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Synthesis, *In Vitro* Antioxidant and Antimicrobial Evaluation of 3-Hydroxy Chromone Derivatives

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Abstract : 3-hydroxy chromones were synthesized by Algar Flynn Oyamada method which includes oxidative cyclization of 2-hydroxy chalcones in basic solution by hydrogen peroxide. Chalcones required were synthesized by Claisen-Schmidt condensation of substituted 2-hydroxy acetophenones with substituted aromatic aldehydes using PEG-400 as recyclable solvent. The synthesized compounds were evaluated for *in vitro* antioxidant activity by 1,1-diphenyl-2-pycrylhydrazyl radical scavenging assay. Additionally, these compounds were also screened for *in vitro* antibacterial and antifungal activity by agar cup method and Poison plate method, respectively. The structures of the synthesized compounds were characterized by IR, ^{1}H NMR and Mass spectra. The antioxidant activity data revealed that all the synthesized derivatives of chromone showed greater antioxidant activity due to presence of phenolic hydroxyl group, 4-oxo group and 2,3-double bond. Further the activity increased with introduction of more phenolic hydroxyl group and adjacent methoxy group in the structure. The antimicrobial activity data showed that the compounds exhibited good antibacterial and antifungal activity which is attributed to the presence of phenolic hydroxyl group and 4-oxo group in the structure.

Keywords : Chromone, Chalcone, Claisen-Schmidt condensation, Algar Flynn Oyamada method, Antioxidant, Antibacterial, Antifungal.

Introduction

Chromones are a group of naturally occurring compounds that are ubiquitous in nature, especially in plants. The word chromone is derived from the Greek word chroma, meaning “color”, which indicates that many chromone derivatives can exhibit a diversity of colors.[1]

Chromones are oxygen-containing heterocyclic compounds with a benzoannelated γ-pyrone ring being chromone (4H-chromen-4-one, 4H-1-benzopyran-4-one) the parent compound (Figure 1).3-hydroxy chromoneis the class of flavonoids structurally related to flavonols (Figure 1). [2]

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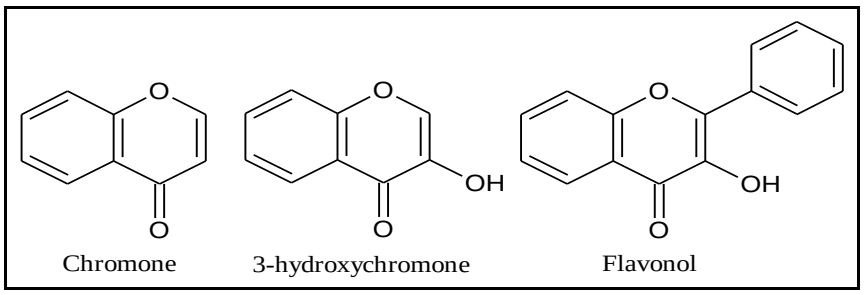


Figure 1: Chromone core, 3-hydroxy chromone and flavonol

Chromones are used as scaffolds for the development of bioactive compounds. These frameworks are naturally occurring derivatives containing anoxa-pyran ring.[3] The most frequently found chromone-based natural products are the 2-arylsubstituted chromones (flavonoids) carrying hydroxy and/or methoxy groups on the aromatic rings.[4] The substitution pattern of the chromone scaffolds determines their different biological effects. Known effects of these types of compounds are antioxidant,[5] antiviral,[6] antimicrobial,[7] anti-inflammatory,[8]antiobesity[9] and kinase inhibition.[10] Hence, chromones can be considered privileged structures, defined as "a single molecular framework ableto provide ligands for diverse receptors".[11]

Prompted by all these observations, we report herein the synthesis, *in vitro* antioxidant and antimicrobial activities of 3-hydroxy chromone derivatives.

Experimental

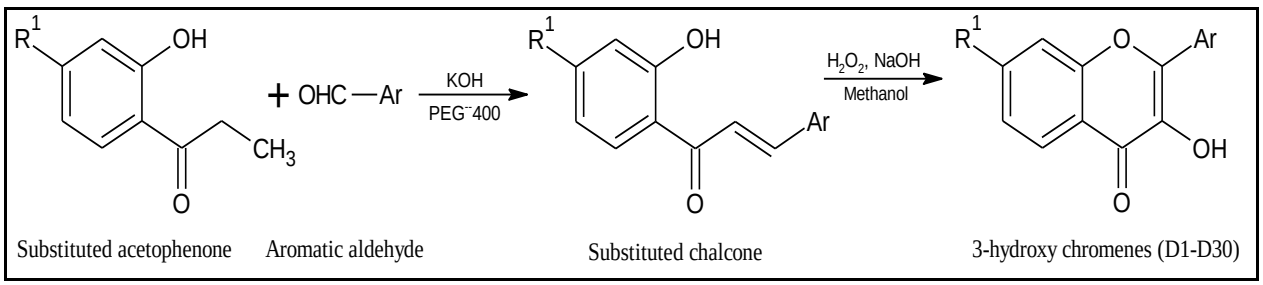
Aldehydes and acetophenones were procured from Sigma-Aldrich and SD fine chemicals. Allother chemicals are of AR grade. Melting points were determined inopen capillaries on a Metal Toledo digital melting point apparatus and areuncorrected. Purity of the compounds was checked using TLC Silica gel 60 F_{254} aluminium sheets procured from Merck and spots were detected in Ultra Violet Fluorescence analysis cabinet. The IR spectra recorded using KBr Pellets on Shimadzu IRAffinity-1 Fourier Transform infrared (IR)spectrophotometer (cm^{-1}). ^1H nuclear magnetic resonance (NMR)spectra recorded on Bruker AVANCE III 500 MHz NMR spectrometer using TMS asinternal standard (chemical shifts in δ ppm) and mass spectra recorded onJEOL GC MATE II GC-MS system.

