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Research Article

Synthesis, Characterization, and Antioxidant Activities of Genistein, Biochanin A, and Their Analogues

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A series of naturally occurring genistein **(3)** and biochanin A **(4)** compounds and their analogues were synthesized from phloroglucinol. The structures of all the synthesized compounds were established by the combined use of ^{1}HNMR, ^{13}CNMR, IR spectral data, and mass spectrometry; their antioxidant activities were investigated. Most of the synthesized compounds show moderate-to-high activity; only two compounds exhibit no significant activity.

1. Introduction

Isoflavonoids **(2)** are one of the main subclasses of flavonoids **(1)** which contain C6-C3-C6 carbon skeleton based on 3-phenylchroman [1]. They are widely distributed in many plants [2, 3] and in various common foods which are particularly abundant in seeds and other parts of *leguminous plants* [4, 5]. Significant amounts of isoflavonoids were found in soybeans [6]. Epidemiological studies show that a high consumption of soybean derived foods correlates to a low incidence of hormone related diseases such as cancers, osteoporosis, and cardiovascular diseases [7]. Genistein **(3)** has been one of the most widely studied natural products and has exhibited a wide range of biological activities such as anticancer [8–11], antioxidant [12–16], and antimicrobial activities [17, 18]. Genistein can bind to both the Estrogen Receptor alpha (ERα) and the Estrogen Receptor beta (ERβ), although it has a higher affinity for the ERβ [19], and genistein is thought to exert its estrogenic effects through mechanisms similar to those of estradiol [20]. Biochanin A **(4)** is the 4′-*O*-methyl derivative of genistein and biochanin A is the predominant isoflavone found in *alfalfa*, *Trifolium pratense*, and *Cicer arietinum* [21] which has an inhibitory and apoptogenic effect on certain cancer cells such as pancreatic cancer and prostate cancer [22, 23].

The biological and biochemical activity, potential chemopreventive property, therapeutic properties, and genistein affinity towards a large variety of molecular targets attracted the interest of many researchers. The number of publications regarding the synthesis and biological evaluation of genistein and its derivatives has increased [24–27]. This paper presents the synthesis of genistein, biochanin A, and their synthetic analogues to investigate the antioxidant activities and the effect of various substituents on the activity of the molecule.

2. Results and Discussion

2.1. Antioxidant Activity

2.1.1. DPPH (1,1-Diphenyl-2-picrylhydrazyl) Radical Scavenging Activity. The DPPH radical scavenging activity of the synthesized compounds was carried out according to the method of [28]. The *in vitro* antioxidant activity of the final compounds **4(a–h)** was evaluated by DPPH (1,1-diphenyl-2-picrylhydrazyl) radical scavenging method. Ascorbic acid was used as the positive control. The DPPH radical scavenging activity was carried out at concentration of 100 μg/ml and the results were reported as average of three replicates. When DPPH reacts with an antioxidant compound, the decrease in absorbance observed because of the reaction

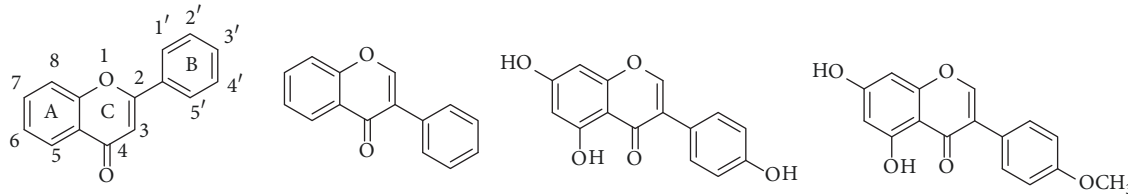


Figure 1: Structure of flavonoid (1), isoflavonoid (2), genistein (3), and biochanin A (4).

between antioxidant molecules and radical progresses, which results in the scavenging of the radical by hydrogen donation. The hydrogen donating activity measured at 517 nm showed a significant relationship between concentration of compounds and percentage of inhibition. The structures of flavonoid, isoflavonoid, genistein, and biochanin A are shown in Figure 1.

The DPPH radical scavenging activity was expressed as % of inhibition and results are tabulated in Table 1. Among the target compounds **4(a–h)**, the compounds 4c (86.95) and **4b** (84.89) exhibited maximum DPPH free radical scavenging activity followed by the compounds **4g** (76.36), **4e** (74.77), **4f** (73.81), and **4h** (65.56) which possess good radical scavenging activity when compared with the reference standard ascorbic acid (92.22). The compounds **4a** and **4d** exhibited no significant radical scavenging activity.

