Synthesis and Chemical Characterisation of Some Novel Substituted Flavone’s for It’s Anti Microbial Activity

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ABSTRACT: The present study reports an experiment on some derivatives of 2-phenyl-chromen-4-one (flavone ring) have a proven inhibitory activity against a variety of human pathogens, including antibiotic-resistant Gram-positive and Gram-negative bacteria and antifungal activities screened against four human pathogenic bacteria and two phytopathogenic fungi. Flavanoid derivatives have been made through Algar–Flynn–Oyamada reaction from hydroxyacetophenones and aromatic-aldehydes. The structures of the synthesized compounds were elucidated by UV, IR and 1H NMR spectroscopic techniques, and elemental analysis. These compounds are potentially useful pharmacologically active compounds and are studied for biological activities like antibacterial and antifungal screens performed in vitro by the plate-hole diffusion method.

KEYWORDS: 2-phenyl-chromen-4-one; Antibacterial; Antifungal; Spectroscopic techniques

Introduction
Medicinal Chemistry itself is concerned mainly with the organic synthesis, analytical and biochemical aspects for alleviating diseases occurring in humans1. Flavanoids comprises of one of the largest group of dietary polyphenolic compounds and natural occurring secondary metabolites in plants existing predominately as O- or C-glycosides2. Chemical structure of Flavanoids is based on C15 flavan skeleton with a chromane ring bearing a second aromatic ring B in position 2, 3 or 4 with a basic ring structure of 2-phenyl -4H-Benzopyran-4-one 2. Authors propose that small structural differences in the compounds are critical to their great variability of activities and their low toxic potential due to differences in aglycone ring structure, state of oxidation / reduction and hydroxyl groups3. Flavanoids contributing towards anti oxidant defense system against oxidative stress by blocking deleterious actions of prooxidants enzymes and thought to possess Antithrombogenic4, cardio-vasculo protective5, vasorelaxant agent4, Antiulcer4, action on cerebellum4, Diuretic5, silicosis6, cirrhosis6, retinopathies6, Antihapatotoxic6, anti neuro-degenerative6 muscular dystrophy6, Premature-antiaging6, Antiinflammatory7, Antiallergic7, Antiproliferative8, immunomodulatory9, Anti spasmodic10, Estrogenic activity11, Thyroid analogue11, Antioxidant12, inhibition of leukotriene B4, and Radio protective properties12. Average daily intake of flavanoid is estimated to be 150-200mg, considering it as a micronutrient13. This paper reports the syntheses of nine derivatives of 2-phenyl-chromen-4-one (flavone) from their corresponding chalcones by using Algar–Flynn-Oyamada reaction where by a chalcone undergoes an oxidative cyclization in presence of hydrogen peroxide and base in ethanol. It is chosen as our primary method to synthesise 3-hydroxy flavones, because it is a modular synthetic method using commercially available starting materials, which makes it an ideal method for combinatorial synthesis. It was felt worthwhile to screen the newly synthesized compounds for their possible antibacterial and anti-fungal properties as it was evident from the literature that amongst all biological activity 3-substitued flavanoids exhibit pronounced antimicrobial activity. The flavones were screened in vitro for their antibacterial and antifungal activity against four human pathogenic bacteria.

Results and discussion
The synthesis of various substituted 3-hydroxy flavones (Compound I to IX) was done by Algar–Flynn-Oyamada reaction as primary method where by a chalcone undergoes an oxidative cyclization to form a flavonol commercially available starting materials. In this procedure aldol condensation between acetophenone derivatives and
different aldehydes to give chalcone products further it was converted to 3-hydroxy flavones by treating with hydrogen peroxide and base in ethanol and the obtained yield was about 80%.

All the newly synthesized compounds were then identified for their structure and functional groups by using various analytical studies like IR, Mass, $^1$H- & $^{13}$C- NMR spectroscopy. Also, various newly synthesized compounds were screened for their invitro antimicrobial against various bacteria’s and fungi using well plate agar diffusion technique by measuring inhibition zone in millimeters.

All compounds have elicited a mild activity against all the bacterial and fungal strains used for the study. All compounds afforded better activity against gram negative bacteria. Compounds I, II, VI, VIII, and I, IV, VII, VIII were found to be equipotent to the anti-bacterial standard used i.e. the Streptomycin, when tested against the strains of gram positive Bacillus subtilis, Staphylococcus Aureus and compound I, II, VII, VIII and I, II, IV, V, VII, VIII were found to elicit potent activity against gram negative Escherichia coli, Shigella sonae whereas some of the synthesized compounds like I, IV and VII and I, II, VII, VIII were found to possess good antifungal activity when tested against Aspergillus niger, Mucor phlei to that of the standard Ketoconazole used.

