	12.00
3a	$C_{16}H_{14}O_3$	254.08	82	125-130	348	0.71	77.42	5.23	20.04	-	-
4a	$C_{17}H_{16}O_3$	268.29	90	90-95	343	0.57	77.44	5.50	19.56	-	-
5a	$C_{17}H_{14}O_4$	282.27	70	110-115	308	0.65	73.48	5.66	21.14	-	-
6a	$C_{16}H_{13}ClO_2$	272.04	80	165-170	328	0.56	71.12	5.00	12.98	-	13.90-
7a	$C_{17}H_{16}O_2$	252.29	90	102-105	336	0.58	82.20	6..10	13.25		-
8a	$C_{16}H_{13}BrO_2$	315.99	70	173-177	344	0.87	61.03	4.57	11.24	-	26.19(Br)
9a	$C_{17}H_{16}O_3$	268.29	90	110-114	345	0.55	77.44	5.50	19.56	-	-
10a	$C_{16}H_{12}O_2$	238.27	80	98-112	310	0.66	80.12	5.94	14.25	-	-

Physical characterizations of 3-methyl flavanone derivatives (TLC Solvent Used: Toluene: Ethyl Acetate 8:2)

Table 2: The physical parameters such as, λ_{max}, and Rf value were determined for the compounds (1a-10a) and summarized in Table 2

CH_3), TOF MS ES+ m/z) 283.5.

2-(2-chlorophenyl)-2,3-dihydro-3-methylchromen-4-one (6a)

Light yellow solid, the physical data summarized in Table 2.

IR Spectra (KBr cm^{-1}): 3050 (ArC-H), 2805 (C–H), 1645 (C=O), 1510 (aromatic C=C), 745 (C-Cl).^{1}H-NMR (400MHz, $CDCl_3$,δ, TMS=0): 8.2 (1H, d, *J*=8.64 Hz, 5-H), 7.8 (1H, d, *J*=8.24 Hz, 7-H), 7.44 (1H, d, *J*=7.6 Hz, 3'-H), 7.23 (1H, d *J*=7.96 Hz, 6'-H), 7.01 (1H, dd, *J*=2.2 Hz, *J*=7.8 Hz, 4'-H), 6.92 (1H, dd, *J*=2.0 Hz, *J*=7.32 Hz, 5'-H), 6.90(1H,d,J=7.89 Hz, 6-H), 6.88 (1H, d, J=7.50 Hz, 8-H), 4.50 (1H, d, 3-H J=7.80 Hz), 5.65 (1H, d, 2-H *J*=12.56Hz), 1.9 (3H, s, 2-CH_3). ^{13}C NMR (400 MHz, δ, $CDCl_3$, TMS=0): Aromatic Ring-A (156.29, 132.24, 131.24, 129.03, 123.94, 116.16,) 182.88 (C=O), 158.26 (2-C), 112.43 (3-C), Aromatic Ring B (136.23, 132.56., 131.89, 129.34, 126.13, 124.68,), (8.23 -3 CH_3), TOF MS ES+ m/z) 273.5.

2,3-dihydro-3-methyl-2-*p*-tolylchromen-4-one (7a)

White yellow solid, the physical data summarized in Table 2.

IR spectra (KBr cm^{-1}): 3080 (ArC-H), 2910 (C-H), 1690 (C=O), 1520 (aromatic C=C), 1182 (C-O). ^{1}H-NMR (400MHz, $CDCl_3$, δ, TMS=0): 8.21(1H, d, *J*=7.72 Hz, 5-H), 7.98 (1H, dd, J=8.64Hz, 7.04Hz,7-H),7.82 (2H, m, 2',6'-H), 7.75 (2H, m, 3', 5', -H), 7.38 (1H,d, J=7.2Hz, 6-H), 7.05(1H,d, J=7.8Hz, 8-H), 4.50 (1H, d, 3-H J=7.80 Hz), 5.65 (1H, d, 2-H *J*=12.56Hz), 2.06 (3H, s, 4'CH_3) 1.9. (3H, s, 3-CH_3) ^{13}C NMR (400 MHz, δ, $CDCl_3$, TMS=0): Aromatic Ring-A (157.29, 135.26, 133.24, 130.03, 125.94, 118.24,) 183.88 (C=O), 159.26 (2-C), 111.43 (3-C), Aromatic Ring B (138.23, 130.56., 129.89, 127.34, 126.13, 125.68,), (30.67-4'CH_3) (10.33 -3 CH_3), TOF MS ES+ m/z) 253.5.