General procedure for synthesis of 2-hydroxy chalcone derivatives (Scheme 1):

An equimolar mixture of substituted acetophenone (1mmol), aromatic aldehyde (1mmol) and potassium hydroxide (2mmol) was stirred in PEG-400 (15 ml) at 40°C for 1 hour. After completion of reaction (monitored by TLC), the crude mixture was worked up in ice-cold water (100ml). The product which separated out was filtered, washed with water and recrystallized with suitable solvent. The filtrate was evaporated to remove water leaving PEG behind. The same PEG was utilized to synthesize further chalcones.[12]

General procedure for synthesis of 3-hydroxy chromone derivatives (Scheme 1, D1-D30):

Hydrogen peroxide (4ml, 35%) added to a mixture of chalcone (10mmol) in methanol (70ml) and dilute sodium hydroxide (35ml, 5%) and cooled in ice bath. The solution was stirred for 5 hours at 0-5°C and then for 16 hours at room temperature. After completion of reaction (monitored by TLC), the reaction mixture was poured into ice water and acidified with dilute hydrochloric acid (6N). The precipitate was collected by filtration, washed with water and recrystallized with suitable solvent.[13]



Scheme 1: Synthesis of substituted chalcones and 3-hydroxy chromones (D1-D30)

3-hydroxy-2-(3-nitrophenyl)-chromone (D1) Yield 85%; m.p. 158-160^{o}C; IR (KBr) υ_{max}: 3647.83 (O-H str), 3080.32 (C-H str), 1716.65 (C=O str), 1608.63 (C=C str), 1529.55 (N=O str),1309.24 (C-N str), 1298.09 (C-O str) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ: 6.971 (s, 1H-OH), 7.792 (dd, J=7.7,1.5, 1H-H5), 7.063 (m, 1H-H6), 7.482 (m, 1H-H7), 7.047 (dd, J=8.2, 1.7, 1H-H8), 7.660 (m, 1H-H2'), 7.265 (m, 1H-H4'), 7.467 (m, 1H-H5'), 7.732 (m, 1H-H6') ppm; Mass m/z: 283.2304 (M-1).

2-(4-chlorophenyl)-3-hydroxy-chromone (D2) Yield: 92%; m.p. 176-178^{o}C; IR (KBr) υ_{max}: 3630.03 (O-H str), 3049.46 (C-H str), 1718.23 (C=O str), 1591.27 (C=C str), 1294.24 (C-O str), 785.03 (C-Cl str)cm^{-1}; ^{1}H NMR ($CDCl_3$) δ: 7.345 (s, 1H-OH), 8.146 (dd, J=8.7, 6.3, 1H-H5), 7.568 (m, 1H-H6), 7.490 (m, 1H-H7), 7.656 (dd, J=9.6,2.6, 1H-H8), 7.943 (m, 2H-H2',H6'), 7.797 (m, 2H-H3',H5') ppm; Mass m/z: 272.6810 (M-1).

3-hydroxy-2-phenyl-chromone (D3) Yield: 76%; 196-198^{o}C; IR (KBr) υ_{max}: 3628.10 (O-H str), 3070.68 (C-H str), 1716.65 (C=O str), 1608.63 (C=C str), 1286.52 (C-O str) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ: 7.401 (s, 1H-OH), 8.256 (dd, J=8.7,6.3, 1H-H5), 7.260 (m, 1H-H6), 7.476 (m, 1H-H7), 7.093 (dd, J=9.6,2.6, 1H-H8), 7.555 (m, 2H-H2',H6'), 7.416 (m, 2H-H3',H5'), 7.405 (m, 1H-H4') ppm; Mass m/z: 238.2402 (M-1).

3-hydroxy-2-(4-methylphenyl)-chromone (D4) Yield: 81%; 202-204^{o}C; IR (KBr) υ_{max}: 3618.46 (O-H str), 3072.60, 2850.79 (C-H str), 1716.65 (C=O str), 1606.70 (C=C str), 1280.73 (C-O str) cm^{-1}; ^{1}H NMR (CDCl3) δ: 6.955 (s, 1H-OH), 7.922 (dd, J=8.7, 6.3, 1H-H5), 6.940 (m, 1H-H6), 7.411 (m, 1H-H7), 6.925 (dd, J=9.6,2.6, 1H-H8), 7.569 (m, 2H-H2',H6'), 7.168 (m, 2H-H3',H5'), 3.743 (s, 3H-CH_3) ppm; Mass m/z: 252.2601 (M-1).

2-(4-bromophenyl)-3-hydroxy-chromone (D5) Yield: 93%; m.p. 284-286^{o}C; IR (KBr) υ_{max}: 3632.53 (O-H str), 3066.82 (C-H str), 1749.44 (C=O str), 1568.13 (C=C str), 1298.09 (C-O str), 625.18 (C-Br str) cm^{-1};^{1}H NMR (CDCl3) δ: 7.369 (s, 1H-OH), 8.055 (dd, J=8.7, 6.3, 1H-H5), 7.355 (m, 1H-H6), 7.644 (m, 1H-H7), 7.341 (dd, J=9.6,2.6, 1H-H8), 7.676 (m, 2H-H2',H6'), 7.667 (m, 2H-H3',H5') ppm; Mass m/z: 317.1304 (M-1).

2-(2-chlorophenyl)-3-hydroxy-chromone (D6) Yield: 72%; m.p. 185-187^{o}C; IR (KBr) υ_{max}: 3630.03 (O-H str), 3061.03 (C-H str), 1716.65 (C=O str), 1587.42 (C=C str), 1296.84 (C-O str), 784.72 (C-Cl str) cm^{-1};^{1}H NMR ($CDCl_3$) δ: 7.031 (s, 1H-OH), 7.952 (dd, J=7.6,1.7, 1H-H5), 7.241(m, 1H-H6), 7.535(m, 1H-H7), 7.096(dd, J=8.3,1.5, 1H-H8), 7.465(m, 1H-H3'), 7.259(m, 1H-H4'), 7.048(m,1H-H5'), 7.745(m, 1H-H6') ppm; Mass m/z: 272.6810 (M-1).

2-(3-chlorophenyl)-3-hydroxy-chromone (D7) Yield: 68%; m.p. 192-194^{o}C; IR (KBr) υ_{max}: 3628.10 (O-H str), 3057.17 (C-H str), 1716.65 (C=O str), 1587.42 (C=C str), 1282.66 (C-O str), 783.68 (C-Cl str) cm^{-1};^{1}H NMR ($CDCl_3$) δ: 7.328 (s, 1H-OH), 8.013 (dd, J=7.7,1.7, 1H-H5), 7.395 (m, 1H-H6), 7.535 (m, 1H-H7), 7.346 (dd, J=8.3,1.9, 1H-H8), 7.555 (m, 1H-H2'), 7.377 (m, 1H-H4'), 7.515 (m,1H-H5'), 7.788 (m, 1H-H6') ppm; Mass m/z: 272.6801 (M-1).

2-(4-fluorophenyl)-3-hydroxy-chromone (D8) Yield: 88%; m.p. 275-277^{o}C; IR (KBr) υ_{max}: 3628.10 (O-H str), 3066.82 (C-H str), 1715.72 (C=O str), 1587.42 (C=C str), 1388.75 (C-F str), 1296.16 (C-O str) cm^{-1};^{1}H NMR ($CDCl_3$) δ: 7.379 (s, 1H-OH), 8.003 (dd, J=8.7, 6.3, 1H-H5), 7.281 (m, 1H-H6), 7.024 (m, 1H-H7), 7.115 (dd, J=9.6,2.6, 1H-H8), 7.607 (m, 2H-H2',H6'), 7.400 (m, 2H-H3',H5') ppm; Mass m/z: 256.2206 (M-1).