**Conclusion**

**Experimentation**

**Materials methods and instruments**

All the chemicals used were of analytical grade are obtained from Thermosticher, and the solvents were procured from Merck and SD Fine Ltd. Melting point was determined in open capillary tubes and is corrected. Thin Layer Chromatography was checked on silica gel-G coated plates by using Iodine vapours as visualizing agent. IR Spectra were recorded on Fourier Transform Infrared Spectrometer (Vmax in cm$^{-1}$), UV Visible spectrometer was recorded on Shimadzu (UV 1700), NMR spectra were recorded in JOEL GCMAT-II GC-MS Spectrometer. Mass Spectra were recorded in BRUKER AV III 500MHz FT-NMR Spectrometer and Mass Spectra were recorded in JOEL GCMAT-II GC-MS Spectrometer.

**Synthesis of 3-[4-(dimethylamino)phenyl]-3-hydroxy-4H-chromen-4-one (Compound I)**

A mixture of 2-hydroxyacetophenone (0.01 mole) and $P$-dimethyl amino benzaldehyde (0.01 mole) was stirred in absolute ethanol (95.0 %, 30 ml) and then an aqueous solution of potassium hydroxide (15 ml) was added to it. The reaction mixture was kept overnight at room temperature and then was poured into crushed ice and acidified with dilute hydrochloric acid. The chalcone derivative precipitates out as solid that was filtered, dried and recrystallized from absolute ethanol as pale yellow crystals, yield 95.00%. The compound was analyzed for $\lambda_{max}$ 323nm (CH$_3$OH), m.p. 140-142°C, $Rf$ 0.72 (benzene: acetone; 8: 1) and Elemental Analysis Calculated (%) C 76.38; H 6.41; O 11.97; N 5.24.

**IR (KBr, cm$^{-1}$)**

1168.90 (C-C Stretch), 1658.84 (Aromatic C=C ring Stretch), 1599.04 (Aromatic C=C-C ring Stretch), 794.70 (Aromatic C-H Bend), 3647.51 (Phenolic O-H Stretch), 1716.70 (C=O Stretch), 1338.64 (Aromatic tertiary amine C-N Stretch).

**Synthesis of 2-[4-(dimethyl amino) phenyl]-3-hydroxy-4H-chromen-4-one (Intermediate I)**

A mixture of 3-[4-(dimethylamino)phenyl]-1-(2-hydroxyphenyl)prop-2-en-1-one (Intermediate I)

A mixture of 2-hydroxyacetophenone (0.01 mole) and $P$-dimethyl amino benzaldehyde (0.01 mole) was stirred in absolute ethanol (95.0 %, 30 ml) and then an aqueous solution of potassium hydroxide (15 ml) was added to it.
Synthesis

General Synthesis:

\[
\begin{align*}
R_1 & = \text{OCH}_3 \\
R_2 & = \text{CH}_3
\end{align*}
\]

2-Hydroxy Acetophenone derivatives

A mixture of 2-hydroxyacetophenone (0.01 mole) and \( p \)-chloro benzaldehyde (0.01 mole) was stirred in absolute ethanol (95.0 %, 30 ml) and then an aqueous solution of potassium hydroxide (15 ml) was added to it. The reaction mixture was kept overnight at room temperature and then poured into crushed ice and acidified with dilute hydrochloric acid. The chalcone derivative precipitates out as solid that was filtered, dried and recrystallized from absolute ethanol as pale yellow crystals, yield 89.00%. The compound was analyzed for \( \lambda_{\text{max}} \) 318nm (CH\textsubscript{3}OH), m.p. 94-96\textdegree C, \( Rf \) 0.66 (benzene : acetone; 8 : 1) and Elemental Analysis Calculated (%): C 69.64; H 4.29; O 12.37; Cl 13.70.

IR (KBr, cm\textsuperscript{-1}): 1155.40 (C-C Stretch), 1639.55 (C=C Stretch), 1473.66 (Aromatic C=C ring Stretch), 1577.82 (Aromatic C=C-C ring Stretch), 794.70 (Aromatic C-H Bend), 3651.37 (Phenolic O-H Stretch), 1734.06 (C=O Stretch), 758.05 (C-Cl Stretch).

3-Hydroxy Flavone derivative

Analysis of 3-(4-chlorophenyl)-1-(2-hydroxyphenyl) prop-2-en-1one (Intermediate II)

A mixture of 2-hydroxyacetophenone (0.01 mole) and \( p \)-chloro benzaldehyde (0.01 mole) was stirred in absolute ethanol (95.0 %, 30 ml) and then an aqueous solution of potassium hydroxide (15 ml) was added to it. The reaction mixture was kept overnight at room temperature and then poured into crushed ice and acidified with dilute hydrochloric acid. The chalcone derivative precipitates out as solid that was filtered, dried and recrystallized from absolute ethanol as pale yellow crystals, yield 89.00%. The compound was analyzed for \( \lambda_{\text{max}} \) 318nm (CH\textsubscript{3}OH), m.p. 94-96\textdegree C, \( Rf \) 0.66 (benzene : acetone; 8 : 1) and Elemental Analysis Calculated (%): C 69.64; H 4.29; O 12.37; Cl 13.70.

IR (KBr, cm\textsuperscript{-1}): 1155.40 (C-C Stretch), 1639.55 (C=C Stretch), 1473.66 (Aromatic C=C ring Stretch), 1577.82 (Aromatic C=C-C ring Stretch), 794.70 (Aromatic C-H Bend), 3651.37 (Phenolic O-H Stretch), 1734.06 (C=O Stretch), 758.05 (C-Cl Stretch).