2.2. Procedure. The synthesized compounds were dissolved in DMSO at a concentration of 100 μg/ml. Ascorbic acid was used as a reference standard. 0.004% of DPPH was freshly prepared in methanol. 2 ml of DPPH was added to each test tube containing 100 μg/ml concentration of synthesized compounds **4(a–h)** (1 ml) and of standard solution (1 ml). It was shaken vigorously. They were then allowed to stand for 30 min at room temperature in dark place. The control was carried without addition of DPPH and the synthesized compounds. DMSO was used for base line corrections and absorbance (OD) of sample was measured at 517 nm. The following formula was used to interpret the value of the sample:

$$\%\ \text{Radical Scavenging Activity} = \left[\frac{(\text{control OD} - \text{sample OD})}{\text{control O.D}}\right] \times 100. \quad (1)$$

2.3. Conclusions. The aim of the present work was to compare the radical scavenging activities of genistein and its analogues, which have various substituents at 4′ position of B-ring, and study the effect of these substituents on antioxidant activity.

The maximum inhibitory effect was exhibited by compound **4c**, (5,7-dihydroxy-3-phenyl-4*H*-chromen-4-one) which lacks hydroxyl substituent on the B-ring, it has two hydroxyl groups on the A-ring (at C-5 and C-7), and the potent activity suggested that, in cases where the B-ring could not contribute to the inhibitory activity of the isoflavonoids,

Table 1: DPPH radical scavenging activity of the target compounds.

Entry	Compound	% inhibition at 100 μg/ml[a]
(1)	Biochanin A (4a)	>100
(2)	Genistein (4b)	84.89 ± 2.155
(3)	4c	86.95 ± 3.94
(4)	4d	>100
(5)	4e	74.77 ± 1.90
(6)	4f	73.81 ± 1.61
(7)	4g	76.36 ± 1.42
(8)	4h	65.56 ± 1.15
(9)	Ascorbic acid	92.22 ± 2.91

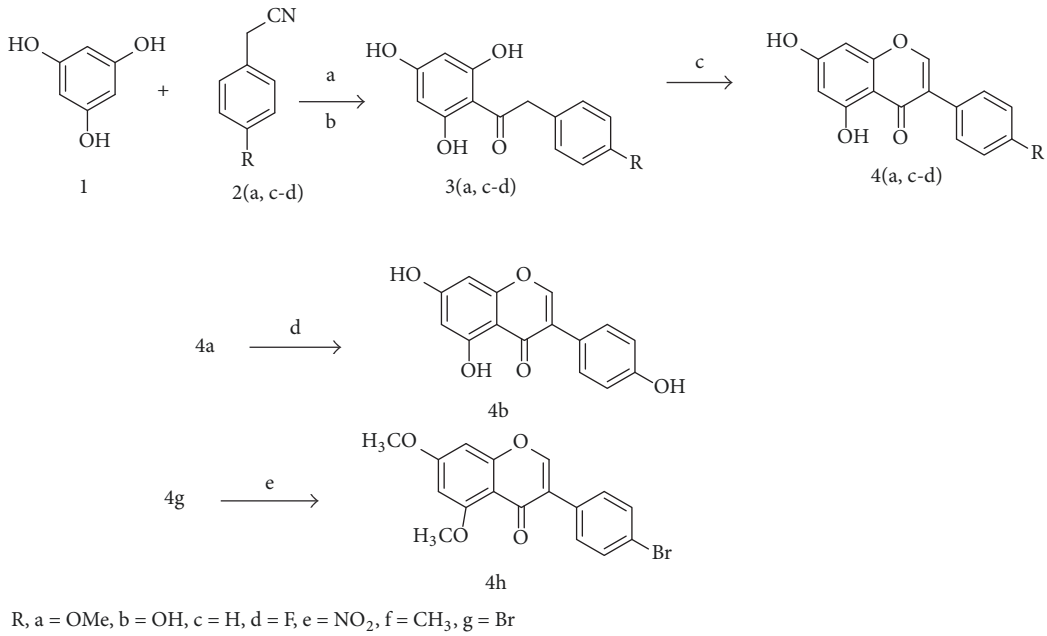
[a]Each value represents mean ± SD of three independent experiments.

the hydroxyl group on the A-ring may become a major factor to show the activity. Compound **4h** which has no hydroxyl group exhibited radical scavenging activity (65.56 ± 1.15). Compounds **4e**, **4f**, and **4g** have comparable inhibitory activities. **4g** (76.36 ± 1.42), **4e** (74.77 ± 1.90), and **4f** (73.81 ± 1.61) exhibited moderate activity. The remaining two compounds, **4a** and **4d**, exhibited no significant radical scavenging activity.