2-(2-bromophenyl)-2,3-dihydro-3-methylchromen-4-one (8a)

Light yellow solid, the physical data summarized in Table 2.

IR spectra (KBr cm^{-1}): 3072 (ArC-H), 2875 (C-H), 1663 (C=O), 1525 (Ar C=C), 1182 (C-O). 612 (C-Br) ^{1}H-NMR (400MHz, $CDCl_3$ δ, TMS=0): 7.92(1H, d, *J*=7.70 Hz, 5-H), 7.82 (1H, dd, J=8.04Hz, 7-H),7.82 (2H, m, 2',6'-H), 7.75 (2H, m, 3', 5', -H), 7.38 (1H,d, J=7.2Hz, 6-H), 7.05(1H,d, J=7.8Hz, 8-H), 4.50 (1H, d, 3-H J=7.80 Hz), 5.65 (1H, d, 2-H *J*=12.56Hz), 2.00 (3H, s, 3-CH_3). ^{13}C NMR (400 MHz, δ, $CDCl_3$, TMS=0): Aromatic Ring-A (156.29, 134.35, 132.79, 129.03, 125.94, 118.24,) 182.88 (C=O), 155.26 (2-C), 110.43 (3-C), Aromatic Ring B (130.83, 130.56., 129.29, 127.24, 127.13, 123.08,), (12.33 -3 CH_3), TOF MS ES+ m/z) 317.5.

2,3-dihydro-2-(4-methoxypenyl)-3-methylchromen-4-one (9a)

Yellow-white solid, physical data summarized in Table 2.

IR spectra (KBr cm^{-1}): 3072 (ArC-H), 2850 (C-H), 16890 (C=O), 1524 (Ar C=C), 1180(C-O). ^{1}H-NMR (400MHz, $CDCl_3$ δ, TMS=0): 8.32(1H, d, *J*=8.32 Hz, 5-H), 7.65 (1H, dd, J=7.08Hz, J=2.1Hz, 7-H), 7.56 (2H, m, 2',6'-H), 7.44 (2H,m,3',5'-H), 6.96 (1H, d, J=7.04Hz, 6-H), 6.71 (1H,d, J=7.8Hz, 8-H), 4.50 (1H, d, 3-H J=7.80 Hz), 5.65 (1H, d, 2-H *J*=12.56Hz), 3.92(3H, s, 4'-OCH_3), 2.1(3H, s, 3-CH_3). ^{13}C NMR (400 MHz, δ, $CDCl_3$, TMS=0): Aromatic Ring-A (156.29, 135.24, 132.24, 129.03, 123.94, 116.06,) 182.88 (C=O), 145.36 (2-C), 112.78 (3-C), Aromatic Ring B (159.47, 131.45, 129.03, 118.34, 115.13, 110.68,), 59.5 –OCH3, (9.09 -3 CH_3), TOF MS ES+ m/z) 269.5.

2,3-dihydro-3-methyl-2-phenylchromen-4-one (10a)

Yellow solid, physical data is summarized in Table 2.

IR spectra (KBr, cm^{-1}): 3085(ArC-H), 2920 (C-H), 1690 (C=O), 1520 (ArC=C), 1182 (C-O). ^{1}H-NMR (400MHz, $CDCl_3$ δ, TMS=0): 7.20(1H, d, *J*=7.70Hz,5-H), 7.09 (1H, dd, J=8.60Hz, 7.04Hz,7-H),7.00 (2H, m, 2',6'-H), 6.98 (2H, m, 3', 5', -H), 6.90 (1H,d,J=7.80Hz, 4'-H), 6.88 (1H,d, J=7.21Hz, 6-H), 6.75(1H,d, J=7.82 Hz, 8-H), 4.50 (1H, d, 3-H J=7.80 Hz), 5.65 (1H, d, 2-H *J*=12.56Hz), 1.98 (3H, s, 3-CH_3).). ^{13}C NMR (400 MHz, δ, $CDCl_3$, TMS=0): Aromatic Ring-A (159.29, 134.24, 132.27, 129.83, 122.94, 117.06,) 183.88 (C=O), 157.36 (2-C), 110.78 (3-C), Aromatic Ring B (160.47, 130.45, 130.03, 128.34, 128.13, 127.68,), (9.09 -3 CH_3), TOF MS ES+ m/z) 239.5.