Synthesis of 2-(4-chlorophenyl)-3-hydroxy-4H-chromen-4-one (Compound II)

A mixture of 3-(4-chlorophenyl)-1-(2-hydroxyphenyl) prop-2-en-1one (0.01 mole), absolute ethanol (50 ml,0.003 mole) and sodium hydroxide solution (5 ml, 1.25N) and
10 ml solution of hydrogen peroxide (30%) was stirred continuously for 2 hrs at room temperature. It was then diluted with ice-cold water and acidified with dilute hydrochloric acid. When solid separated, it was filtered, washed well with water, dried and crystallized from isopropyl alcohol as pale yellow crystals, yield 88.23%. The compound was analyzed for \( \lambda_{\text{max}} \) 351 nm (CH$_2$OH), \textit{m.p.} 105-107°C, \textit{Rf} 0.48 (benzene: acetone; 8: 1) and Elemental Analysis Calculated (%) C 72.71; H 6.44; O 16.14; N 4.71.

IR, KBr \( \nu_{\text{max}} \) : IR (KBr, cm

IR (KBr, cm

IR (KBr, cm

\textit{IR} (KBr, cm

\textit{IR} (KBr, cm

\textit{IR} (KBr, cm

\textit{IR} (KBr, cm

The compound was analyzed for \( \lambda_{\text{max}} \) 348 nm (CH$_2$OH), \textit{m.p.} 110-112°C, \textit{Rf} 0.59 (benzene: acetone; 8: 1) and Elemental Analysis Calculated (%) C 68.42; H 3.53; O 28.04.

IR, KBr \( \nu_{\text{max}} \) : IR (KBr, cm

Synthesis of 3-(2-furyl)-1-(2-hydroxyphenyl) prop-2-en-1-one (Intermediate III)

A mixture of 2-hydroxyacetophenone (0.01 mole) and furfuraledehyde (0.01 mole) was stirred in absolute ethanol (95.0%, 30 ml) and then an aqueous solution of potassium hydroxide (15 ml) was added to it. The reaction mixture was kept overnight at room temperature and then was poured into crushed ice and acidified with dilute hydrochloric acid. The chalcone derivative precipitates out as solid that was filtered, dried and recrystallized from absolute ethanol as pale yellow crystals, yield 86.00%. The compound was analyzed for \( \lambda_{\text{max}} \) 331 nm (CH$_2$OH), \textit{m.p.} 96-98°C, \textit{Rf} 0.79 (benzene: acetone; 8: 1) and Elemental Analysis Calculated (%) C 72.71; H 6.44; O 16.14; N 4.71.

IR (KBr, cm

Synthesis of 3-(2-furyl)-1-(2-hydroxyphenyl) prop-2-en-1-one (Compound III)

A mixture of 3-(2-furyl)-1-(2-hydroxyphenyl) prop-2-en-1-one (0.01 mole), absolute ethanol (50 ml, 0.003 mole) and sodium hydroxide solution (5 ml, 1.25N) and 10 ml solution of hydrogen peroxide (30%) was stirred continuously for 2 hrs at room temperature. It was then diluted with ice-cold water and acidified with dilute hydrochloric acid. When solid separated, it was filtered, washed well with water, dried and crystallized from isopropyl alcohol as pale yellow crystals, yield 91.00%.

\textit{IR} (KBr, cm

Synthesis of 3-[4-(dimethylamino) phenyl]-1-(2-hydroxy-4-methoxy phenyl)prop-2-en-1-one (Intermediate IV)

A mixture of p-methoxy-2-hydroxyacetophenone (0.01 mole) and \textit{p}-dimethyl amino benzaldehyde (0.01 mole) was stirred in absolute ethanol (95.0%, 30 ml) and then an aqueous solution of potassium hydroxide (15 ml) was added to it. The reaction mixture was kept overnight at room temperature and then was poured into crushed ice and acidified with dilute hydrochloric acid. The chalcone derivative precipitates out as solid that was filtered, dried and recrystallized from absolute ethanol as pale yellow crystals, yield 76.00%. The compound was analyzed for \( \lambda_{\text{max}} \) 331 nm (CH$_2$OH), \textit{m.p.} 96-98°C, \textit{Rf} 0.79 (benzene: acetone; 8: 1) and Elemental Analysis Calculated (%) C 72.71; H 6.44; O 16.14; N 4.71.

IR (KBr, cm

Synthesis of 3-[4-(dimethylamino) phenyl]-3-hydroxy-7-methoxy-4H-chromen-4-one (Compound IV)

A mixture of 3-[4-(dimethylamino) phenyl]-1-(2-hydroxy-4-methoxy phenyl)prop-2-en-1-one (0.01 mole), absolute ethanol (50 ml, 0.003 mole) and sodium hydroxide solution (5 ml, 1.25N) and 10 ml solution of hydrogen peroxide (30%) was stirred continuously for 2 hrs at room temperature. It was then diluted with ice-cold water and acidified with dilute hydrochloric acid. When solid separated, it was filtered, washed well with water, dried and crystallized from isopropyl alcohol as pale yellow crystals, yield 86.00%. The compound was analyzed for...
\[ \lambda_{\text{max}} 343 \text{nm} \ (\text{CH}_2\text{OH}), \ \text{m.p.} \ 168-170^\circ \text{C}, \ \text{Rf} \ 0.56 \] (benzene : acetone ; 8 : 1) and Elemental Analysis Calculated (%) C 69.44; H 5.50; O 20.56; N 4.50.

