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Synthesis, Characterization and Biological Activity Study of New Flavones.

V.K.Kannan [1]*, D.V. Patil [2], Samadhan R. Patil [3], R.M.Patil [4], R.S.Lokhande[5]

[1*.] Department of Chemistry, Jaipur National University- Agra – Jaipur Rd Jaipur, Rajasthan, INDIA.

[2.] Herbert Brown Pharmaceutical and Research Laboratories, Mumbai, Maharashtra (M.S.) INDIA.

[3] Herbert Brown Pharmaceutical and Research Laboratories, Mumbai, Maharashtra (M.S.) INDIA.

[4.] Institute of Science, Mumbai, Maharashtra (M.S.), INDIA.

[5.] Department of Chemistry, Jaipur National University- Jaipur, Rajasthan, INDIA.

Abstract

The flavones are certainly occurring heterocyclic compounds belonging to the flavonoid group. These are accumulating in almost any part of plant and it is medicinal natural products. A series of 6, 7 dimethyl substituted flavones derivatives (F-1 to F-8) were synthesized and their antimicrobial activity was evaluated. The Flavone derivatives are synthesized by oxidative cyclization of 2-hydroxy-4, 5-dimethyl substituted chalcones in presence of Selenium dioxide and DMSO -Iodine. The structure of synthesized Flavones derivatives was elucidated by spectroscopic techniques like ^{1}H-NMR, IR, UV and Mass spectral analysis. Purity of the substances was determined by high performance liquid chromatography (HPLC). Physical parameters like melting point, solubility in solvents like Acetone Chloroform, DMSO, Ethanol Ethyl acetate Methanol and Pyridine are also documented. The results of antimicrobial assessment revealed that some of the synthesized compounds were good in their antibacterial and antifungal actions against some selected microbes.

Keywords: *Chalcone, flavone, Selenium oxide, Antibacterial, Antifungal.*

1. Introduction

A class of flavonoids based on the backbone of 2-phenylchromen-4-one are Flavones. Two phenyl ring and one heterocyclic ring are in Flavone. It is composed of a C_6-C_3-C_6 backbone. Flavones are found in cereals and herbs. Due to its wide range of application it attracts many researchers of the world. Flavones are related with human dietary ingredients and health directly. Naturally occurring flavones like **Apigenin** [1] 4', 5, 7 Trihydroxy Flavones are isolated from parsley & celery and this has been used to dye wool. Moreover Apigenin contribute to the cellular antioxidant defense system [2] in the body. **Luteolin** [3] (5, 7, 3', 4'-Tetrahydroxy flavones) Play an important role in the human body as an antioxidant. A free radical scavenger and an agent in the prevention of inflammation. **Tangerine** [4] (4'5, 6, 7, 8 Pentamethoxy Flavone), citrus peels, commercially available as a dietary supplement, Cholesterol lowering agent, Potential as an anti-cancer agent. **Chrysin** [5] (5, 7 di-hydroxy Flavones), present in carrots and flowers of some plants and isolated from honey. It is used as dietary supplements. Some of the synthetic flavones have wide range of medicinal application such as **Diosmin** [6] also known as venosmine. It is occurring mainly in the citrus family rutaceae, used as Anti-inflammatory, Anti-tumor and Neurodegeneration .Flavoxte [7] treat urinary bladder spasms. It is available under the trade name Urispas (Paladin).5, 7-Dihydroxy-3, 6, 8-trimethoxyflavone is reported to possess anti-inflammatory and anticancer [8] activity. Flavones are considered to play an important role in

prevention of oxidative damage in living system by capturing free radicals [9].

Flavones are synthesized by two routes i.e. 1. Cyclodehydration of l, 3-diphenylpropane-l, 3-diones 2. By oxidative cyclisation of 2'-hydroxychalcones.
1. Generally, flavones have been synthesized by Baker venkatraman rearrangement, which involves the conversion of 2-hydroxy acetophenone to benzoyl esters, followed by rearrangement in base to 1, 3-diphenylpropan-1, 3-diones, which upon cyclization under acidic conditions provides flavones [10]. **2**. Oxidative cyclisation of 2'-hydroxychalcones is an important and simple route for the synthesis of flavones. A brief review of the various reagents used for this reaction is given below.