2-(4-(dimethylamino)phenyl)-3-hydroxy-4*H*-chromen-4-one (1b)

Pale yellow solid, physical data summarized in Table 3.

IR (KBr, cm^{-1}): 3355 (Ar-OH), 1556 (Ar C=C str), 1689 (C=5O str), 1327 (C-O str), 2895, (C-H str), 3027(Ar-H), 1318, (C-N).^{1}H NMR(400 MHz, DMSO δ, TMS=0): δ=2.97 (6H, s, 4'-Dimethyl aimno), 6.74 (2H, m, 3'5'-H) 6.97 (1H, d, 8-H, J=8.23 Hz), 7.39 (1H, dd, 6-H,J=7.76 Hz), 7.44 (2H, m, 2',6'-H), 7.51 (1H,dd, 7-H *J*=8.24 Hz), 7.59.(1H, d, 5-H, *J*=8.42 Hz), 12.69 (1H,s, 3-OH, Exchangeable with D_2O).^{13}CNMR (400 MHz, δ, $CDCl_3$, TMS=0): Aromatic Ring-A (152.24, 132.12, 131. 87, 124.43, 122.49, 117.10) 178.88 (C=O), 148.32 (2-C), 138.35 (3-C), Aromatic Ring B (153.44, 147.89, 127.35, 127.36, 118.68, 118.68,) 40.16, 40.17, N-$(CH_3)_2$. TOF MS ES+ (m/z)=282.

2-(4-chlorophenyl)-3-hydroxy-4*H*-chromen-4-one (2b)

Brownish solid, physical data summarized in Table 3.

IR (KBr, cm^{-1}): 3388 (Ar-OH), 1528 (Ar C=C str), 1685 (C=O str), 1333 (C-O str), 3061 (Ar-H), 776 (C-Cl).^{1}H NMR(400MHz, DMSO δ, TMS=0): δ=6.94(1H, d,8-H, J=8.04 Hz),7.03(1H, dd,6 -H, J=3.05 Hz), 7.19 (2H, m, 3',5'-H,), 7.25 (2H, m, 2',6'-H,), 7.35 (1H, dd, 7-H,

S. No	Compd Code	Molecular Formula	Molecular Weight	(%) Yield	Melting Point (°C)	λ_{max} nm	R_f Value	Elemental Analysis Calculated (%)				
								C	H	O	N	Cl
1.	1c	$C_{17}H_{15}NO_3$	281.32	88.24	134-136	341	0.63	72.58	5.37	17.06	4.98	-
2.	2c	$C_{15}H_9ClO_3$	272.68	88.23	105-107	351	0.48	696.07	3.33	17.60	-	13.00
3.	3c	$C_{13}H_8O_4$	228.20	91.00	110-112	348	0.59	68.42	3.53	28.04	-	-
4.	4c	$C_{18}H_{17}NO_4$	311.33	86.00	168-170	343	0.56	69.44	5.50	20.56	4.50	-
5.	5c	$C_{16}H_{11}ClO_4$	302.70	83.00	107-109	308	0.44	63.48	3.66	21.14	-	11.71
6.	6c	$C_{14}H_{10}O_5$	258.22	90.32	120-122	328	0.50	65.12	3.90	30.98	-	-
7.	7c	$C_{18}H_{17}NO_3$	295.33	79.00	180-182	336	0.57	73.20	5..80	16.25	4.74	-
8.	8c	$C_{16}H_{11}ClO_3$	286.70	70.00	112-114	344	0.42	67.03	3.87	16.74	-	12.37
9.	9c	$C_{14}H_{10}O_4$	242.22	79.00	147-149	345	0.49	69.42	4.16	26.42	-	-
10	10c	$C_{15}H_9NO_5$	283.05	85	135-139	310	0.67	64.12	4.14	29.25	5.28	-

Physical characterization of 3-hydroxy flavone derivatives (TLC Solvent Used: Toluene: Ethyl Acetate 8:2)

Table 3: The physical parameters such as, λ_{max}, and Rf value were determined for the compounds (1b-10b) and summarized in Table 3.