IR, KBr \[ \nu_{\text{max}} : \ \text{IR (KBr, cm}-1) \ 1166.97 (\text{C-C Stretch}), 1678.13 (\text{C=C Stretch}), 1502.60 (\text{Aromatic C=C ring Stretch}), 1560.46 (\text{Aromatic C=C ring Stretch}), 796.63 \] (Aromatic C-H Bend), 3668.73 (Phenolic O-H Stretch), 1678.13 (C=O Stretch), 1317.43 (Ar- tertiary amine C-N Stretch), 2848.96 (N-CH3 Stretch, C-H Stretch), 2848.96 [Methoxy C-H Stretch (O-CH3)], 1205.55 (C-O Stretch).

\[ \lambda_{\text{max}} 308 \text{nm} \ (\text{CH}_2\text{OH}), \ \text{m.p.} \ 107-109^\circ \text{C}, \ \text{Rf} \ 0.44 \] (benzene : acetone ; 8 : 1) and Elemental Analysis Calculated (%) C 63.481; H 3.66; O 21.14; Cl 11.71.

IR, KBr \[ \nu_{\text{max}} : \ \text{IR (KBr, cm}-1) \ 1161.19 (\text{C-C Stretch}), 1687.77 (\text{C=C Stretch}), 1498.74 (\text{Aromatic C=C ring Stretch}), 1531.53 (\text{Aromatic C=C ring Stretch}), 796.63 (\text{Aromatic C-H Bend}), 3661.01 (Phenolic O-H Stretch), 1716.07 (C=O Stretch), 754.19 (C-CI Stretch), 2843.17 [Methoxy C-H Stretch (O-CH3)], 1201.69 (C=O Stretch), 1687.77 (C=O Stretch, 1.4 quinones), 1608.69 (C=O Stretch 1.4 quinones). MASS 302 [M+H]+, 271.5 [M+H-CH2OH]+, 166.3 [M+H-CH2OH-HCI]+, 166.3 [M+H-HCl- CH2OH]+, 123.1, 1498.74 (Aromatic C=C ring). 1H-NMR 6.46-7.91 (7 H-benzene, m), 3.88 (O-CH3, s), 13.90 (OH-enol, s), 3.08-3.10 (6H-N(CH3)2, dd).

13C-NMR 40.18 (C2), 130.94 (C6 benzene), 131 (C=O), 145 (C=O), 55.53 (C=O-C).

Synthesis of 3-(4-chlorophenyl)-1-(2-hydroxy-4-methoxyphenyl) prop-en-1-one (Intermediate V)

A mixture of P-methoxy-2-hydroxyacetophenone (0.01 mole) and p-chloro benzaldehyde (0.01 mole) was stirred in absolute ethanol (95.0 %, 30 ml) and then an aqueous solution of potassium hydroxide (15 ml) was added to it. The reaction mixture was kept overnight at room temperature and then was poured into crushed ice and acidified with dilute hydrochloric acid. When solid separated, it was filtered, washed well with water, dried and recrystallized from isopropyl alcohol as pale yellow crystals, yield 83.00%. The compound was analyzed for \[ \lambda_{\text{max}} 313 \text{nm} \ (\text{CH}_4\text{OH}), \ \text{m.p.} \ 92-94^\circ \text{C}, \ \text{Rf} \ 0.64 \] (benzene: acetone; 8: 1) and Elemental Analysis Calculated (% C 68.85; H 4.95; O 26.20.

IR (KBr, cm-1) 1128.39 (C-C Stretch), 1631.83 (C=C Stretch), 1575.99 (Aromatic C=C ring Stretch), 796.63 (Aromatic C-H Bend), 3674.51 (Phenolic O-H Stretch), 1716.07 (C=O Stretch), 756.12 (C-CI Stretch), 2843.17 [Methoxy C-H Stretch (O-CH3)].

Synthesis of 3-((furan-2-yl)-1-(2-hydroxy-4-methoxyphenyl)prop-en-2-1-one (Intermediate VI)

A mixture of p-methoxy-2-hydroxyacetophenone (0.01 mole) and furfuraldehyde (0.01 mole) was stirred in absolute ethanol (50 ml, 0.003 mole) and sodium hydroxide (30 %) was stirred continuously for 2 hrs at room temperature. It was then diluted with ice-cold water and acidified with dilute hydrochloric acid. When solid separated, it was filtered, washed well with water, dried and recrystallized from isopropyl alcohol as pale yellow crystals, yield 83.00%. The compound was analyzed for \[ \lambda_{\text{max}} 308 \text{nm} \ (\text{CH}_2\text{OH}), \ \text{m.p.} \ 107-109^\circ \text{C}, \ \text{Rf} \ 0.44 \] (benzene : acetone ; 8 : 1) and Elemental Analysis Calculated (%) C 63.481; H 3.66; O 21.14; Cl 11.71.