By Using Selenium dioxide
Venkatraman et al. [11] reported the first cyclodehydrogenation of 2'-hydroxychalcones to flavones by heating them with selenium dioxide in Isoamyl alcohol medium. Using this method 2', 4'-dimethoxyflavone was obtained in 25% yield from 2'-hydroxy-2, 4-dimethoxychalcone. This reaction was believed to proceed via formation of flavanones by cyclisation, which further undergoes oxidation to give flavone. Further on Seshadri et al. [12] extended the use of this method for the synthesis of a number of naturally occurring flavones. But this method suffers from disadvantage of prolonged refluxing for 12-48 hours, which decreases the yield of flavones. This method was modified by carrying out the reaction in dimethyl sulphoxide (DMSO) medium[13], when the oxidative cyclisation was found to be completed in much shorter time 3 to 4 hours. Using this method differently substituted flavones were obtained in 60-70% yield.

By using Palladium compounds
2'-Hydroxychalcones on heating with Pd-C (10%) in equal proportions at 45°C above the melting point of Chalcone for one hour under reduced pressure were converted in to flavones in 50-60% yield [14].

Use of **lithium chloropalladite** or palladium (II) acetate [15] has also been reported for the synthesis of flavones by this route. But in this case formation of flavones is also accompanied by a small amount of flavanones.
By using Iodine: Doshi et al. [16] reported the cyclisation of 2'-hydroxychalcones by heating them with iodine in dimethylsulphoxide medium under refluxing conditions to form flavones. Various substituted flavones such as 5-methyl, 4'miethoxy-5-methyl, 7-bromo-5-methyl and 4'-methoxyflavone were synthesized by this method.

By using 2,3-Dichloro-5,6-dicyanobenzoquinone (DDQ) 2'-Hydroxychalcones when refluxed with DDQ in dioxane medium for 20-72 hours gave mixture of compounds like flavones (28-42%), flavanones (3-13%) and aurones (3-17%).[17]

By using Nickel Peroxide 2'-Hydroxychalcones when heated with Nio_2 in dioxane medium also gave a mixture of flavones, flavanones and aurones [18].

By using Sodium Periodate 2'-Hydroxychalcones on prolonged heating (24 to 48 hours) with sodium Periodate in DMSO at 100-120°C produced flavones [19]

By using Ferric chloride Ferric Chloride Oxidative cyclisation of 2'-hydroxychalcones with ferric chloride in dimethylsulphoxide medium has been reported to afford flavones in low yield (20-30%)[20]
By using **Organic disulphides** 2'-Hydroxychalcones when heated with disulphides at 260-290°C under nitrogen atmosphere also produced flavones[21]

By using Indium halides 2'-Hydroxychalcones dissolved in ethyl acetate and silica gel supported Indium halides (InBr3 and InCls) were heated with stirring at 130 to 140°C in an inert atmosphere for 45-120 minutes to yield flavones [22].

By using Sodium Tellurite (Na2TeO3)- Tellurium is the second heaviest element of the chalcogens it has a silvery white appearance. Its abundance is rare as gold. Tellurium forms compounds in different oxidation states such as + 2, + 4, + 6. Te° is comparatively more stable oxidation state. So TeO2 & TeO3 act as oxidizing agent. Sodium tellurite as an oxidizing agent in aqueous organic biphase medium using phase transfer catalyst [23]. Tellurite ion is extracted in the organic medium as ion pair with quaternary ammonium cation [Q+ TeO_3^{2-}], where the reaction takes place in homogenous manner.2Q + X " + Na2Te03 [(Q^+)2Te03^{2-}] + 2NaX. Using this oxidation of 2-hydroxy -4, 5-dimethyl substituted Chalcone could be done.

2. Result and Discussion

2.1 Preparation of Starting materials.

The 2-hydroxy-4, 5-dimethyl substituted Chalcones (C-1 to C-8) were prepared by reacting stoichiometry mole ratio of 2'-Hydroxy-4, 5-dimethylacetophenone (0.01mole) and corresponding substituted aromatic benzaldehyde (0.01 mol) in presence of aqueous Sodium hydroxide (NaOH 50 %, moles 5 eq.) or KOH (50% 10 eq.) or piperidine as base and Ethanol (20 ml) or Methanol or as solvent at 25-30°C (ambient temperature) for 8-24 hrs. The reactions progress was monitored by TLC (Hexane: Ethyl

acetate 90:10). The reaction after ~ 8-12 hrs was quenched, depending on the progress of reaction, into ice water and pH adjusted (~ 1-2) with dilute Hydrochloric acid (10% ~ 100 ml). The precipitated yellow colored product was filtered, washed with water till washings are neutral and dried (~ 60°C under vacuum 100 mm for ~ 8 hrs). The crude product was purified in Ethyl acetate and re-precipitated by addition of n-Hexane. All the substituted Chalcones were purified by crystallization technique only and achieved more yield. All Chalcone derivatives characterized by using spectral like ^{1}H NMR,(hydroxy protons are D_2O exchangeable) ^{13}C NMR, IR,UV,HPLC & physical constant were recorded such as Melting point and solubility in various solvents. [Refer reaction Scheme-1] –Eq(1)