2-(3-chlorophenyl)-3,7-dihydroxy-chromone (D9) Yield: 75%; m.p. 216-21^{o}C; IR (KBr) υ_{max}: 3634.45 (O-H str), 3049.46 (C-H str), 1714.72 (C=O str), 1573.91 (C=C str), 1294.45 (C-O str), 783.10 (C-Cl str) cm^{-1};^{1}H NMR ($CDCl_3$) δ: 7.412 (s, 2H-OH), 8.023 (dd, J=8.6, 6.4, 1H-H5), 7.424 (td, J=8.3,2.2, 1H-H6), 7.409 (dd, J=9.6,2.2, 1H-H8), 7.559 (m, 1H-H2'), 7.468 (m, 1H-H4'), 7.493 (m, 1H-H5'), 7.761 (m, 1H-H6') ppm; Mass m/z: 288.6801 (M-1).

2-(3-bromophenyl)-3-hydroxy-chromone (D10) Yield: 90%; m.p. 318-320^{o}C; IR (KBr) υ_{max}: 3647.39 (O-H str), 3062.96 (C-H str), 1714.72 (C=O str), 1596.20 (C=C str), 1294.95 (C-O str), 628.30 (C-Br str) cm^{-1};^{1}H NMR ($CDCl_3$) δ: 7.439 (s, 2H-OH), 8.120(dd, J=8.6, 6.4, 1H-H5), 7.422 (m, 1H-H6), 7.417 (m, 1H-H7), 7.405(dd,J=9.6,2.2, 1H-H8), 7.562(m, 1H-H2'), 7.470(m, 1H-H4'), 7.490(m, 1H-H5'), 7.768(m,1H-H6') ppm; Mass m/z: 317.1302 (M-1).

2-(3,4-dimethoxyphenyl)-3-hydroxy-chromone (D11) Yield: 80%; m.p. 287-289^{o}C; IR (KBr) υ_{max}: 3639.68 (O-H str), 3078.39, 2841.15 (C-H str), 1716.01 (C=O str), 1598.99 (C=C str), 1292.31 (C-O str), 1028.06 (C-O-C) cm^{-1};^{1}H NMR ($CDCl_3$) δ: 6.937 (s, 1H-OH), 7.938 dd, J=7.4,1.6, 1H-H5), 7.167 (m, 1H-H6), 7.532 (m, 1H-

H7), 7.029 (dd, J=8.4,1.6, 1H-H8), 7.501 (m, 1H-H2'), 3.964 (s, 6H-OCH3), 7.013 (m, 1H-H5'), 7.865 (m, 1H-H6') ppm; Mass m/z: 298.2910 (M-1).

3,7-dihydroxy-2-(4-methylphenyl)-chromone (D12) Yield: 72%; m.p. 256-258^{o}C; IR (KBr) υ_{max}: 3618.46 (O-H str), 3026.31, 2852.72 (C-H str), 1716.65 (C=O str), 1589.34 (C=C str), 1284.59 (C-O str) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ: 7.180 (s, 2H-OH), 7.902 (dd, J=8.7, 6.3, 1H-H5), 7.159 (td, J=8.3,2.2,1H-H6), 6.800(dd, J=9.6,2.6, 1H-H8), 7.799(m, 2H-H2',H6'), 7.474(m, 2H-H3',H5'), 3.837(s, 3H-CH3) ppm; Mass m/z: 268.2601 (M-1).

3-hydroxy-2-(3-methylphenyl)-chromone (D13) Yield: 78%; m.p. 224-226^{o}C; IR (KBr) υ_{max}: 3639.68 (O-H str), 3026.31, 2999.31 (C-H str), 1716.65 (C=O str), 1600.92 (C=C str), 1271.09 (C-O str) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ: 7.313 (s, 1H-OH), 8.066 (dd, J=7.7,1.7, 1H-H5), 7.457 (m, 1H-H6), 7.769 (m, 1H-H7), 7.330 (dd, J=8.3,1.9, 1H-H8), 7.789 (m, 1H-H2'), 7.438 (m, 1H-H4'), 7.493 (m, 1H-H5'), 7.809 (m, 1H-H6'), 3.322 (s, 3H-CH3) ppm; Mass m/z: 252.2601 (M-1).

3,7-dihydroxy-2-(3-nitrophenyl)-chromone (D14) Yield: 77%; m.p. 244-246^{o}C; IR (KBr) υ_{max}: 3647.83 (O-H str), 3080.32 (C-H str), 1710.86 (C=O str), 1598.99 (C=C str), 1529.55 (N=O str), 1309.24 (C-N str) 1282.99 (C-O str) cm^{-1};^{1}H NMR ($CDCl_3$) δ: 7.415 (s, 2H-OH), 8.016 (dd, J=8.6, 6.4, 1H-H5), 7.427 (td, J=8.3,2.2, 1H-H6), 7.405 (dd, J=9.6,2.2, 1H-H8), 7.558 (m, 1H-H2'), 7.463 (m, 1H-H4'), 7.491 (m, 1H-H5'), 7.767 (m, 1H-H6') ppm; Mass m/z: 299.2304 (M-1).

2-(4-chlorophenyl)-3,7-dihydroxy-chromone (D15) Yield: 75%; m.p. 188-190^{o}C; IR (KBr) υ_{max}: 3630.03 (O-H str), 3093.82 (C-H str), 1718.23 (C=O str), 1593.20 (C=C str), 1282.66 (C-O str), 761.88 (C-Cl str) cm^{-1};^{1}H NMR ($CDCl_3$) δ: 7.183 (s, 2H-OH), 7.907 (dd, J=8.7, 6.3, 1H-H5), 7.155 (td, J=8.3,2.2, 1H-H6), 6.802 (dd, J=9.6,2.6, 1H-H8), 7.798 (m, 2H-H2',H6'), 7.473 (m, 2H-H3',H5') ppm; Mass m/z: 288.6810 (M-1).

3,7-dihydroxy-2-phenyl-chromone (D16) Yield: 72%; m.p. 262-264^{o}C; IR (KBr) υ_{max}: 3628.10 (O-H str), 3080.32 (C-H str), 1716.65 (C=O str), 1604.77 (C=C str), 1294.24 (C-O str) cm^{-1};^{1}H NMR ($CDCl_3$) δ: 7.405 (s, 2H-OH), 8.257 (dd, J=8.7, 6.3, 1H-H5), 7.263 (td, J=8.4,2.6, 1H-H6), 7.099(dd, J=9.6,2.6, 1H-H8), 7.551(m, 2H-H2',H6'), 7.419(m, 2H-H3',H5'), 7.405(m, 1H-H4') ppm; Mass m/z: 254.2306 (M-1).