IR, KBr \[ \nu_{\text{max}} : \ \text{IR (KBr, cm}-1) \ 1161.19 (\text{C-C Stretch}), 1687.77 (\text{C=C Stretch}), 1498.74 (\text{Aromatic C=C ring Stretch}), 1531.53 (\text{Aromatic C=C ring Stretch}), 796.63 (\text{Aromatic C-H Bend}), 3661.01 (Phenolic O-H Stretch), 1716.07 (C=O Stretch), 754.19 (C-CI Stretch), 2843.17 [Methoxy C-H Stretch (O-CH3)], 1201.69 (C=O Stretch), 1687.77 (C=O Stretch, 1.4 quinones), 1608.69 (C=O Stretch 1.4 quinones). MASS 302 [M+H]+, 271.5 [M+H-CH2OH]+, 166.3 [M+H-CH2OH-HCI]+, 166.3 [M+H-HCl- CH2OH]+, 123.1, 1498.74 (Aromatic C=C ring). 1H-NMR 6.46-7.91 (7 H-benzene, m), 3.75 (O-CH3, s), 12.5 (OH-enol. 13C-NMR 130.26 (C6 benzene), 131 (C=O), 127.15 (C6 benzene), 76.75 (C=O-C).

Synthesis of 3-((furan-2-yl)-1-(2-hydroxy-4-methoxyphenyl)prop-en-2-1-one (Intermediate VI)

A mixture of p-methoxy-2-hydroxyacetophenone (0.01 mole) and furfuraldehyde (0.01 mole) was stirred in absolute ethanol (95.0 %, 30 ml) and then an aqueous solution of potassium hydroxide (15 ml) was added to it. The reaction mixture was kept overnight at room temperature and then was poured into crushed ice and acidified with dilute hydrochloric acid. The chalcone derivative precipitates out as solid that was filtered, dried and recrystallized from absolute ethanol as pale yellow crystals, yield 87.00%. The compound was analyzed for \[ \lambda_{\text{max}} 313 \text{nm} \ (\text{CH}_4\text{OH}), \ \text{m.p.} \ 92-94^\circ \text{C}, \ \text{Rf} \ 0.64 \] (benzene: acetone; 8: 1) and Elemental Analysis Calculated (% C 68.85; H 4.95; O 26.20.

IR (KBr, cm-1) 1128.39 (C-C Stretch), 1631.83 (C=C Stretch), 1575.99 (Aromatic C=C ring Stretch), 794.70 (Aromatic C-H Bend), 3672.59 (Phenolic O-H Stretch), 1716.70 (C=O Stretch), 1869.08 (Five-membered ring anhydride), 2848.96 [Methoxy C-H Stretch (O-CH3)].

Synthesis of 2-(furan-2-yl)-3-hydroxy-7-methoxy-4H-chromen-4-one(Compound VI)

A mixture of 3-(furan-2-yl)-1-(2-hydroxy-4-methoxyphenyl)prop-en-2-1-one (0.01 mole), absolute ethanol (50 ml, 0.003 mole) and sodium hydroxide solution (5 ml,1.25N) and 10ml solution of hydrogen peroxide (30 %) was stirred continuously for 2 hrs at room temperature. It was then diluted with ice-cold water and...
acidified, it was filtered, washed well with water, dried and crystallized from isopropyl alcohol as pale yellow crystals, yield 90.32%. The compound was analyzed for \( \lambda_{\text{max}} \) 328 nm (CH\textsubscript{3}OH), \text{m.p.} 120-122°C, \( R_f \) 0.50 (benzene: acetone; 8 : 1) and Elemental Analysis Calculated (%C 65.12; H 3.90; O 30.98).

IR, KBr \( \nu_{\text{max}} \) : IR (KBr, cm\textsuperscript{-1}) 1126.47 (C-C Stretch), 1681.98 (C=O Stretch), 1577.82 (Aromatic C=C ring Stretch), 796.35 (Aromatic C-H Bend), 3661.01 (Phenolic O-H Stretch), 1726.35 (C=O Stretch), 1872.94 (Five-membered ring anhydride), 2848.96 [Methoxy C-H Stretch (O-CH\textsubscript{3})], 1209.41 (C-O Stretch), 1681.98 (C=O Stretch, 1,4 quinones), 1610.61 (C=O Stretch 1,4 quinones). MASS 258 [M+H]+, 228 [M+H-CH\textsubscript{2}OH]+, 161.3 [M+H-CH\textsubscript{2}OH-C\textsubscript{4}H\textsubscript{4}O]+, 161.3 0.2A+, 106 0.4A+. 1H-NMR 6.76-7.88 (6 H, m), 3.86 (O-CH\textsubscript{3}, s), 13.5 (OH-enol. 13C-NMR 55.59 (C-O-C), 143.89 (C-O), 191.49 (C=O), 151.69 (C=C benzene), 145.12 (C4 furan), 145.12 (C-O-C furan), 145.12 (C=O furan), 111.98 (C-C furan).