2.2 Synthesis of 6, 7-dimethyl substituted Flavones

2'hydroxy -4', 5'-dimethyl substituted Chalcone (3.7mm), selenium dioxide (9.0mm) and 1-pentanol were heated on an oil bath at external temperature of ~150- 160°C and refluxed for 20.0hrs.Reaction progress were monitored by TLC. Chalcone were completely disappeared. Cooled and filtered the solution under hot condition and washed the catalyst bed with pentanol. The clear filtrate was concentrated to low volume. Cooled the material to room temperature and allowed to stand overnight for natural Crystillation. Next day material were filtered and washed with Hexane. The Flavone is light yellow in color and needle like crystal. The compound is dried. By this method few Flavones were prepared and other one Flavones are synthesized by DMSO/Iodine method. [Refer Reaction scheme -2- Eq (2)] Physical and analytical properties of Flavones are mentioned in Table no.1.and refer experimental procedure (8.1 to 8.8**)**

All synthesized novel Flavones derivatives were characterized by UV, FTIR, LCMS, ^{1}H NMR, HPLC and melting point. The Flavones showed the characteristics bands in FTIR between 1633 to 1788cm-1(C=O stretching in Flavones), the characteristic –CH3 stretching in between 2731 to 2941 cm-1 and C-O-C of heterocyclic ring of Flavone in the range of 1111, 1180.The wave numbers changing according to Flavone structure. In ^{1}H NMR $-CDCl_3$ Aliphatic protons singlet corresponding to methyl group appears at δ 2.34,2.38 (6H, 2-CH3-), singlet at δ 6.88ppm 1H,singlet at δ7.16ppm 1H,multiplet at δ7.20,7.32ppm 2H,duplet of doublet at δ7.44,7.86 ppm 2H and aromatic proton due to cyclisation singlet at δ7.89 ppm 1H. The mass spectrum showed molecular ion peak which corresponds to molecular weight of the compound**.** The UV absorption of Flavones consists of two essential absorption bands, band I and band II. The UV spectra of the Flavones in Acetonitrile were recorded; Flavone in acetonitrile solution shows two main bands**.** One in the range of 300 to 315 nm (referred to as Band I or Band K) arising probably, due to $\pi - \pi^*$ electronic transition of the whole molecule, while the other absorption band lies in the range of 210 to 250 nm assigned as band II. The intensity of K band is observed stronger than the band II. The most of the Flavones showed biologically activity against various bacterial species as E.coli, Pseudomonas aeruginosa and Staphylococcus aureus and fungi types like Aspergillus Niger, Penecillium crysogenum and Candida albicans. The concentration of the molecules were taken as 0.5 % (5 mg of sample added in 1ml of DMSO) and 1.0 % (10mg of sample added in 1 ml of DMSO) each. The antimicrobial and antifungal activity was performed by agar plate testing diffusion method. The concentration used for screening was established after estimating the Minimum inhibitory Concentration (MICs) of each compound. The solvent used for dilution was Dimethyl Sulfoxide (DMSO). For study an antibacterial activity 1-Loopful of micro-organism were incubated into sterile glucose broth and incubated for 24.0 hrs at 37°C. After 24 hrs of incubation broth containing the microorganism was added to peptone water and mixed well. 10 fold serial dilutions were made in the range of 10^{-1} to $10^{-10.}$ The results were compared with standard drug Chloramphenicol (1% solution in DMSO) for antibacterial activity by measuring the zone of inhibition in mm on mullelhinton agar plate by using 0.5% & 1.0% solution. The Zone of inhibition of all Flavones molecules is shown in [**Refer Table no.2**]. Most of the Flavones showed maximum zone of inhibition.

For Antifungal activity evaluation, Sabouraud Dextrose Agar (SDA) is used as fungal cultures and this was prepared by mixing of Peptone, Dextrose and Agar, distilled water and adjusted the pH to 6.8 then autoclaved the agar media at 121°C for 15 lbs. for 20 minutes. For study an antifungal activity 1-loopful of micro-organism were incubated into sterile glucose broth and incubated for 24 hrs at 22^{0}C. After 24 hrs of incubation broth containing the micro-organism was added to peptone water and mixed well. 10 fold serial dilutions were made in the range of 10^{-1} to 10^{-10}. The result were compared with standard drug fluconazole (100mg of fluconazole added in 10 ml of methanol) for antifungal activity by measuring the zone of inhibition of all Chalcone molecules. Most of the Flavones showed maximum zone of inhibition. After Autoclaved cool the

media to 40°C and mixed the fungal cultures. Prepared plates by pour plate method. Refrigerate all the plates for 30 minutes then kept the plates in laminar air flow and rest for a minutes. By sterile cork borer was used to prepare four cups of 6mm diameter in the agar plates. 5.0 µl diluents of bacterial culture of 0.5% and 1.0% were added in all respective plates. Incubate all the plates for 24 hrs at 37°C. Most of the Flavones showed maximum zone of inhibition. [Refer **Table no. 03**]