2-(4-bromophenyl)-3,7-dihydroxy-chromone (D17) Yield: 92%; m.p. 326-328^{o}C; IR (KBr) υ_{max}: 3639.68 (O-H str), 3064.89 (C-H str), 1714.72 (C=O str), 1596.20 (C=C str), 1293.17 (C-O str), 644.22 (C-Br str) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ: 7.224 (s, 2H-OH), 8.008 (dd, J=8.7, 6.3, 1H-H5), 6.543 (td, J=8.3,2.7, 1H-H6), 6.439 (dd, J=9.6,2.6, 1H-H8), 7.554 (m, 2H-H2',H6'), 7.354 (m, 2H-H3',H5') ppm; Mass m/z: 333.1301 (M-1).

2-(4-fluorophenyl)-3,7-dihydroxy-chromone (D18) Yield: 88%; m.p. 272-274 ^{o}C; IR (KBr) υ_{max}: 3628.10 (O-H str), 3066.82 (C-H str), 1716.01 (C=O str), 1578.42 (C=C str), 1398.39 (C-F str), 1271.09 (C-O str) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ: 6.971 (s, 2H-OH), 8.004 (dd, J=8.7, 6.3, 1H-H5), 7.262 (td, J=8.3,2.7, 1H-H6), 6.795 (dd, J=9.6,2.6, 1H-H8), 7.739 (m, 2H-H2',H6'), 7.357 (m, 2H-H3',H5') ppm; Mass m/z: 272.2201 (M-1).

3-hydroxy-2-(2-nitrophenyl)-chromone (D19) Yield: 70%; m.p. 285-287^{o}C; IR (KBr) υ_{max}: 3608.81 (O-H str), 3032.10 (C-H str), 1710.22 (C=O str), 1598.99 (C=C str), 1529.55 (N=O str), 1340.53 (C-N str), 1288.45 (C-O str) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ: 6.975(s, 1H-OH), 7.962 (dd, J=7.6,1.7, 1H-H5), 7.174(m, 1H-H6), 7.536(m, 1H-H7), 7.101(dd, J=8.3,1.5, 1H-H8), 7.502(m, 1H-H3'), 7.260(m, 1H-H4'), 7.062(m, 1H-H5'), 7.743(m, 1H-H6') ppm; Mass m/z: 283.2312 (M-1).

2-(3,4-dimethoxyphenyl)-3,7-dihydroxy-chromone (D20) Yield: 72%; m.p. 258-260^{o}C; IR (KBr) υ_{max}: 3628.10 (O-H str), 3078.39, 2995.45 (C-H str), 1716.65 (C=O str), 1575.84 (C=C str), 1286.52 (C-O str), 1026.13 (C-O-C) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ: 6.998 (s, 2H-OH), 7.792 (dd, J=8.8, 6.2, 1H-H5), 6.842 (td, J=8.1,2.4, 1H-H6), 6.804 (dd, J=9.5,2.5, 1H-H8), 7.480 (m, 1H-H2'), 3.883 (s, 6H-OCH_3), 7.108 (m, 1H-H5'), 7.747 (m, 1H-H6') ppm; Mass m/z: 314.2814 (M-1).

3,7-dihydroxy-2-(4-nitrophenyl)-chromone (D21) Yield: 75%; m.p. 236-238^{o}C; IR (KBr) υ_{max}: 3618.32 (O-H str), 3032.62 (C-H str), 1716.65 (C=O str), 1587.42 (C=C str), 1529.42(N=O str), 1311.59 (C-N str), 1288.45 (C-O str) cm^{-1};^{1}H NMR ($CDCl_3$) δ: 6.983 (s, 2H-OH), 7.822 (dd, J=8.7, 6.3, 1H-H5), 6.968 (td, J=8.3,2.7, 1H-H6), 6.587 (dd, J=9.6,2.6, 1H-H8), 7.561 (m, 2H-H2',H6'), 7.282 (m, 2H-H3',H5') ppm; Mass m/z: 299.2301 (M-1).

3,7-dihydroxy-2-(2-nitrophenyl)-chromone (D22) Yield: 71%; m.p. 240-242^{o}C; IR (KBr) υ_{max}: 3614.60 (O-H str), 3032.10 (C-H str), 1716.65 (C=O str), 1598.99 (C=C str), 1529.55 (N=O str), 1340.53 (C-N str), 1244.09 (C-O str) cm^{-1};^{1}H NMR ($CDCl_3$) δ: 6.973 (s, 2H-OH), 7.965 (dd, J=7.3,1.9, 1H-H5), 7.177 (td, J=8.1,2.6, 1H-H6), 7.107 (dd, J=8.4,1.8, 1H-H8), 7.503 (m, 1H-H3'), 7.264 (m, 1H-H4'), 7.069 (m, 1H-H5'), 7.742 (m, 1H-H6') ppm; Mass m/z: 299.2304 (M-1).

3-hydroxy-2-(3-hydroxy-4-methoxyphenyl)-chromone (D23) Yield: 80%; m.p. 256-258^{o}C; IR (KBr) υ_{max}: 3628.10 (O-H str), 3072.39, 2991.59 (C-H str), 1716.65 (C=O str), 1541.12 (C=C str), 1276.88 (C-O str), 1022.27 (C-O-C) cm^{-1};^{1}H NMR ($CDCl_3$) δ: 6.987 (s, 2H-OH), 7.919 (dd, J=7.1,1.9, 1H-H5), 7.086 (m, 1H-H6), 7.582 (m, 1H-H7), 7.083 (dd, J=8.4,1.5, 1H-H8), 7.516 (m, 1H-H2'), 3.982 (s, 3H-OCH_3), 7.032 (m, 1H-H5'), 7.855 (m, 1H-H6') ppm; Mass m/z: 284.2602 (M-1).

2-(3-bromophenyl)-3,7-dihydroxy-chromone (D24) Yield: 94%; m.p. 324-326^{o}C; IR (KBr) υ_{max}: 3608.81 (O-H str), 3064.89 (C-H str), 1716.65 (C=O str), 1570.06 (C=C str), 1261.45 (C-O str), 661.27 (C-Br str) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ: 7.189(s,2H-OH), 7.813(dd, J=8.2, 6.3, 1H-H5), 6.632(td, J=8.5,2.4, 1H-H6), 6.479(dd, J=9.7,2.8, 1H-H8), 7.551(m, 1H-H2'), 7.203(m, 1H-H4'), 7.454(m, 1H-H5'), 7.742(m, 1H-H6') ppm; Mass m/z: 333.1304 (M-1).

2-(2-chlorophenyl)-3,7-dihydroxy-chromone (D25) Yield: 66%; m.p. 272-274^{o}C; IR (KBr) υ_{max}: 3628.10 (O-H str), 3064.89 (C-H str), 1716.65 (C=O str), 1541.12 (C=C str), 1281.09 (C-O str), 756.10 (C-Cl str) cm^{-1};^{1}H NMR ($CDCl_3$) δ: 6.991 (s, 2H-OH), 8.081 (dd J=7.3,1.9, 1H-H5), 7.177 (td J=8.1,2.6, 1H-H6), 7.132 (dd, J=8.4,1.8, 1H-H8), 7.535 (m, 1H-H3'), 7.284 (m, 1H-H4'), 7.023 (m, 1H-H5'), 7.754 (m, 1H-H6') ppm; Mass m/z: 288.6800 (M-1).