3. Experimental Section

3.1. Materials and Methods. All chemicals and solvents were purchased from Sigma-Aldrich and used without further purification; the reaction process was monitored by TLC silica gel plates; the purification of the products was performed using column chromatography using silica gel (100–200 mesh). Melting points were measured in open capillary tubes and were uncorrected; infrared (IR) spectra were recorded using FT-IR Bruker Alpha spectrometer. NMR spectra were recorded on Bruker (400 MHz) spectrometer using TMS as the internal standard; mass spectra were recorded on an Agilent 110 Lc/MSD. Elemental analyses were performed on a Vario EL-III. The antioxidant activity of all the target compounds **(4a–h)** was investigated using DPPH (1,1-diphenyl-2-picrylhydrazyl) radical method.

3.2. Chemistry. The titled compounds **(4a–h)** described in this study were prepared as outlined in Scheme 1, according to the literature method [29]. The intermediate, substituted trihydroxybenzoin **(3a, 3c–g)** was prepared by acylation of phloroglucinol **(1)** with appropriately substituted phenyl acetonitrile **(2a**, **2c–g)**, catalyzed by HCl gas and anhydrous



Scheme 1: Reagent and condition: (a) $HCl_{(gas)}$, anhydrous $ZnCl_2$, dry Et_2O, 0°C; (b) H_2O, reflux; (c) $Et_2O{\cdot}BF_3$, DMF, $POCl_3$, 60–70°C, 4 h; (d) $AlCl_3$, toluene, 140°C, 6 h; (e) DMS, K_2CO_3, Me_2CO, 60°C, 2 h.

$ZnCl_2$ in dry ether. Cyclization of the intermediate **(3a**, **3c–g)** with reagents of $Et_2O{\cdot}BF_3$ and DMF/$POCl_3$ yielded the desired substituted isoflavonoids in good yield. There are several reagents for the demethylation of methyl aryl ethers; we used anhydrous $AlCl_3$ to synthesize genistein **(4b**) from biochanin A (**4a**) by demethylation of 4′-O-methyl of biochanin A. **4h** was prepared by methylation of **4g** using dimethyl sulphate in acetone in the presence of K_2CO_3.

3.3. Synthesis and Characterization

*3.3.1. General Procedure for the Synthesis of Substituted 2′,4′,6′-Trihydroxydeoxybenzoins (**3a**, **3c–g**).* To a solution of phloroglucinol (1) (5 g, 0.039 mol) and substituted phenyl acetonitrile (2a, 2c–g) (0.044 mol), in 100 ml dry ether in an ice-salt bath, 2 g anhydrous zinc chloride was added. A steady stream of dry hydrogen chloride gas was passed through the solution for 2 hrs of stirring continuously. The mixture was allowed to stand in refrigerator overnight and again dry hydrogen chloride gas was passed through the mixture for another 2 hours. After keeping the mixture in a refrigerator for three days, the ether was decanted and washed twice with ether; the solid obtained was hydrolyzed by refluxing with 100 ml 2% HCl water for 2 hours. After completion of the reaction the mixture was cooled, filtered, and dried to yield the target compounds.

*1-(2,4,6-Trihydroxy)-2-(4-methoxyphenyl)ethanone (**3a**).* Yield: 52%; Mp: 190–194°C; Anal. Calcd for $C_{15}H_{14}O_5$: C, 65.69; H, 5.15; O, 29.17; found: C, 65.62; H, 5.19; O, 29.19; ^{1}H NMR (DMSO-d_6, 400 MHz): δ 12.94 (s, 2 H, -OH), 10.92 (s, 1H, -OH), 7.2 (d, J = 8.0 Hz, 2H, Ar-H), 6.8 (d, J = 8.0 Hz, 2H, Ar-H), 5.8 (s, 2H, Ar-H), 4.2 (s, 2H), 3.8 (s, 3H); ^{13}C NMR (DMSO-d_6, 100 MHz): δ 202.6, 164.7, 164.2, 157.8, 130.5, 127.7, 113.5, 103.6, 94.7, 54.9, 47.9; ESI-MS: m/z 275 $[M + H]^+$.