J=7.68Hz), 7.62(1H,d, 5-H *J*=8.00 Hz), 12.16 (1H,s, 3-OH, Exchangeable with D_2O), ^{13}C NMR (400 MHz, δ, $CDCl_3$, TMS=0): Aromatic Ring-A (153.23, 132.56, 131.81, 125.17, 121.49, 115.37), 187.49 (C=O), 153.36 (2-C), 145.59 (3-C), Aromatic Ring B (146.09, 138.79, 135.20, 135.91, 126.67, 126.37) TOF MS ES+ (m/z)=273.

2-(furan-2-yl)-3-hydroxy-4*H*-chromen-4-one (3b)

Brownish yellow solid, physical data summarized in Table 3.

IR (KBr, cm^{-1}): 3388 (Ar-OH), 1527(Ar C=C str), 1685 (C=O str), 1352 (C-O str), 3071 (Ar-H).^1H NMR(400MHz, DMSO δ, TMS=0): δ=6.77(1H,m, 4'-H), 6.99(1H, d,8-H, J=8.04 Hz),7.09 (1H, d, 3'-H, J=8.5Hz) 7.20 (1H, dd, 6-H, J=4.04Hz), 7.38 (1H, dd, 7-H, J=10.60Hz), 7.69(1H,d, 5-H *J*=8.20 Hz), 7.70(1H, d,5'-H, J=5.08 Hz). 11.90 (1H,s, 3-OH, Exchangeable with D_2O), ^{13}C NMR (400 MHz, δ, $CDCl_3$, TMS=0): Aromatic Ring-A (152.85, 133.03, 130.31, 129.54, 119.58, 116.31), 187.38 (C=O), 155.67 (3-C), 140.59 (2-C), Aromatic Ring B (15.416, 142.68, 123.86, 112.73), TOF MS ES+ (m/z)=227.5.

2-(4-(dimethylamino) phenyl)-3-hydroxy-7-methoxy-4*H*-chromen-4-one (4b)

Yellow white solid, physical data summarized in Table 3.

IR (KBr, cm^{-1}): 3356 (Ar-OH), 1570 (Ar C=C str), 1688 (C=O str), 1340 (C-O str), 2930,(H str), 3025 (Ar-H),1247 (O-C), 1313, (C-N). ^1H NMR(400MHz, DMSO δ, TMS=0): δ=3.06(6H, s,4'-Dimethyl aimno), 3.89 (3H,s, 7-H), 6.95 (1H, s, 8-H), 6.98 (1H, d, 6-H, J=7.76 Hz), 7.05 (2H, m, 3'5'-H) 7.24 (2H, m, 2',6'-H), 7.57 (1H, d, 5-H, *J*=8.00 Hz), 12.00(1H,s, 3-OH, Exchangeable with water). ^{13}C NMR (400 MHz, δ, $CDCl_3$, TMS=0): Aromatic Ring-A (157.77, 152.34, 132. 43, 122.12, 110.34, 108.30, 60.09) 188.73 (C=O), 153.36 (2-C), 144.78 (3-C), Aromatic Ring B (145.34, 134.75, 127.23, 127.33, 115.68, 115.50,) 40.01, 39.98, N-$(CH3)_2$. TOF MS ES+ (m/z)=312.

2-(4-chlorophenyl)-3-hydroxy-7-methoxy-4*H*-chromen-4-one (5b)

Brownish solid, physical data summarized in Table 3.