3,7-dihydroxy-2-(4-methoxyphenyl)-chromone (D26) Yield: 86%; m.p. 296-298^{o}C; IR (KBr) υ_{max}: 3628.10 (O-H str), 3072.39, 2985.81 (C-H str), 1701.22 (C=O str), 1541.12 (C=C str), 1294.24 (C-O str), 1033.85 (C-O-C) cm^{-1};^{1}H NMR ($CDCl_3$) δ: 6.957 (s, 2H-OH), 7.878 (dd, J=8.5, 6.1, 1H-H5), 7.262 (td, J=8.7,2.6, 1H-H6), 6.890 (dd, J=9.6,2.8, 1H-H8), 7.820 (m, 2H-H2',H6'), 7.467 (m, 2H-H3',H5'), 3.835 (s, 3H-OCH_3) ppm; Mass m/z: 284.2610 (M-1).

2-(furan-2-yl)-3,7-dihydroxy-chromone (D27) Yield: 92%; m.p. 316-318^{o}C; IR (KBr) υ_{max}: 3612.67 (O-H str), 3076.46 (C-H str), 1716.65 (C=O str), 1541.05 (C=C str), 1265.30 (C-O str), 1020.34 (C-O-C) cm^{-1};^{1}H NMR ($CDCl_3$) δ: 7.264 (s, 2H-OH), 7.815 (dd, J=8.8, 6.6, 1H-H5), 6.731 (td, J=8.4,2.9, 1H-H6), 6.724 (dd, J=9.5,2.6, 1H-H8), 7.538 (m, 1H-H3'), 7.439 (m, 1H-H4'), 7.469 (m, 1H-H5') ppm; Mass m/z: 244.1906 (M-1).

3-hydroxy-2-(4-methoxyphenyl)-chromone (D28) Yield: 85%; m.p. 265-267^{o}C; IR (KBr) υ_{max}: 3628.10 (O-H str), 3066.82, 2947.23 (C-H str), 1716.65 (C=O str), 1541.12 (C=C str), 1296.16 (C-O str), 1022.27 (C-O-C) cm^{-1};^{1}H NMR ($CDCl_3$) δ: 6.993 (s, 1H-OH), 7.931 (dd, J=7.6,1.8, 1H-H5), 7.127 (m, 1H-H6), 7.625 (m, 1H-H7), 7.110 (dd, J=8.3,1.7, 1H-H8), 7.638 (m, 2H-H2',H6'), 7.249 (m, 2H-H3',H5'), 3.863 (s, 3H-OCH_3) ppm; Mass m/z: 268.2609 (M-1).

2-(furan-2-yl)-3-hydroxy-chromone (D29) Yield: 93%; m.p. 310-312^{o}C; IR (KBr) υ_{max}: 3649.32 (O-H str), 3095.75 (C-H str), 1716.65 (C=O str), 1568.13 (C=C str), 1298.09 (C-O str), 1016.49 (C-O-C) cm^{-1};^{1}H NMR ($CDCl_3$) δ: 6.53 (s, 1H-OH), 7.930 (dd, J=7.8,1.6, 1H-H5), 7.260 (m, 1H-H6), 7.572 (m, 1H-H7), 7.027 (dd, J=8.3,1.9, 1H-H8), 7.542 (m, 1H-H3'), 7.125 (m, 1H-H4'), 7.491 (m, 1H-H5')ppm; Mass m/z: 228.2010 (M-1).

3-hydroxy-2-(4-nitrophenyl)-chromone (D30) Yield: 84%; m.p. 254-256^{o}C; IR (KBr) υ_{max}: 3614.60 (O-H str), 3032.10 (C-H str), 1714.72 (C=O str), 1566.20 (C=C str), 1539.20 (N=O str), 1336.67 (C-N str), 1269.16 (C-O str) cm^{-1};^{1}H NMR ($CDCl_3$) δ: 6.996 (s, 1H-OH), 7.963 (dd, J=8.7, 6.3, 1H-H5), 7.281 (m, 1H-H6), 7.028 (m, 1H-H7), 7.046 (dd, J=9.6,2.6, 1H-H8), 7.608 (m, 2H-H2',H6'), 7.469 (m, 2H-H3',H5') ppm; Mass m/z: 283.2310 (M-1).

***In vitro*antioxidant study**

The synthesized compounds were evaluated for their *in vitro* antioxidant activity by 1,1-diphenyl-2-picrylhydrazyl(DPPH)radical scavenging method. DPPH is a stable free radical that can accept an electron or hydrogen radical to become a stable diamagnetic molecule. Due to its odd electron, the methanolic solution of DPPH shows a strong absorption band at 517 nm. DPPH radical reacts with various electron donating

molecules (reducing agents or antioxidants). When electrons become paired off, bleaching of the DPPH solution is the result. This results in the formation of the colourless 1,1-diphenyl-1-picryl hydrazine. Reduction of the DPPH radicals can be estimated quantitatively by measuring the decrease in absorbance at 517 nm.[14] A radical scavenging antioxidant reacts with DPPH stable free radical and converts to DPPH-H. The change in the absorbance produced in this reaction has been used to measure antioxidant properties.

Stock solution of DPPH (1.3 mg/mL) in methanol was prepared. Stock solution of DPPH 100 µL was added to 3.0 mL of methanol and absorbance was recorded at 517 nm. The various concentrations of compounds (20, 40, 60, 80 and 100µg/mL) were prepared. All sample solutions 1.0 mL each is diluted with 3.0 mL with methanol and 100 µL of stock solution of DPPH was added. Test tubes were kept for 30 min in light to complete the reaction. After 30 min, absorbance of each test tube was recorded at 517 nm on UV-VIS spectrophotometer against methanol as a blank.[15]Control experiment was carried out with solvent only, and ascorbic acid was used as reference standard. All the measurements were performed in triplicate, and the mean of triplicate measurements was used to calculate the percentage reduction of DPPH by the following formula.

$$\% \text{ scavenging} = \frac{\text{Absorbance of control - Absorbance of test sample}}{\text{Absorbance of control}} \times 100$$

Where,
Control is absorbance of a DPPH solution without compound;
Test is the absorbance of the test compound with DPPH.

The degree of discoloration indicates the free radical scavenging efficiency of the compound. The effective concentration of sample required to scavenge DPPH radical by 50% (IC_{50} value) was obtained by linear regression analysis of dose-response curve plotted between % inhibition and concentrations.