**Synthesis of 3-(4-(dimethylamino)phenyl)-1-(2-hydroxy-5-methyl phenyl) prop-2-en-1-one (Intermediate VII)**

A mixture of 5-methyl-2-hydroxyacetophenone (0.01 mole) and \( p \)-dimethyl amino benzaldehyde (0.01 mole) was stirred in absolute ethanol (95.0 %, 30 ml) and then an aqueous solution of potassium hydroxide (15 ml) was added to it. The reaction mixture was kept overnight at room temperature and then was poured into crushed ice and acidified with dilute hydrochloric acid. The chalcone derivative precipitates out as solid that was filtered, washed well with water, dried and crystallized from isopropyl alcohol as pale yellow crystals, yield 83.02%. The compound was analyzed for \( \lambda_{\text{max}} \) 336 nm (CH\textsubscript{3}OH), \text{m.p.} 180-182°C, \( R_f \) 0.57 (benzene : acetone; 8 : 1) and Elemental Analysis Calculated (%C 73.20; H 5.80; O 16.25; N 4.74).

IR, KBr \( \nu_{\text{max}} \) : IR (KBr, cm\textsuperscript{-1}) 1166.97 (C-C Stretch), 1691.63 (C=C ring Stretch), 1489.10 (Aromatic C=C ring Stretch), 1568.18 (Aromatic C-C ring Stretch), 794.70 (Aromatic C-H Bend), 3620.51 (Phenolic O-H Stretch), 1726.35 (C=O Stretch), 1363.72 (Ar- tertiary (C=O Stretch, 1,4 quinones), 1608.69 (C=O Stretch 1,4 quinones). MASS 295 [M+H]+, 277.5 [M+H-H\textsubscript{2}O]+, 263 [M+H-H\textsubscript{2}O-CH\textsubscript{3}]+, 235 [M+H-H\textsubscript{2}O-CH\textsubscript{3}-NHCH\textsubscript{2}]+, 160.3 [M+H-H\textsubscript{2}O-CH\textsubscript{3}-NHCH\textsubscript{2}-C\textsubscript{6}H\textsubscript{6}]+, 144.5 [M+H-H\textsubscript{2}O-CH\textsubscript{3}-NHCH\textsubscript{2}-C\textsubscript{6}H\textsubscript{6}-CH\textsubscript{3}]+, 220 [M+H-H\textsubscript{2}O-CH\textsubscript{3}-NHCH\textsubscript{2}-C\textsubscript{6}H\textsubscript{6}]+, 144.5 [M+H-H\textsubscript{2}O-CH\textsubscript{3}-NHCH\textsubscript{2}-C\textsubscript{6}H\textsubscript{6}-CH\textsubscript{3}]+, 220 [M+H-H\textsubscript{2}O-CH\textsubscript{3}-NHCH\textsubscript{2}-C\textsubscript{6}H\textsubscript{6}]+, 144.5 [M+H-H\textsubscript{2}O-CH\textsubscript{3}-NHCH\textsubscript{2}-C\textsubscript{6}H\textsubscript{6}]+. 1H-NMR 6.48-7.9 (7 H-benzene, m), 3.87 (OH-enol, s), 3.075 (6H-N(CH\textsubscript{3})\textsubscript{2}, dd). 13C-NMR 166.49 (C=O), 130.94 (C-O), 152.17 (C-O-C), 130.09 (C=C benzene), 122.27 (C=C benzene), 144.61 (C=C benzene), 22.70 (C=C benzene), 40.12 (C2).

**Synthesis of 3-(4-(chlorophenyl)-1-(2-hydroxy-5-methyl phenyl) prop-2-en-1-one (Intermediate VIII)**

A mixture of 5-methyl-2-hydroxyacetophenone (0.01 mole) and \( p \)-chloro benzaldehyde (0.01 mole) was stirred in absolute ethanol (95.0 %, 30 ml) and then an aqueous solution of potassium hydroxide (15 ml) was added to it. The reaction mixture was kept overnight at room temperature and then was poured into crushed ice and acidified with dilute hydrochloric acid. The chalcone derivative precipitates out as solid that was filtered, dried and recrystallized from isopropyl alcohol as pale yellow crystals, yield 82.23%. The compound was analyzed for \( \lambda_{\text{max}} \) 312 nm (CH\textsubscript{3}OH), \text{m.p.} 118-120°C, \( R_f \) 0.75 (benzene : acetone; 8 : 1) and Elemental Analysis Calculated (%C 73.20; H 5.80; O 16.25; N 4.74).

IR (KBr, cm\textsuperscript{-1}) 1163.11 (C-C Stretch), 1681.96 (C=C Stretch), 1487.17 (Aromatic C=C ring Stretch) 1523.82 (Aromatic C=C ring Stretch), 792.77 (Aromatic C-H Bend), 3616.65 (Phenolic O-H Stretch), 1716.70 (C=O Stretch), 1342.50 (Artertiary amine C-N Stretch), 2802.66 (N-CH\textsubscript{3} Stretch, C-H Stretch).