*1-(2,4,6-Trihydroxyphenyl)-2-phenylethanone (**3c**).* Yield: 47%, Mp: 158–161°C; Anal. Calcd for $C_{14}H_{12}O_4$: C, 68.85; H, 4.95; O, 26.20; found: C, 68.81; H, 4.98; O, 26.21; ^{1}H NMR (DMSO-d_6, 400 MHz,): δ12.22 (s, 2H, -OH), 10.39 (s, 1H, -OH), 7.31–7.19 (m, 5H, Ar-H), 5.83 (s, 2H, Ar-H), 4.35 (s, 2H); ^{13}C NMR (DMSO-d_6, 100 MHz): δ 202.2, 164.8, 164.2, 135.9, 129.6, 128.0, 126.1, 103.7, 94.7, 48.8; ESI-MS: m/z 245 $[M + H]^+$.

*2-(4-Fluorophenyl)-1-(2,4,6-trihydroxyphenyl)ethanone (**3d**).* Yield: 40%, Mp: 194–196°C; Anal. Calcd for $C_{14}H_{11}FO_4$: C, 64.12; H, 4.23; O, 24.40; found: C, 64.07; H, 4.25; O, 24.43; ^{1}H NMR (DMSO-d_6, 400 MHz,): δ12.19 (s, 2H, -OH), 10.39 (s, 1H, -OH), 7.27–7.23 (m, 2H, Ar-H), 7.11 (t, J = 9.2, 2H, Ar-H), 5.83 (s, 2H, Ar-H), 4.34 (s, 2H); ^{13}CNMR (DMSO-d_6, 100 MHz): δ 202.0, 164.8, 164.2, 160.9 (d, $^1J_{CF}$ = 241 Hz, 1C), 132.0 (d, $^4J_{CF}$ = 3 Hz, 1C), 131.4 (d, $^3J_{CF}$ = 8.0 Hz, 2C), 114.6 (d, $^2J_{CF}$ = 21 Hz, 2C,) 103.6, 94.7, 48.0; ESI-MS: m/z 263 $[M + H]^+$.

*1-(2,4,6-Trihydroxyphenyl)-2-(4-nitrophenyl)ethanone (**3e**).* Yield: 58%, Mp: 222–224°C; Anal. Calcd for $C_{14}H_{11}NO_6$: C, 5.13; H, 3.83; N, 4.84; O, 33.19; found: C, 5.09; H, 3.84; N, 4.85; O, 33.21; ^{1}H NMR (DMSO-d_6, 400 MHz): δ 12.21 (s, 2H, -OH), 10.92 (s, 1H, -OH), 8.22 (d, J = 8.8 Hz, 2H, Ar-H), 7.55 (d, J = 8.8 Hz, 2H, Ar-H), 5.89 (s, 2H, Ar-H), 4.57 (s, 2H,); ^{13}C NMR (DMSO-d_6, 100 MHz): δ = 200.8, 165.1, 164.2, 146.2, 144.2, 131.1, 123.0, 103.7, 94.7, 48.83; ESI-MS: m/z 290 $[M + H]^+$.

*1-(2,4,6-Trihydroxyphenyl)-2-p-tolylethanone (**3f**)*. Yield: 56%, Mp: 168–170°C; Anal. Calcd for $C_{15}H_{14}O_4$: C, 69.76; H, 5.46; O, 24.78; found: C, 69.72; H, 5.48; O, 24.80; ^{1}H NMR (DMSO-d_6, 400 MHz): δ 12.22 (s, 2H, -OH), 10.38 (s, 1H, -OH), 7.09 (s, 4H, Ar-H), 5.81 (s, 2H, Ar-H), 4.28 (s, 2H,), 3.01 (s, 3H, CH_3); ^{13}C NMR (DMSO-d_6, 100 MHz): δ202.5, 164.8, 164.2, 135.1, 132.8, 129.4, 128.6, 103.6, 94.6, 48.4, 20.6; ESI-MS: m/z 259 $[M + H]^+$.