IR (KBr, cm^{-1}): 3356 (Ar-OH), 1527 (Ar C=C str), 1689 (C=O str), 1328(C-O str), 2939, (C-H str), 3083 (Ar-H), 1245(O-C), 777 (C-Cl).^1H NMR(400MHz, DMSO δ, TMS=0): δ=3.88(3H,s, 6.98 (1H, s, 8-H,),7.03(1H, d, 6 -H, J=8.04Hz), 7.26 (2H, m, 3',5'-H,), 7.35 (2H, m, 2',6'-H,), 7.68 (1H,d, 5-H *J*=8.00 Hz), 12.11 (1H,s, 3-OH, Exchangeable with water). ^{13}C NMR (400 MHz, δ, $CDCl_3$, TMS=0): Aromatic Ring-A (160.94, 153.82, 132.88, 127.89, 118.60, 117.13, 59.89), 188.38 (C=O), 141.36 (3-C), 155.59 (2-C), Aromatic Ring B (160.43, 145.67, 131.66, 131.56, 124.37, 124.29,) TOF MS ES+ (m/z)=303.

2-(furan-2-yl)-3-hydroxy-7-methoxy-4*H*-chromen-4-one (6b)

Brownish yellow solid, physical data summarized in Table 3.

IR (KBr, cm^{-1}): 3365 (Ar-OH), 1521 (Ar C=C str), 1659 (C=O str), 1309 (C-O str), 2892, (C-H str), 3090 (Ar-H), 7625 (C-Cl).^1H NMR(400 MHz, δ, $CDCl_3$, TMS=0): 3.82 (3H,s, 7-OCH_3), 5.88 (1H, s,3-OH) Exchangeable with D_2O, 6.58(1H, s,8-H), 6.75(1H, dd, 4'-H,J=3.00Hz), 6.83(1H, d,6-H,J=8.60 Hz), 7.61(IH, d, 3-H,J=8.0Hz), 8.06 (1H,d,5-H,J=8.84 Hz), ^{13}C NMR (400 MHz, δ, $CDCl_3$, TMS=0): Aromatic Ring-A (164.35, 151.23, 135.69, 119.36, 114.26, 108.70, 60.35), 188.87 (C=O), 135.33 (3-C), 145.47 (2-C), Aromatic Ring B (148.36, 103.09, 112.36, 111.16,) GC-MS, m/e M^{+1}=259.5.

2-(4-(dimethylamino)phenyl)-3-hydroxy-6-methyl-4*H*-chromen-4-one (7b)

Yellow white solid, physical data summarized in Table 3.

IR (KBr, cm^{-1}): 3405 (Ar-OH), 1533(Ar C=C str), 1690 (C=5O str), 1360 (C-O str), 2932, (C-H str), 3033 (Ar-H), 1319 (C-N) ^1H NMR(400MHz, DMSO δ, TMS=0): δ=2.44(3H,s,6-CH_3), 3.08 (6H, s,4'-Dimethyl aimno), 6.70 (2H,m,3'5'-H), 6.94 (1H, d, 8-H, J=8.20 Hz), 7.45 (1H, d, 7-H, J=7.80 Hz), 7.48 (2H, m, 2',6'-H), 7.59 (1H, d, 5-H, *J*=8.40 Hz), 12.7 (1H,s, 3-OH, Exchangeable with D_2O), ^{13}C NMR (400 MHz, δ, $CDCl_3$, TMS=0): Aromatic Ring-A (152.35, 151.38, 128.20, 122.34, 116.05, 110.47, 30.57) 187.31 (C=O), 153.36 (2-C), 147.78 (3-C), Aromatic Ring B (151.41, 143.36, 123.24, 123.23, 116.68, 116.90,) 41.56, 41.49, N-$(CH3)_2$. TOF MS ES+ (m/z)=296.

2-(4-chlorophenyl)-3-hydroxy-6-methyl-4*H*-chromen-4-one (8b)

Brownish solid, physical data summarized in Table 3.