***In vitro* antibacterial activity**

The antibacterial activity of synthesized compounds was measured by agar cup method. Nutrient agar (Himedia) was prepared and sterilized at 15psi for 15 minutes in the autoclave. It was allowed to cool below 45^{o}C and seeded with turbid suspension of test bacteria separately, prepared from 24 hours old slant cultures. 3% inocula were used every time. The bacterial cultures selected were, two Gram negative cultures viz. Escherichia coli, Salmonella typhi and two Gram positive cultures viz. Staphylococcus aureus, Bacillus subtilis. This seeded preparation was then poured in sterile petri plate under aseptic condition and allowed to solidify.

Cups of 10mm diameter were borered in the agar plate with sterile cork borer, 100µl of compound solution prepared in dimethyl sulphoxide (1%) was added in the cup under aseptic condition with the help of micropipette. 100µl of DMSO was also placed in one of the cup as blank (negative control). A standard antibiotic disk impregnated with 10 units of Penicillin was also placed on the seeded nutrient agar surface as standard reference antibiotic (positive control).

The plates were kept in refrigerator for 15 minutes to allow diffusion of the compound from agar cup into the medium. Then the plates were shifted to incubator at 37^{o}C and incubated for 24 hours.[16]

After incubation plates were observed for the zone of inhibition of bacterial growth around the agar cup. Results were recorded by measuring the zone of inhibition in millimeter (mm) using zone reader.

***In vitro* antifungal activity**

Antifungal activity of title compounds was performed by Poison plate method. The medium used was Potato dextrose agar (Himedia). The medium was prepared and sterilized at 10psi in autoclave for 15 minutes. Then the compound to be tested is added to the sterile medium in aseptic condition so as to get final concentration at 1%. A plate with DMSO was prepared as blank (negative control) similarly a plate with 1% Greseofulvin was prepared as standard reference plate (positive control).

Aspergillus niger, Penicillium chrysogenum, Fusarium moneliforme and Aspergillus flavus were selected as test fungal cultures. They were allowed to grow on slant for 48 hours so as to get profuse sporulation. 5ml of 1:100 aqueous solution of Tween 80 was added to the slant and spores were scraped with the help of nicrome wire loop to form suspension.

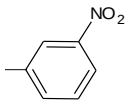
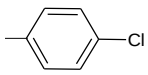
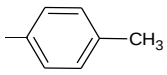
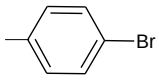
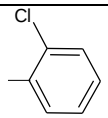
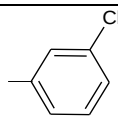
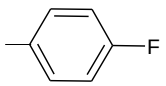
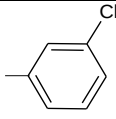
The fungal suspension was spot inoculated on the plates prepared using compound with the help of nicrome wire loop. The plates were incubated at room temperature for 48 hours.[16]

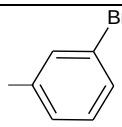
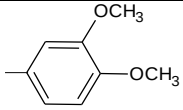
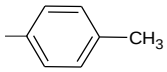
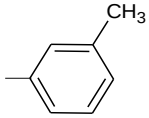
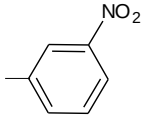
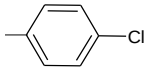
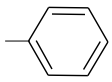
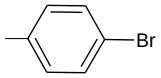
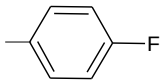
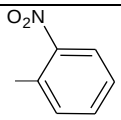
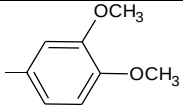
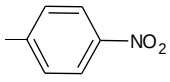
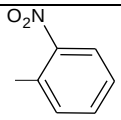
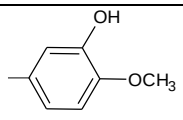
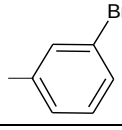
After incubation plates were observed for the growth of inoculated fungi. Results were recorded as growth of fungi (no antifungal activity), reduced growth of fungi (moderate antifungal activity), and no growth of inoculated fungi (antifungal activity).

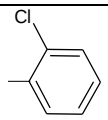
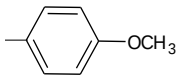
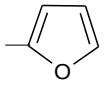
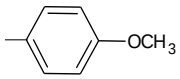
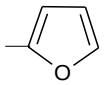
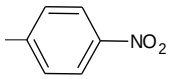
Results and Discussion

In our laboratory, a facile method has been adopted for the synthesis of 3-hydroxy chromones by base catalyzed cyclization of chalcones in the presence of hydrogen peroxide. The respective chalcones has been synthesized by Claisen-Schmidt condensation of substituted 2-hydroxy acetophenones with substituted aromatic aldehydes using PEG-400 as recyclable solvent. The reaction was simple and efficient and yields the title compounds almost in pure form. However the resultant compounds were purified by recrystallization with suitable solvent. The compounds obtained in good yields ranging from 66% to 94%. The physical data of the synthesized compounds were given in Table 1. The structures of the synthesized compounds were confirmed by IR, ^{1}H NMR, and mass spectra.

Table 1: Physical data of synthesized 3-hydroxy chromone derivatives

Compound code	R^1	Ar	Molecular formula	Molecular Weight (g)	Yield (%)	Melting Point (^{o}C)	Rf value*
D1	H		$C_{15}H_9NO_5$	283.23	85	158-160	0.65
D2	H		$C_{15}H_9ClO_3$	272.68	92	176-178	0.51
D3	H		$C_{15}H_{10}O_3$	238.24	76	196-198	0.71
D4	H		$C_{16}H_{12}O_3$	252.26	81	202-204	0.75
D5	H		$C_{15}H_9BrO_3$	317.13	93	284-286	0.78
D6	H		$C_{15}H_9ClO_3$	272.68	72	185-187	0.53
D7	H		$C_{15}H_9ClO_3$	272.68	68	192-194	0.57
D8	H		$C_{15}H_9FO_3$	256.22	88	275-277	0.65
D9	OH		$C_{15}H_9ClO_4$	288.68	75	216-218	0.72

D10	H		$C_{15}H_9BrO_3$	317.13	90	318-320	0.86
D11	H		$C_{17}H_{14}O_5$	298.29	80	287-289	0.82
D12	OH		$C_{16}H_{12}O_4$	268.26	72	256-258	0.77
D13	H		$C_{16}H_{12}O_3$	252.26	78	224-226	0.76
D14	OH		$C_{15}H_9NO_6$	299.23	77	244-246	0.69
D15	OH		$C_{15}H_9ClO_4$	288.68	75	188-190	0.76
D16	OH		$C_{15}H_{10}O_4$	254.23	72	262-264	0.82
D17	OH		$C_{15}H_9BrO_4$	333.13	92	326-328	0.71
D18	OH		$C_{15}H_9FO_4$	272.22	88	272-274	0.79
D19	H		$C_{15}H_9NO_5$	283.23	70	285-287	0.81
D20	OH		$C_{17}H_{14}O_6$	314.28	72	258-260	0.67
D21	OH		$C_{15}H_9NO_6$	299.23	75	236-238	0.70
D22	OH		$C_{15}H_9NO_6$	299.23	77	240-242	0.71
D23	H		$C_{16}H_{12}O_5$	284.26	80	256-258	0.73
D24	OH		$C_{15}H_9BrO_4$	333.13	94	324-326	0.83