3. Experimental

Melting points were recorded on a DBK instrument and temperature rise per minute is 2◦C. IR spectra of the compound were recorded on Shimadzu FTIR - 8400S, UV spectra of the compound were analyzed in Shimadzu UV-1800. The purity of substances was analyzed by Shimadzu-1200 series HPLC. The mass spectra of the compound were analyzed in Agilent Single Quadruple LCMS. 1H NMR Spectra were recorded on Bruker–Avance II-300 MHz & 400 MHz.

3.1. General Synthetic Procedure for various Flavone derivatives (F-1)

2'hydroxy -4', 5'-dimethyl-2-fluro Chalcone (1.0g, 3.7mm), selenium oxide (1.0g, 9.0mm) and 1-pentanol 30 mL were heated on an oil bath at external temperature of 150- 159°C and refluxed for 20.0hrs.Reaction progress were monitored by TLC(Mobile phase:1:1 Toluene & Ethyl acetate or 100% Toluene).Chalcone were completely disappeared. Cooled to 75°C and filtered the solution under hot condition and washed the catalyst bed with 10 ml of n-pentanol. The clear filtrate was concentrated to low volume i.e. 30mL of pentanol were distilled out. Cooled the material to room temperature and allowed to stand overnight for natural Crystillation. Next day material were filtered and washed with Hexane. The Flavone is light yellow in color and needle like crystal. The compound is dried and weight of substance is 0.585g, yield 59%.By this method most of the Flavones were prepared and one Flavones were synthesized by DMSO/Iodine method.

3.2: Spectral data of Flavones (F-1 to F-8)

3.2.1: 2-(2-flurophenyl)-6, 7-dimethyl -4H-chromen-4-one {F-1}

Molecular Formula: $C_{17}H_{13}FO_2$; **Formula Weight:** 268.28; **Color**: Light Yellow powder. Solubility: Acetone, chloroform, DMSO, ethyl acetate Pyridine; **^{1}H-NMR (**($CDCl_3$) 300 MHz) δ ppm 7.89 (s, 1H,), 7.44, 7.86, (dd, 2H), δ7.32-7.20 (m 2H), δ6.88, 7.16 (S- 2 H), δ 2.38, 2.34 (S-6H).**MS** m/z= 269.50 $[M+H]^{+1}$,**UV** Bands λmax in nm Band-I &II in Acetonitrile: 253.60 and 289.0 its **Molar absorptivity is** 22057.1 & 17463.6 **(L mol^{-1} cm^{-1}).IR** (KBr,cm^{-1}): 1633.71,1788 (C=O of Flavone), 2731,2796,2916,2941,2974 (-CH3 stretching), 1512, 1531,1537,1566,1573,1618,1633(C=C of aromatic), 1111,1180 (C-O-C of Flavone ring), 831,995 (Ar-H bending), 690.52-894.97 (C-F stretching and bending vibration).**HPLC purity** -97.82% **Melting point**: 138 to 140 °C.

3.2.2: 2-(3-flurophenyl)-6, 7-dimethyl -4H-chromen-4-one {F-2}

Molecular Formula: $C_{17}H_{13}FO_2$; **Formula Weight**: 268.28; **Color**: off white powder. Solubility: Acetone, chloroform, DMSO, ethyl acetate Pyridine. **^{1}H-NMR (**($CDCl_3$) 300 MHz) δ ppm 7.94 (s, 1H,), 7.19, 7.27, (d, 2H), δ7.58-7.69 (t 1H), δ7.52 -7.44 (S-1 H),δ 7.34,6.76 (s-2 H)δ 2.36, 2.40(s 6 H,2CH3), **MS** m/z= 269.5 $[M+H]^{+1}$,**UV** Bands λmax in nm Band-I &II in Acetonitrile: 259.8 and 294.8- its **Molar absorptivity is** 23485.4 & 20127.5 **(L mol^{-1} cm^{-1}). IR** (KBr, cm^{-1}): 1782. 1691 (C=O of Flavone), 2916, 2943, 2972 (-CH3 stretching), 3049 (=C-H aromatic) 1512, 1564, 1579, 1608(C=C of aromatic), 1153, 1178 (C-O-C of Flavone ring), 904,997,850,875 (=C-H stretching of aromatic), 698,761 (C-F stretching and bending vibration). **HPLC purity** -99.83% **Melting point:** 152 to 155 °C.