IR (KBr, cm^{-1}): 3395 (Ar-OH), 1565 (Ar C=C str), 1688 (C=O str), 1324 (C-O str), 2960, (C-H str), 3070 (Ar-H), 776 (C-Cl). ^1H NMR(400 MHz, δ, $CDCl_3$, TMS=0): 2.64 (3H,s, 6-CH_3), 6.05 (1H, d, 8-H,J=8.02Hz), 6.92(1H, d,7-H, J=8.00 Hz), 7.18(2H, m, 3',5'-H), 7.31(2H, m. 2',6'-H), 7.65(IH, d, 5-H,J=8.04Hz), 12.09 (1H,s,3-OH, Exchangeable with D_2O).^{13}C NMR (400 MHz, δ, $CDCl_3$, TMS=0): Aromatic Ring-A (154.09, 133.24, 131.37, 130.77, 126.31, 116.34, 108.47, 26.78), 188.44 (C=O), 144.67 (3-C), 148.34 (2-C), Aromatic Ring B (151.09, 148.05, 127.28, 127.16, 117.24, 117.34,). TOF MS ES+ (m/z)=287.

2-(furan-2-yl)-3-hydroxy-7-methoxy-4*H*-chromen-4-one (9b)

Brownish yellow solid, physical data summarized in Table 3.

IR (KBr, cm^{-1}): 3355 (Ar-OH), 1528 (Ar C=C str), 1690 (C=O str), 1332 (C-O str), 2937 (C-Hstr), 3082 (Ar-H).^{1}H-NMR(400MHz, DMSO, δ, TMS=0): δ=2.48(3H, s, 6-CH_3), 6.76(1H,m, 4'-H), 6.87 (1H, d,8-H, J=8.01Hz),7.20 (1H, d, 3'-H, J=8.0Hz), 7.40 (1H, d, 7-H, J=8.50Hz), 7.71(1H,s, 6'-H), 11.98 (1H,s, 3-OH, Exchangeable with D_2O), ^{13}C-NMR (400 MHz, δ, $CDCl_3$, TMS=0): Aromatic Ring-A (162.45, 140.36, 132.46, 131.62, 125.27, 116.58, 25.02), 188.87 (C=O), 149.54 (3-C), 143.80 (2-C), Aromatic Ring B (153.09, 145.80, 112.98, 112.790,). TOF MS ES+ (m/z)=243.

3-hydroxy-2-phenyl-4*H*-chromen-4-one (10b)

Dark brownish solid, physical data summarized in Table 3.

IR (KBr, cm^{-1}): 3350 (Ar-OH), 1552 (Ar C=C str), 1688 (C=5O str), 1325 (C-O str), 2892, (C-H str), 3025(Ar-H), 1317, (C-N).^{1}H NMR(400MHz, DMSO, δ, TMS=0): δ=6.74 (1H, d, 8-H, J=7.50 Hz), 6.97 (1H, d, 6-H, J=8.23 Hz), 7.10(1H,m, 4'-H), 7.39 (1H, dd, 7-H, J=7.76 Hz), 7.44 (2H, m, 2', 6'-H), 7.51 (1H, d, 5-H *J*=8.24 Hz), 7.59. (2H, m, 3'5,-H,), 12.69 (1H,s, 3-OH, Exchangeable with D_2O).^{13}C NMR (400 MHz, δ, $CDCl_3$, TMS=0): Aromatic Ring-A (152.24, 132.12, 131. 87, 124.43, 122.49, 117.10) 178.88 (C=O), 148.32 (2-C), 138.35 (3-C), Aromatic Ring B (153.44, 147.89, 127.35, 127.36, 118.68, 118.68,) 40.16, 40.17, N-$(CH3)_2$. TOF MS ES+ (m/z)=282.

1. The physical parameter, λ_{max}, and Rf value were determined and for the compounds (**1a-10a)** and summarized in Table 2.
2. The physical parameter, λ_{max}, and Rf value were determined and for the compounds (**1b-10b)** and summarized in Table 3.

Biological activity

All the 20 test compounds were subjected for their antibacterial and antifungal activity. The zone of inhibition was determined and the results were shown in the (Tables 4 and 5)**.**

1. Antimicrobial Activity of test compounds (1a-10a) were screened against Gram positive, Gram negative and fungi and compared with standard drugs.
2. Antimicrobial Activity of test compounds (1b-10b) Antimicrobial Activity of test compounds (1a-10a) were screened against Gram positive, Gram negative and fungi and compared with standard drugs.