**Synthesis of 2-[4-(dimethylamino) phenyl]-3-hydroxy-6-methyl-4H-chromen-4-one (Compound VII)**

A mixture of 3-[4-(dimethylamino) phenyl]-1-(2-hydroxy-5-methylphenyl) prop-2-en-1-one (0.01 mole), absolute ethanol (50 ml, 0.003 mole) and sodium hydroxide solution (5 ml, 1.25N) and 10ml solution of hydrogen peroxide (30 %) was stirred continuously for 2 hrs at room temperature. It was then diluted with ice-cold water and acidified with dilute hydrochloric acid. When solid separated, it was filtered, washed well with water, dried and crystallized from isopropyl alcohol as pale yellow crystals, yield 79.00%. The compound was analyzed for \( \lambda_{\text{max}} \) 336 nm (CH\textsubscript{3}OH), \text{m.p.} 180-182°C, \( R_f \) 0.57 (benzene : acetone; 8 : 1) and Elemental Analysis Calculated (%C 73.20; H 5.80; O 16.25; N 4.74).

IR (KBr, cm\textsuperscript{-1}) 1176.62 (C-C Stretch), 1678.13 (C=C Stretch), 1489.10 (Aromatic C=C ring Stretch), 1587.47 (Aromatic C=C-C ring Stretch), 794.70 (Aromatic C-H Bend), 3672.59 (Phenolic O-H Stretch), 1747.57 (C=O Stretch), 756.12 (C-Cl Stretch), 2850.88 (N-CH\textsubscript{3} Stretch, C-H Stretch).
Synthesis of 2-(4-chlorophenyl)-3-hydroxy-6-methyl-4H-chromen-4-one (Compound VIII)

A mixture of 3-(4-chlorophenyl)-1-(2-hydroxy-5-methylphenyl) prop-2-en-1-one (0.01 mole), absolute ethanol (50 ml, 0.003 mole) and sodium hydroxide solution (5 ml, 1.25N) and 10 ml solution of hydrogen peroxide (30%) was stirred continuously for 2 hrs at room temperature. It was then diluted with ice-cold water and acidified with dilute hydrochloric acid. When solid separated, it was filtered, washed well with water, dried and crystallized from isopropyl alcohol as pale yellow crystals, yield 70.00%. The compound was analyzed for \( \lambda_{\text{max}} \) 344nm(CH3OH), m.p. 112-114°C, \( R_f \) 0.42 (benzene: acetone; 8:1) and Elemental Analysis Calculated (% C 67.03; H 3.87; O 16.74; Cl 12.37.

IR, KBr \( \nu_{\text{max}} \) : IR (KBr, cm-1) 1170.83 (C-C Stretch), 1691.63 (C=O Stretch), 1487.17 (Aromatic C=C ring Stretch), 1575.89 (Aromatic C=C-C ring Stretch), 781.20 (Aromatic C-H Bend), 3664.87 (Phenolic O-H Stretch), 1923.09 (C=O Stretch), 752.26 (C=O Stretch), 2850.88 (N-CH3 Stretch, C-H Stretch), 1213.27 (C-O Stretch), 1616.40 (C=O Stretch 1,4 quinines), 1614.47 (C=O Stretch, 1,4 quinoines). MASS 286 [M+H]+, 257.6 [M+H+CH3OH]+, 146.3 [M+H+CH3OH-C6H5Cl]+, 175.5 [M+H-HCl-C6H6]+, 162.3 [M+H-HCl-C6H6-C3H5]+, 162.3 [M+H+CH3-C6H6]+, 146.4 0.2A+, 200 0.4B+, 138.4 1,3A+, 105 1.4A+, 175.2 [M+H-B ring]+, 113 [M+H-A ring]+. 1H-NMR 6.81-7.79 (7 H-benzene, m), 2.19 (CH3, s), 13.81 (OH-enol. 13C-NMR 20.95 (C-CH3), 188.219 (C=O), 135.290 (C-O), 158.82 (C-O-C), 135.290 (CH=CH benzene), 118.67 (C=C benzene), 157.22 (CH=CH benzene), 126.36 (C=C benzene), 130.350 (CH=CH benzene).

Synthesis of 3-(furan-2-yl)-1-(2-hydroxy-5-methylphenyl) prop-2-en-1-one (Intermediate IX)

A mixture of 5-methyl-2-hydroxyacetophenone (0.01 mole) and furfuraldehyde (0.01 mole) was stirred in absolute ethanol (95.0%, 30 ml) and then an aqueous solution of potassium hydroxide (15 ml) was added to it. It was then diluted with ice-cold water and acidified with dilute hydrochloric acid. The chalcone derivative precipitates out as a solid that was filtered, Adried and recrystallized from absolute ethanol as pale yellow crystals, yield 88.00%. The compound was analyzed for \( \lambda_{\text{max}} \) 344nm (CH3OH), m.p. 102-104°C, \( R_f \) 0.65 (benzene: acetone; 8: 1) Elemental Analysis Calculated (% C 73.67; H 5.30; O 21.03.