3.2.3: 6, 7-dimethyl-2-(3-nitrophenyl)-4H-chromen-4-one {F-3}

Molecular Formula: $C_{17}H_{13}NO_2$; **Formula Weight**: 295.28; **Color**: Light grey color. Solubility: Soluble in DMSO, acetone, chloroform, ethyl acetate Pyridine. **^{1}H-NMR (**(DMSO) 300 MHz) δ ppm 7.90 (s, 1H,), 8.55,8.82 (d, 2H), δ8.44-8.41 (m 1H), δ,7.20,7.70,7.87 (S- 3 H),δ 2.0-2.50(s 6 H,2CH3), **MS** m/z= 296.5 $[M+H]^{+1}$, **UV** Bands λmax in nm Band-I &II in Acetonitrile: 257.4 and 285.4 its **Molar absorptivity is** 29526.1 & 18192.5 **(L mol^{-1} cm^{-1}).IR** (KBr,cm^{-1}): 1346,1369,1529,1577 (NO_2 Stretching), 2862,2924, 2976(-CH3 stretching), 3086,3203(C-H stretching of aromatic), 1691,1720,1737, (C=O of Flavone), 1105,1161,1582 (C-O-C of Flavone), 806,844,867 (C-N Stretching), **HPLC purity** -99.74% **Melting point:** 256 to 258 °C.

3.2.4: 2-(3-hydroxyphenyl)-6, 7-dimethyl -4H-chromen-4-one {F-4}

Molecular Formula: $C_{17}H_{14}O_3$; **Formula Weight**: 266.29; **Color**: Light brown color powder. Solubility: Sparingly soluble in DMSO and very

poor soluble Acetone, chloroform, ethyl acetate Pyridine.**^{1}H-NMR** ((TFA) 400 MHz) δ ppm 2.44,2.52 (s, 6H, 2-CH_3), δ7.46(s,1H), 7.24, δ7.68(s, 2H-ArH), δ7.26, δ 8.09 (s, 2H), δ7.72 (d,1 ArH), δ7.48 (t, 1H), δ 11.5(s,1H).**MS** m/z= 267.3 $[M+H]^{+1}$,**UV** Bands λmax in nm Band-I &II in Acetonitrile: 261 and 296- its **Molar absorptivity is** 19492.7 & 20148 **(L mol^{-1} cm^{-1}).IR** (KBr) in cm^{-1}: 3140 (-OH stretching), 3061(=C-H stretching of aromatic), 2862, 2945,2976(-CH3 stretching),1710, 1788 (C=O of flavone), 1502, 1537, 1571,1610,1625 (C=C of aromatic),1157,1195(C-O-C of Flavone),950-995,1018(=C-H of Alkene) 702,756,785 (C-H bending of aromatic). **HPLC purity** -99.56% **Melting point**: 250 to 253 °C.

3.2.5: 6, 7-dimethyl-2-(naphthalen 2-yl)-4H-chromen-4-one – {F-5}

Molecular Formula: $C_{21}H_{16}O_2$; **Formula Weight**: 300.355, **Color**: off white powder. Solubility: Highly soluble in Chloroform, sparingly soluble in Toluene, Methanol, DMSO, acetone, ethyl acetate, Pyridine.**^{1}H-NMR** ($CDCl_3$)300 MHz) δ ppm 2.40-2.41 (s, 6H,2-CH_3), δ 6.64 (s, 1H), δ 7.25,7.31 (s, 2H-ArH), δ 8.13,7.95 (t 2H), δ 7.76,(d,1H). δ 7.59, (s,1H), δ 7.57, 7.55,756 (d, 3H, ArH)..**MS** m/z= 301.0 $[M+H]^{+1}$,**UV** Bands λmax in nm Band-I &II in Acetonitrile: 217.2 and 305.6- its **Molar absorptivity is** 60588 & 16292.7 **(L mol^{-1} cm^{-1}).IR** ($KBrcm^{-1}$): 3055 (=C-H stretching), 2862,2920,2945,2970(-CH_3 Stretching),1647 (=C=O of Flavone), 1508,1570,1631 (-C=C of aromatic). 1105, 1153, 1178 (-C-O-C of aromatic flavone) 893,910,972 (=C-H bending of aromatic), **HPLC purity** -98.62% **Melting point**: 130 to 132°C.

3.2.6: 2(5-bromo-2-hydroxyphenyl)-6, 7-dimethyl 4H-chromen-4-one –{C-6}.