Discussion

Antimicrobial activity of series (1a-10a)

The synthesized test compounds were evaluated for their antibacterial and antifungal activity against Gram-positive Gram-negative organisms and fungi. Results were expressed as a zone of inhibition (mm=millimeter) as shown in the (Table 4). Out of 10 test compounds 3a showed the marked antibacterial activity against *Bacillus cereus, Bacillus subtilis, Staphylococcus aureus* (Gram+ve) and *Escherichia Coli, Klebsiella pneumonia. Pseudomonas aeruginosa* organism (Gram-ve) showing a zone of inhibition 20, 19, 18 and 13, 11, 8 mm respectively. The antifungal activity of 3a was also promising when compared with that of standard drugs. The broad spectrum activity shown by 3a was attributed due to the presence of hydroxyl group at 4'position of ring B. Further, compounds such as 1a, 2a, and 4a have exhibited promising activity against all Gram-positive and Gram-negative bacteria. The compound 1a was shown to be more active against both fungal strains as compared to 2a and 3a. The potential nature of the activity was retained as 1a, 2a and 4a possessed electron withdrawing groups at 4'-position of ring B. However, compounds 8a, 6a, 5a and 9a exhibited moderate activity against Gram-positive and Gram-negative bacteria while 8a was found to be inactive against fungal strains. The results revealed that compounds such as 7a and 10a have shown least activity against all microorganisms as compared with that of standard drugs. This is probably because of 10a has no substitution at any position of ring B while 7a has methyl (Electron donating group) at 4′ of ring B. The results also revealed that all the compounds have a common substitution at 3-position of methyl group, which provides more metabolic stability towards the ring C, that indirectly influence antimicrobial activity. Thus 3-methyl flavanones with various substitutions at ring B have exhibited comparatively marked antibacterial, antifungal activity than that of no substitution at the 3-position in ring C.

It was evident from the data that all the test compounds were active against all Gram-positive organisms selected as compared with that of the standard as shown in Table 4. However, out of the three Gram-negative organism selected, 80% test compounds showed activity against *K pneumonia*. 60% against *E. coli* and only 30% were active against *P. aeruginosa.* However 70% of the test compounds were active against *C. albicans* while only 30% of the test compounds were active against *A. fumigatus*.

Antimicrobial activity of series (1b-10b)

We have evaluated biological screening with antibacterial and anti-fungal activity and the result as substituted flavone derivatives were active against microorganisms (Bacteria and Fungi), showed good zone of inhibition for each compound. Most of the have shown moderate to good antimicrobial activity. The activity is attributed may be due to the substitution of dimethyl amino, chloro, methoxy groups in addition with the hydroxyl group present at 3-position in each member of 1b-10b series. Compounds such as 1b, 3b, 4b, and 5b were found to elicit potent activity against Gram-positive (*Staphylococcuss aureus, Bacillus cereus* and *Bacillus subtilis,*) and Gram-negative (*E. coli, K. pneumonia* and *S. typhi*) bacteria and also against fungal strain probably because of the presence of hydroxyl group at 3-position, methoxy group at 7-position of ring A and halogen group at the *para* position of ring B. The remaining member of this series showed moderate anti-bacterial and anti-fungal activity. From the above findings, it has been concluded halogen, methoxy and hydroxyl groups located at different positions of ring A and B greatly affect antibacterial and antifungal activity. It was clear from the data that the presence of hydroxyl group at 3-position in ring C, greatly influences antibacterial and antifungal activity. Al most all (90% of the test compounds) compounds have shown promising antimicrobial activity. In addition to the hydroxyl group at 3-position, the halogens, methoxy, hydroxyl and nitro groups located at different positions (especially 7 and 4') of ring A and B enhances antibacterial and antifungal activity.

It was evident from the literature survey that amongst the all biological activities, the substituted flavones exhibit pronounced antimicrobial activity. Therefore, the present study has been performed to screen the newly synthesized compounds for their possible anti-bacterial and anti-fungal properties.