D25	OH		$C_{15}H_9ClO_4$	288.68	66	272-274	0.77
D26	OH		$C_{12}H_{16}O_5$	284.26	86	296-298	0.75
D27	OH		$C_{13}H_8O_5$	244.19	92	316-318	0.84
D28	H		$C_{16}H_{12}O_4$	268.26	85	265-267	0.74
D29	H		$C_{13}H_8O_4$	228.20	93	310-312	0.81
D30	H		$C_{15}H_9NO_5$	283.23	84	254-256	0.73

*Solvent system-4:1 ratio of n-Hexane and ethyl acetate

The IR spectra of final compounds showed an absorption band at 3649.32-3608.81 cm^{-1} indicative of O-H stretching of a phenolic group. The absorption bands in the region of 3095.75-2841.15 cm^{-1} indicative of C-H stretching and in the region of 1298.09-1244.09 cm^{-1} corresponds to C-O stretching. The absorption band corresponding to carbonyl group appeared in the region of 1749.44-1701.22 cm^{-1}. The absorption peaks at 1608.63-1541.05 cm^{-1} indicate the C=C stretching vibrations. The absorption band representing N=O stretching was appeared in the region of 1539.20-1529.42 $cm^{-1}$and those representing C-N stretching was appeared in the region of 1340.53-1309.24 cm^{-1}. The compounds containing halogen group viz. fluoro, chloro and bromo showed an absorption band in the region of 1398.39-1388.75 cm^{-1}, 785.03-756.10cm^{-1} and 661.27-625.18 cm^{-1}, respectively. The compounds with methoxy substitution exhibited absorption band in the region of 1033.85-1016.49 cm^{-1} due to C-O-C stretching vibration.

The NMR spectra of title compounds showed singlets in the region of δ 6.937-7.439 due to the protons of phenolic hydroxy group. The spectra of the compounds showed singlets in the region of δ 3.322-3.743 indicative of methyl protons. The compounds containing methoxy group exhibited characteristic signals in the region of δ 3.835-3.982. The spectra also exhibited double doublets, triple doublets and multiplets in the region of δ 6.439-8.257 assignable to aromatic protons in all the NMR spectra of final compounds confirm the structures of title compounds.

The mass spectra of final compounds showed their characteristic molecular ion peak. Thus, the structures of the compounds were confirmed by IR, ^{1}H NMR and mass spectral data.

In vitro antioxidant studies

The synthesized compounds, 3-hydroxy chromones were evaluated for their *in vitro* antioxidant properties at 20, 40, 60, 80, and 100μM by DPPH radical scavenging model. The activity data are presented in Table 2.

The study revealed that all the synthesized 3-hydroxy chromones exhibited potent antioxidant activity with IC_{50} below 70 μM. As all the compounds contain 2,3 double bond, one phenolic hydroxyl group and adjacent to that is the presence of α,β-unsaturated keto group. These structural features were responsible for the presence of antioxidant activity. According to literature, the 2,3 double bond in conjugation with a 4-oxo function is responsible for electron delocalization from aromatic ring at 2nd position. The antioxidant potency is related to structure in terms of electron delocalization of the aromatic nucleus. When these compounds react with free radicals, the phenoxyl radicals produced are stabilized by the resonance effect of the aromatic nucleus.

Additionally, the 3-OH and 4-oxo functional groups are required for maximum radical scavenging potential.[17]Among the synthesized compounds, the compound D23, 3-hydroxy-2-(3-hydroxy-4-methoxyphenyl)-chromone showed highest activity with IC_{50} at 10.04μM as compared to standard. The reason may be due to the presence of methoxy group, adjacent to phenolic hydroxyl group making the molecule as sterically hindered phenol. This observation is in confirmation with the literature that steric hindrance of phenolic moiety is one of the factors governing antioxidant efficiency.[18] The presence of more phenolic hydroxyl group resulted in increase of antioxidant activity and indicated that the phenolic moiety is necessary to confer better antioxidant and radical scavenging properties.

Table 2: *In vitro* antioxidant activity of 3-hydroxy chromones

↓Compound Concentration→	% scavenging					IC_{50}
	20	40	60	80	100	
D1	40.58	52.64	60.95	69.54	80.21	37.57
D2	35.71	47.62	55.98	69.21	78.45	46.18
D3	22.95	34.58	46.85	60.07	67.74	66.19
D4	30.58	38.21	50.13	58.21	67.54	62.27
D5	34.27	41.85	49.65	60.32	68.74	57.78
D6	42.58	50.94	62.87	70.18	77.28	35.69
D7	39.13	42.84	52.94	60.13	68.49	52.87
D8	33.84	40.26	48.54	56.87	67.65	61.34
D9	46.24	55.19	64.32	83.48	91.24	29.40
D10	28.57	35.48	47.69	55.87	64.88	67.53
D11	31.57	40.98	52.16	64.81	75.26	54.68
D12	44.96	58.32	67.19	77.46	85.21	26.62
D13	28.54	42.67	58.13	70.54	84.76	50.12
D14	48.51	59.17	66.78	78.59	87.33	22.75
D15	46.34	58.17	70.98	81.44	90.16	24.98
D16	43.59	54.63	66.98	77.25	85.49	30.67
D17	45.17	54.09	64.83	75.54	81.60	29.78
D18	47.58	59.21	67.99	76.84	82.53	21.54
D19	40.51	53.82	65.20	85.99	94.26	34.28
D20	49.21	62.87	75.49	85.44	91.63	17.30
D21	50.71	59.21	69.45	78.68	85.44	17.94
D22	48.97	55.46	65.82	73.54	81.24	23.67
D23	52.47	66.29	75.82	85.21	91.62	10.04
D24	47.54	61.87	74.58	87.25	93.55	26.88
D25	49.08	64.97	72.84	81.15	89.55	15.68
D26	50.87	64.22	76.97	86.68	92.45	14.11
D27	41.27	50.23	57.42	65.88	72.97	40.88
D28	31.48	38.52	46.13	56.28	64.75	66.09
D29	30.87	41.68	50.98	62.49	75.64	55.86
D30	44.15	53.97	63.25	71.11	80.43	31.94
Standard	51.95	65.18	74.11	84.97	89.24	11.06

***In vitro* antibacterial activity:**

The synthesized 3-hydroxy chromones were evaluated for their *in vitro* antibacterial activity measured by agar cup method against two Gram negative cultures viz. Escherichia coli, Salmonella typhi and two Gram positive cultures viz. Staphylococcus aureus, Bacillus subtilis. The activity data are presented in Table 3.