Molecular Formula: $C_{17}H_{13}$ BrO_3; **Formula Weight**: 345.18, **Color**: Light brown powder. Solubility: Highly soluble in Chloroform, sparingly soluble in Toluene, Methanol, DMSO, acetone, ethyl acetate, Pyridine and TFAA.**^{1}H-NMR** (TFA- 400 MHz) δ ppm 2.48,2.56, (s, 6H, 2 CH_3), δ 6.96,7.57 (d, 2H-ArH), δ 7.78, 8.10,8.24,8.42 (s, 4H), 11.49,(s,1H,OH).**MS** m/z= 343.1 $[M-H]^{-2}$,**UV** Bands λmax in nm Band-I &II in Acetonitrile: 241.0 and 319- its **Molar absorptivity is** 21503.1 & 14680.6 **(L mol^{-1} cm^{-1}).IR** (KBr cm^{-1}): 3134 (-C-OH stretching), 2852,2918(-CH_3 Stretching),1622 (=C=O of Flavone), 1469,1560 (-C=C of aromatic).1469,1560 (Aromatic C=C stretching)1130,1093,1159 (-C-O-C of aromatic flavone) 925,999 (=C-H bending of aromatic),655,686,765 (C-Br stretching).**HPLC purity** -98.19%, Melting **point**: 290 to 294 °C.

3.2.7: 2(2, 5-dimethoxyphenyl)-6, 7-dimethyl-4H chrome-4-one– {F-7}.

Molecular Formula: $C_{19}H_{18}$ O_4; **Formula Weight**: 310.348, **Color**: Light pale green powder. Solubility: Highly soluble in Chloroform, sparingly soluble in Toluene, Methanol, DMSO, acetone, ethyl acetate, Pyridine and TFAA. **^{1}H-NMR** ($CDCl_3$- 300 MHz) δ ppm 2.35,2.38 (s, 6H,2-CH_3), δ 3.84,3.88 (s,6H,2-CH_3), 6.99,7.02(d,2H),δ7.10,7.30,7.45(s,3H), δ 7.94(s,1H).**MS** m/z= 311.1 $[M+H]^{+1}$,**UV** Bands λmax in nm Band-I &II in Acetonitrile: 245.6 and 290.2- its **Molar absorptivity is** 21145.5 & 13612.4 **(L mol^{-1} cm^{-1}).IR** (KBr, cm^{-1}): 2831,2904,2945,(-CH_3 stretching),2999.31(=C-H Stretching of aromatic),1631 (C=O of Flavone), 1502,1581,1597(C=C of Aromatic), 1058,1151,1180(C-O-C of Flavone ring), 792,812(=C-H bonding of aromatic), 1300,1373 -(-OCH3 stretching), **HPLC purity** -99.09% **Melting point**: 162 to 164 °C.

3.2.8: 6, 7-dimethyl-2-(2-(trifluromethyl) Phenyl)-4H-chromen-4-one –{C-8}.

Molecular Formula: $C_{18}H_{13}F_3$ O_2; **Formula Weight**: 318.28, **Color**: Light brown color powder. Solubility: Highly soluble in Chloroform, DMSO, sparingly soluble in Toluene, Methanol, acetone, ethyl acetate, Pyridine and TFAA.**^{1}H-NMR** ($CDCl_3$-300 MHz) δ ppm 2.37,2.39(s, 6H, 2-CH_3), 6.46-7.26 (s, 2H-ArH), 7.98, (s,1H),7.82,7.85 (dd, 2H), 7.69,7.62 (m-2H). **MS** m/z= 319.1 $[M\ ^{+}H]^{+1}$,**UV** Bands λmax in nm Band-I &II in Acetonitrile: 243.8 and 281.0- its **Molar absorptivity is** 20702.7 & 9480.8 **(L mol^{-1} cm^{-1}).IR** (KBr, cm^{-1}): 3105,3059(=C-H Stretching of Aromatic),2927,2978 (-CH3 Stretching),1645,1680 (=C=O of Flavone),1566,1614,1631(Ar-C=C stretching), 1109,1128,1168 (C-O-C of flavone),1037,1070(C-F stretching),698,738 (C-H bending of Aromatic) **HPLC purity** -97.23% **Melting point**: 154 to 160 °C.

4. Conclusion

We synthesized novel series of 6, 7 dimethyl substituted flavone derivatives are screened for antibacterial and antifungal activity. From the antimicrobial study results it revealed that, most of the compounds were most effective against all the tested pathogens compared with the other tested compounds. In case of antioxidant screening, compounds does not show any activity.