Conclusion

In the present study, we have depicted the synthesis of 20 3-substituted flavone analogues (3-methyl flavanones and 3-hydroxy flavones). The structure of all the synthesized compounds were established and characterized by TLC, melting point, elemental analysis,

Compound	Gram Positive			Gram Negative			Fungi	
	B.s	*S.a*	*B.c*	*E.c*	*K.p*	*P.a*	*C.a*	*A.f*
1a	18	12	13	11	-	7	7	5
2a	15	18	19	10	10	-	6	-
3a	19	18	20	13	11	8	7	5
4a	15	13	10	9	8	-	4	-
5a	6	-	7	-	6	-	-	-
6a	11	9	8	7	4	-	4	-
7a	6	5	8	-	-	-	5	3
8a	4	5	-	-	4	-	-	-
9a	7	9	8	3	4	-	3	-
10a	4	6	7	-	-	-	-	-
Ciprofloxacin	27	28	27	25	26	28	-	-
Griseofulvin	-	-	-	-	-	-	20	23

S.a: *Staphylococcus aureus*; *B.s*: *Bacillus subtilis; B.c*: *Bacillus cereus*, *E.c*: *Escherichia coli*, *P.a*: *Pseudomonas aeruginosa*, *K.p*: *Klebsiella pneumoni*, *C.a*: *Candida albicans*, *A.f*. *Aspergilus fumigatus*; Absence of zone of inhibition of microbial growth. All the zone of inhibition was determined at 100 µg/ml.

Table 4: Zone of Inhibition (mm) of bacteria, fungi and standard drugs.

Compound	Gram Positive			Gram Negative			Fungi	
	B.s	*S.a*	*B.c*	*E.c*	*K.p*	*P.a*	*C.a*	*A.f*
1b	18	19	17	17	19	7	7	5
2b	11	12	11	12	-	8	4	3
3b	20	22	20	14	15	8	7	5
4b	18	20	11	19	18	6	4	-
5b	12	13	7	-	16	-	8	-
6b	11	9	8	10	-	-	4	4
7b	12	10	7	10	-	9	7	6
8b	12	11	-	13	14	10	8	5
9b	11	-	4	-	4	-	3	-
10b	18	16	17	10	12	8	7	8
Ciprofloxacin	28	28	27	26	26	28	-	-
Griseofulvin	-	-	-	-	-	-	21	23

S.a: *Staphylococcus aureus*, *B.s*: *Bacillus subtilis*, *B.c*: *Bacillus cereus*, *E.c*: *Escherichia coli*, *P.a*: *Pseudomonas aeruginosa*, *K.p*: *Klebsiella pneumonia*, *C.a*: *Candida albicans*, *A.f*: **Aspergilus** *fumigatus*; Absence of zone of inhibition of microbial growth. All the zone of inhibition was determined at 100 µg/ml

Table 5: Zone of Inhibition (mm) of bacteria, fungi and standard drugs.

IR, ^{1}HNMR, ^{13}CNMR and Mass spectrometry. Most of the compounds have shown good to moderate antimicrobial activity, while some of the 3-hydroxyl flavone derivatives (1b, 3b, 4b, and 5b) were found to elicit potent antibacterial activity against Gram positive, Gram negative and fungi. The new series of 3-methyl flavanone derivatives (3a, 1a, 2a and 4a) exhibited marked antibacterial activity against Gram positive and moderate against fungi. The study revealed that 3-hydroxy flavone derivatives were found to be most active against Gram negative, while 3-methyl flavanone derivatives were active against Gram positive. However, further study needed for the *in-vivo* antimicrobial activity and toxicity studies. The results obtained from this study can be used as guidelines for further development of new antimicrobial agents.

Current and Future development

In current era, the derivatives of synthesized compounds (Flavonoids) have been associated with various pharmacological activities such as, antibacterial, antioxidant, anticancer, anti-diabetic [14,25]. The 3-methyl flavanones and 3-hydroxy flavones may become the probable potential class of compounds for future study. The recent reports available on analogues of these compounds for their glutathione transferase [32] and farnesyl transferase [33] inhibitors, will initiate our study to synthesize many more of such substituted flavanones and flavones and test them for such activity, there is a future scope for synthetic flavones to be targeted for newer targets such as CYP-450 aromatase to exploit their anticancer activity [34].

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