*2-(4-Bromophenyl)-1-(2,4,6-trihydroxyphenyl)ethanone (**3g**)*. Yield: 48%, Mp: 218–220°C; Anal. Calcd. for $C_{14}H_{11}BrO_4$: C, 52.04; H, 3.43; Br, 24.73; O, 19.80; found: C, 52.01; H, 3.44; O, 19.82; ^{1}H NMR (DMSO-d_6, 400 MHz): δ 12.12 (s, 2H, -OH), 10.41 (s, 1H, -OH), 7.45 (d, J = 8.4 Hz, 2H, Ar-H), 7.18 (d, J = 8.8 Hz, 2H, Ar-H), 5.82 (s, 2H, Ar-H), 4.33 (s, 2H); ^{13}C NMR (DMSO-d_6, 100 MHz): δ201.6, 164.9, 164.2, 135.3, 131.9, 130.8, 119.4, 103.6, 94.7, 48.31; ESI-MS: m/z 323 $[M + H]^+$.

*3.3.2. General Procedure for the Cyclization of Substituted 2′,4′,6′-Trihydroxydeoxybenzoins (Synthesis of **4a**, **4c–g**)*. With cooling and vigorous stirring (3 mL, 24 mmol), etherated boron trifluoride was added drop wise to 8 mmol of 3a, 3c–g in 3 ml of anhydrous DMF. The cooling was stopped and phosphorus oxychloride (0.9 ml, 9.6 mmol) was added dropwise; after mixing all the components the reaction mixture was stirred at 60–70°C for 2 h and then poured into acidified water; the precipitate was filtered off and purified by column chromatography using hexane and ethylacetate in the ratio of 8 : 2 as eluents.

*5,7-Dihydroxy-3-(4-methoxyphenyl)-4H-chromen-4-one (**4a**)*. Yield: 61%, Mp: 212–214°C; Anal. Calcd. for $C_{16}H_{12}O_5$: C, 67.60; H, 4.25; O, 28.14; found: C, 67.57; H, 4.27; O, 28.15; ^{1}H NMR (DMSO-d_6, 400 MHz): δ12.94 (s, 1H, 5-OH), 10.92 (s, 1H, 7-OH), 8.38 (s, 1H, 2-H), 7.50 (d, J = 8.0 Hz, 2H, Ar-H), 7.0 (d, J = 8.0 Hz, 2H, Ar-H), 6.40 (1H, Ar-H), 5.77 (s, 1H, Ar-H), 3.79 (s, 3H); ^{13}CNMR (DMSO-d_6, 100 MHz,): δ 180.0, 164.3, 161.9, 159.17, 157.5, 154.2, 130.1, 122.9, 121.9, 113.7, 104.4, 99.0, 93.6, 55.1; 24; ESI-MS: m/z 285 $[M + H]^+$; FT-IR (KBr, Cm^{-1}): 3312 (O-H), 3007, (C-H aromatic), 2950 (C-H aliphatic), 1642 (C=O);

*5,7-Dihydroxy-3-phenyl-4H-chromen-4-one (**4c**)*. Yield: 76%, Mp: 194–196°C; Anal. Calcd. for $C_{15}H_{10}O_4$: C, 70.86; H, 3.96; O, 25.17; found: C, 70.82; H, 3.98; O, 25.19; ^{1}H NMR (DMSO-d_6, 400 MHz): δ10.81 (s, 1H, 7-OH), 8.39 (s, 1H, 2-H), 8.0 (d, J = 8.8 Hz, 2H, Ar-H), 7.58 (d, J = 8.0 Hz, 2H, Ar-H), 6.97 (d, J = 2.0 Hz, 1H, Ar-H), 6.88 (d, J = 2 Hz, 1H, Ar-H); ^{13}CNMR (DMSO-d_6, 22.5 MHz): δ 174.3, 162.6, 157.4, 153.6, 153.5, 132.1, 128.8, 127.6, 123.58; ESI-MS: m/z 255 $[M + H]^+$; FT-IR (KBr, Cm^{-1}): 3198 (O-H), 3062, (C-H aromatic), 2925 (C-Haliphatic), 1626 (C=O).