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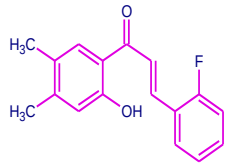
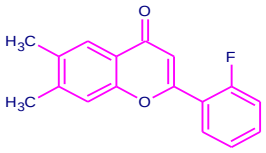
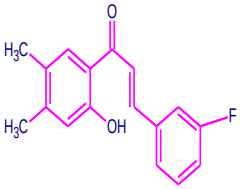
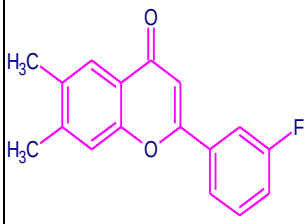
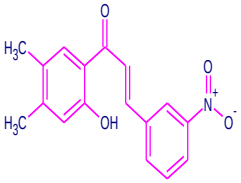
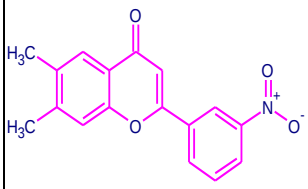
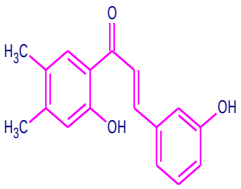
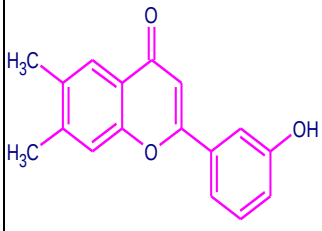
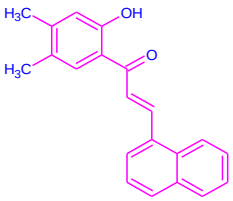
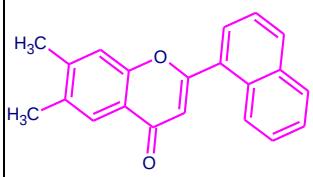
5. Tables & Equations.

5.1 Table 1: The physical and analytical data of synthesized compounds

Chalcone	Code No	Flavone	Reaction Time (hrs)	catalyst	Isolated Yield	Melting Point
	**F-1**		**20.0**	**SeO_2**	**59%**	138-140°C
	**F-2**		**20.0**	**SeO_2**	**62%**	152-155°C
	**F-3**		**18.0**	**SeO_2**	**68%**	256-258°C
	**F-4**		**18.0**	**SeO_2**	**54%**	250-253°C
	**F-5**		**2.0**	**Iodine**	**69%**	130-132°C

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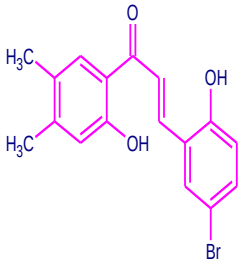
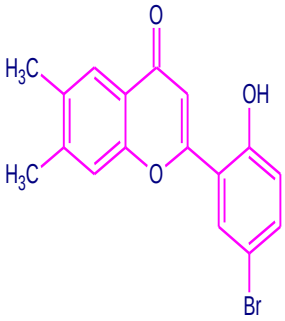
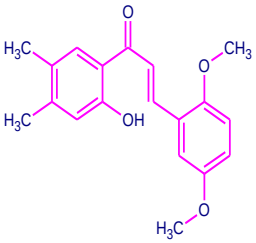
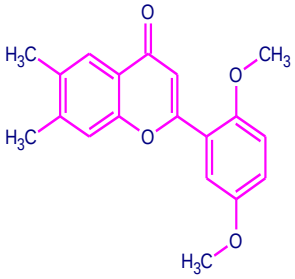
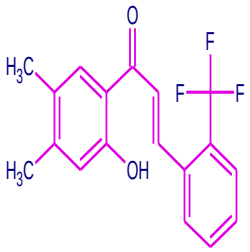
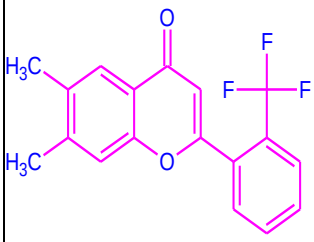
	**F-6**		**20.0**	**SeO_2**	**47%**	290-294°C
	**F-7**		**18.0**	**SeO_2**	**55%**	162-164°C
	**F-8**		**16.0**	**SeO_2**	**54%**	154-160°C

(F-1 to F-8) have been given in below Table)