IR (KBr, cm-1) 1132.25 (C-C Stretch), 1668.48 (C=C Stretch), 1487.17 (Aromatic C=C ring Stretch), 1595.18 (Aromatic C=C-C ring Stretch), 792.77 (Aromatic C-H Bend), 3616.65 (Phenolic O-H Stretch), 1734.06 (C=O Stretch), 1857.51 (Five-membered ring anhydride), 2850.88 (N-CH3 Stretch, C-H Stretch).

Synthesis of 2-(furan-2-yl)-3-hydroxy-6-methyl-4H-chromen-4-one (Compound IX)

A mixture of 3-(furan-2-yl)-1-(2-hydroxy-5-methylphenyl) prop-2-en-1-one (0.01 mole), absolute ethanol (50 ml, 0.003 mole) and sodium hydroxide solution (5 ml, 1.25N) and 10 ml solution of hydrogen peroxide (30% ) was stirred continuously for 2 hrs at room temperature. It was then diluted with ice-cold water and acidified with dilute hydrochloric acid. When solid separated, it was filtered, washed well with water, dried and crystallized from isopropyl alcohol as pale yellow crystals, yield 79.00%. The compound was analyzed for \( \lambda_{\text{max}} \) 345nm (CH3OH), m.p. 147-149°C, \( R_f \) 0.49 (benzene: acetone; 8:1) and Elemental Analysis Calculated (% C 69.42; H 4.16; O 26.42.

IR, KBr \( \nu_{\text{max}} \) : IR (KBr, cm-1) 1132.25 (C-C Stretch), 1668.48 (C=C Stretch), 1487.17 (Aromatic C=C ring Stretch), 1595.18 (Aromatic C=C-C ring Stretch), 792.77 (Aromatic C-H Bend), 3616.65 (Phenolic O-H Stretch), 1712.85 (C=C Stretch), 1859.44 (Five-membered ring anhydride), 3107.43 (N-CH3 Stretch, C-H Stretch), 1203.62 (C-O Stretch), 1668.48 (C=O Stretch, 1,4 quinoines), 1614.47 (C=O Stretch 1,4 quinoines). MASS 242 [M+H]+, 225 [M+H+CH3]+, 214 [M+H+CH3OH]+, 151 0.2A+, 151 0.4B+. 1H-NMR 6.86-7.21 (3H-furan, dd), 2.33 (CH3, s), 12.72 (OH-enol. 13C-NMR 20.491 (C-CH3), 188.219 (C=O), 135.290 (C-O), 158.82 (C-O-C), 135.290 (CH=CH benzene), 118.67 (C=C benzene), 157.22 (CH=CH benzene), 126.36 (C=C benzene), 130.350 (CH=CH benzene).

Pharmacology:

Antibacterial screening:

Synthesized compounds in DMSO (200 μg/ml). Streptomycin (200 μg/ml) is used as a standard for both gram positive and gram negative bacteria and, Molten Hinton (MH) agar (25 ml)

Microbes used (200 μg/ml):

Gram positive (Bacillus subtilis, Staphylococcus Aureus) and Gram negative bacteria (Escherichia coli, Shigella sonei).

Experimental Design for Anti-bacterial studies: Agar media was poured into sterile universals and was inoculated with different bacterial species. After setting, it is incubated at 37 °C for 24 hr. A well was prepared in the bacterial agar culture. 0.2 ml test solution of synthesized compounds as well as standard was poured into the wells, using a dropping pipette under...
aseptic condition and labeled accordingly. The plates were maintained at room temperature for 3-5 hrs to allow diffusion into the medium and were incubated at 37 ± 1°C for 24 hr. Diameter of zones of inhibition (mm) surrounding each of the well was recorded and the results were compared to Streptomycin for antibacterial activity. Effectiveness of susceptibility is proportional to the diameter of inhibition of zone was measured.

**Anti fungal Screening**

Synthesized compounds in DMSO (200 μg/ml). Ketoconazole (200 μg/ml) is used as a standard for fungus studies by plate hole diffusion technique. Sabouraud dextrose agar medium (25 ml).

**Microbes used (200 μl):** Phytopathogenic fungi (*Aspergillus niger, Rhizopus nigricans*)

**Experimental for Anti-fungal studies:** Universals containing the broth was inoculated with different species of fungus and spreaded well. After setting, it is incubated at 28°C overnight. Using a sterile cork borer (6 mm), four holes per plate were made in the fungal culture. 0.2 ml of test solution of synthesized compounds was poured into the wells, using a dropping pipette under aseptic condition and labeled accordingly. The plates were maintained at room temperature for 4-5 hr to allow diffusion into the medium and were incubated at 28 ± 1°C overnight for 36 to 48 hr and the zone diameter was then recorded. The results were compared to Ketoconazole for antifungal activity. Effectiveness of susceptibility is proportional to the diameter of inhibition of zone was measured.

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<tr>
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**Analyzed data for anti bacterial screening**

<table>
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Acknowledgement

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References