The study revealed that the compounds with phenolic hydroxyl group exhibited greater antibacterial activity in both gram positive and gram negative bacteria. Among these, the compound D23, 3-hydroxy-2-(3-hydroxy-4-methoxyphenyl)-chromone showed potent antibacterial activity against all the four strains of bacteria. The compound D12, 3,7-dihydroxy-2-(4-methylphenyl)-chromone exhibited greater antibacterial

activity against Salmonella typhi as compared to standard with zone of inhibition of 25mm. The compounds 2-(3-chlorophenyl)-3,7-dihydroxy-chromone (D9), 3,7-dihydroxy-2-(4-methylphenyl)-chromone (D12), 3,7-dihydroxy-2-(3-nitrophenyl)-4H-1-benzo pyran-4-one (D14), 2-(4-bromophenyl)-3,7-dihydroxy-chromone (D17), 3-hydroxy-2-(3-hydroxy-4-methoxyphenyl)-chromone (D23) and 3,7-dihydroxy-2-(4-methoxyphenyl)-chromone (D26) showed maximum activity against Escherichia coli as compared to standard with zone of inhibition of 16mm, 17mm, 12mm, 15mm, 20mm and 13mm respectively. Thus the main structural feature responsible for antibacterial activity is thehydroxyl group and the 4-oxo group. The weaker antibacterial activity of compounds against gram positive bacteria may be due to presence of 2,3-double bond as mentioned in literature.[19] The presence of more phenolic hydroxyl group resulted in increase of antibacterial activity and indicated that the phenolic moiety is necessary to confer better antibacterial properties.

Table 3: *In vitro* antibacterial activity of 3-hydroxy chromones

Compound	Zone of Inhibition (mm)			
	Escherichia coli	**Salmonella typhi**	**Staphylococcus aureus**	**Bacillus subtilis**
D1	-ve	-ve	11	17
D2	-ve	-ve	12	11
D3	-ve	12	16	16
D4	-ve	12	17	17
D5	-ve	-ve	12	12
D6	-ve	-ve	18	20
D7	-ve	-ve	11	11
D8	-ve	-ve	20	20
D9	16	-ve	22	26
D10	-ve	12	15	16
D11	-ve	-ve	11	11
D12	17	25	23	15
D13	-ve	-ve	18	17
D14	12	-ve	21	23
D15	-ve	-ve	22	18
D16	-ve	-ve	20	21
D17	15	-ve	20	25
D18	-ve	-ve	18	21
D19	-ve	-ve	16	20
D20	-ve	-ve	19	20
D21	-ve	-ve	20	17
D22	-ve	-ve	20	23
D23	20	19	23	25
D24	-ve	-ve	20	20
D25	-ve	-ve	22	19
D26	13	-ve	12	-ve
D27	-ve	-ve	20	21
D28	-ve	-ve	12	15
D29	-ve	-ve	14	14
D30	-ve	-ve	-ve	20
DMSO	-ve	-ve	-ve	-ve
Penicillin	11	24	36	30

-ve: No antibacterial activity

***In vitro* antifungal activity:**

The synthesized 3-hydroxy chromones were evaluated for their *in vitro* antifungal activity measured by poison plate method against Aspergillus niger, Penicillium chrysogenum, Fusarium moneliforme and Aspergillus flavus. The activity data are presented in Table 4.

The study revealed that the almost all the synthesized compounds exhibited greater antifungal activity in all four strains of fungi. Among these, the compound 3-hydroxy-2-(3-hydroxy-4-methoxyphenyl)-chromone (D23), 2-(2-chlorophenyl)-3,7-dihydroxy-chromone (D25), 3,7-dihydroxy-2-(4-methoxyphenyl)-chromone (D26) and 2-(furan-2-yl)-3,7-dihydroxy-chromone (D27) showed more than 90% reduction in growth in all the four strains. Thus the presence of phenolic hydroxyl group and 4-oxo group is also responsible for antifungal activity of title compounds.

Table 4: *In vitro* antifungal activity of 3-hydroxy chromones

Compound	Aspergillus niger	Penicillium chrysogenum	Fusarium moneliforme	Aspergillus flavus
D1	RG	RG	RG	RG
D2	-ve	RG	-ve	RG
D3	RG	RG	RG	RG
D4	RG	RG	RG	RG
D5	RG	RG	RG	RG
D6	RG	-ve	-ve	RG
D7	RG	RG	RG	RG
D8	RG	-ve	-ve	RG
D9	RG	RG	-ve	RG
D10	RG	-ve	-ve	RG
D11	RG	-ve	-ve	RG
D12	RG	RG	RG	RG
D13	RG	-ve	-ve	RG
D14	RG	RG	RG	RG
D15	RG	-ve	-ve	RG
D16	RG	RG	RG	12
D17	RG	-ve	-ve	RG
D18	RG	-ve	-ve	RG
D19	RG	-ve	-ve	RG
D20	RG	RG	RG	RG
D21	-ve	-ve	-ve	-ve
D22	RG	RG	RG	RG
D23	-ve	-ve	-ve	-ve
D24	RG	-ve	-ve	RG
D25	-ve	-ve	-ve	-ve
D26	-ve	-ve	-ve	-ve
D27	-ve	-ve	-ve	-ve
D28	-ve	-ve	-ve	RG
D29	RG	-ve	-ve	-ve
D30	RG	-ve	-ve	RG
DMSO	+ve	+ve	+ve	+ve
Greseofulvin	-ve	-ve	-ve	-ve

+ve: Growth (Antifungal activity absent); -ve: No growth (More than 90% reduction in growth); RG: Reduced growth (More than 50% and less than 90% reduction in growth)

Conclusion

An eco-friendly and easy method has been used to synthesize the title compounds. The method includes mild reaction conditions, use of recyclable solvent and easy work-up procedure for the isolation of products. The reaction led to the expected products with high yield and in all most all cases the products obtained in pure form.

The present research work revealed that the compounds of 3-hydroxy chromones containing 2,3-double bond, phenolic substitution and α,β-unsaturated keto group showed greater antioxidant activity in DPPH radical

scavenging model. These active compounds also exhibited statistically significant antibacterial and antifungal activity. Hence, these compounds can be developed as useful therapeutic agents after establishing their safety pharmacology and toxicity profile. Nevertheless, the obtained results in all these assays are advocating in terms that additional synthesis of new derivatives and further investigations in this therapeutic area might provide interesting and potentially promising results that can finally be applied for enriching our knowledge and experience in the development of new chemical leads with this specific biological activity.

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Conflict of Interest

The authors confirm that this article content has no conflict of interest.

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