5.2 Table: 2 Antibacterial Activity Of Flavones.

Compound Name	Compound Code	Escherichia Coli (NCIM 2685)		Pseudomonas aeruginosa (NCIM- 5029)		Staphylococcus aureus (NCIM-5021)	
		1 % sample dilution	0.5% sample dilution	1 % sample dilution	0.5% sample dilution	1 % sample dilution	0.5% sample dilution
		Zone of inhibition in mm		Zone of inhibition in mm		Zone of inhibition in mm	
2FF	F-1	15	11	13	10	15	No Zone
3FF	F-2	10	10	11	10	12	11
3NF	F-3	25	19	27	22	23	20
3HF	F-4	22	20	25	20	18	10
1-NAPH-F	F-5	15	19	27	17	22	18
BSF	F-6	14	10	No zone	No zone	20	10
DMF	F-7	15	10	27	15	16	10
TFF	F-8	25	19	16	10	22	17
Chloramphenicol	Standard	28		28		28	

Refer: [Fig. S-1f to S-8f] & [Fig.S-1fR to S-8fR].

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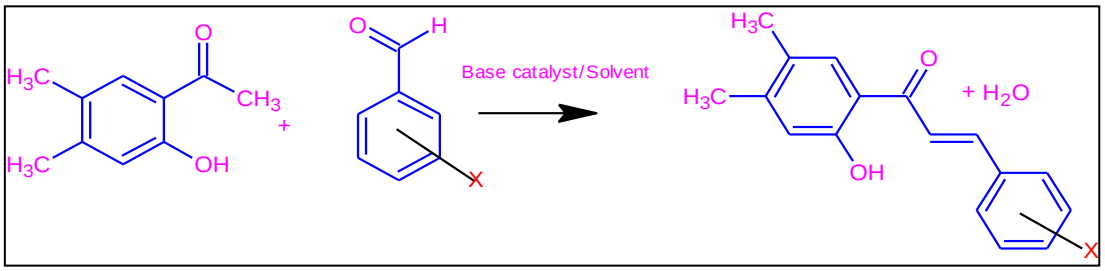
5.3 Table:3 ANTIFUNGAL ACTIVITY OF FLAVONES.

Compound Name	Compound Code	Aspergillus niger (ATCC: 16838)		Penicilium crysogenum (ATCC: 10106)		Candida albicans (ATCC: 18804)	
		1 % sample dilution	0.5% sample dilution	1 % sample dilution	0.5% sample dilution	1 % sample dilution	0.5% sample dilution
		Zone of inhibition in mm		Zone of inhibition in mm		Zone of inhibition in mm	
2FF	F-1	19	11	19	11	20	10
3FF	F-2	20	17	14	10	17	16
3NF	F-3	17	10	20	19	15	11
3HF	F-4	15	10	19	16	No Zone	No Zone
1-NAPH-F	F-5	12	No Zone	15	13	20	12
BSF	F-6	22	19	12	10	20	14
DMF	F-7	21	17	18	17	20	16
TFF	F-8	19	15	18	17	18	14
Fluconazole	Standard	22		22		22	

Refer: [Fig. S-1f to S-8f] & [Fig.S-1fR to S-8fR].

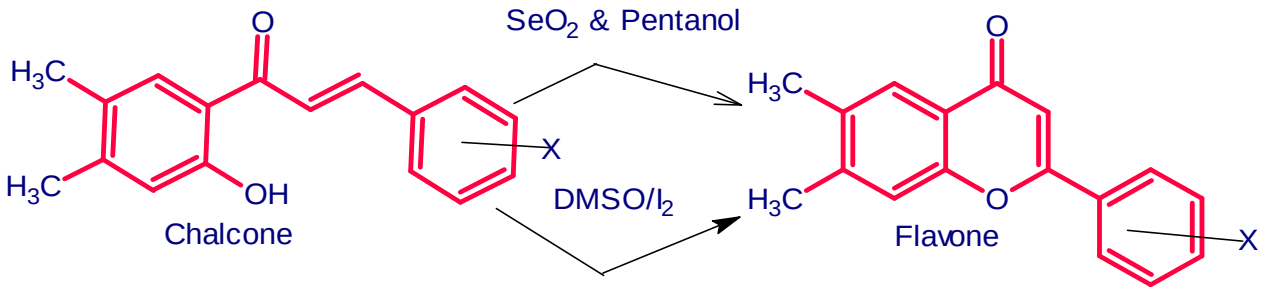
5.4 Equation-(1)



Scheme-1: Reaction Scheme for substituted 2, hydroxy 4, 5-dimethyl Chalcone.

Where X=2- F, 3-F, 3-NO2, 3-OH, Naphthyl, 5-Br, 2-CF3, 2, 5-OCH3

Equation-(2)



Scheme-2**:** Reaction Scheme for 6, 7-dimethyl substituted flavones
Where X=2- F, 3-F, 3-NO2, 3-OH, Naphthyl, 5-Br, 2-CF3, and 2, 5-OCH3

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