*3-(4-Fluorophenyl)-5,7-dihydroxy-4H-chromen-4-one (**4d**)*. Yield: 54%, Mp: 188–190°C; Anal. Calcd. for $C_{15}H_9FO_4$: C, 66.18; H, 3.33; F, 6.98; O, 23.51 found: C, 66.13; H, 3.34; O, 23.55; ^{1}H NMR (DMSO-d_6, 400 MHz): δ 12.83 (s, 1H, 5-OH), 10.93 (s, 1H, 7-OH), 8.44 (s, 1H, 2-H), 7.63 (t, J = 8.8 Hz, 2H, Ar-H), 7.31 (t, J = 9.2 Hz, 2H, Ar-H), 6.42 (d, J = 1.6 Hz, 1H, Ar-H), 6.25 (d, J = 1.6 Hz, 1H, Ar-H); ^{13}CNMR (DMSO-d_6, 22.5 MHz): δ 179.1, 164.6, 161.8, 156.2, 157.3, 147.01, 157.2, 156.2, 147.0, 137.8, 123.10; ESI-MS: m/z 273 $[M + H]^+$; FT-IR (KBr, Cm^{-1}): 3299 (O-H), 3077, (C-H aromatic), 2924 (C-H aliphatic), 1664 (C=O).

*5,7-Dihydroxy-3-(4-nitrophenyl)-chroman-4-one (**4e**)*. Yield: 63%, Mp: 286–288°C; Anal. Calcd: for $C_{15}H_9NO_6$: C, 60.21; H, 3.03; N, 4.68; O, 32.08; found: C, 60.17; H, 3.05; N, 4.69; O, 32.09; ^{1}H NMR (DMSO-d_6, 400 MHz): δ 12.70 (s, 1H, 5-OH), 11.01 (s, 1H, 7-OH), 8.63 (s, 1H, 2-H), 8.32 (d, J = 8.8 Hz, 2H, Ar-H), 7.91 (d, J = 8.8 Hz, 2H, Ar-H) 6.46 (d, J = 1.6 Hz, 1H, Ar-H), 6.28 (d, J = 2 Hz, 1H, Ar-H); ^{13}C NMR (DMSO-d_6, 22.5 MHz): δ 179.1, 164.6, 161.9, 157.4, 156.1, 146.8, 137.9, 123.15, 120.3, 104.3, 99.2; ESI-MS: m/z 300 $[M + H]^+$.; FT-IR (KBr, Cm^{-1}): 3418 (O-H), 1654 (C=O).

*5,7-Dihydroxy-3-tolyl-4H-chromen-4-one (**4f**)*. Yield: 68%, Mp: 193–195°C; Anal. Calcd: for $C_{16}H_{12}O_4$; C, 71.64; H, 4.51; O, 23.86; found: C, 71.61; H, 4.53; O, 23.87; ^{1}H NMR (DMSO-d_6, 400 MHz): δ 12.90 (s, 1H, 5-OH), 10.89, (s, 1H, 7-OH), 8.38 (s, 1H, 2-H), 7.46 (d, J = 8.0 Hz, 2H, Ar-H), 7.26 (d, J = 8.0 Hz, 2H, Ar-H), 6.40 (d, J= 2.0 Hz, 1H, Ar-H), 6.24 (d, J = 2.0 Hz, 1H, Ar-H), 2.34 (s, 3H,); ^{13}CNMR (DMSO-d_6, 100 MHz): δ 179.9, 164.5, 161.99, 157.5, 157.4, 154.5, 137.3, 128.8, 128.7, 127.8, 122.2, 104.4, 99.0, 93.7, 20.7; ESI-MS: m/z 269 $[M + H]^+$; FT-IR (KBr, Cm^{-1}): 3264 (O-H), 3073, (C-H aromatic), 2921 (C-Haliphatic), 1643 (C=O).

*3-(4-Bromophenyl)-5,7-dihydroxy-4H-chromen-4-one (**4g**)*. Yield: 66%, Mp: 212–214°C; Anal. Calcd for $C_{15}H_{14}BrO_5$: C, 54.08; H, 2.72; Br, 23.99; O, 19.21; found: C, 54.06; H, 2.73; O, 19.22; ^{1}H NMR (DMSO-d_6, 400 MHz): δ 12.79 (s, 1H, 5-OH), 10.94, (s, 1H, 7-OH), 8.47 (s, 1H, 2-H), 7.66 (d, J = 8.8 Hz, 2H, Ar-H), 7.55 (d, J = 8.4 Hz, 2H, Ar-H), 6.42 (d, J = 1.6 Hz, 1H, Ar-H), 6.25 (d, J = 1.6 Hz, 1H, Ar-H); ^{13}C NMR (DMSO-d_6, 100 MHz): δ 179.5, 164.5, 161.9, 155.1, 131.1, 130.9, 121.3, 121.1, 99.2, 93.8; ESI-MS: m/z 332 $[M + H]^+$.; FT-IR (KBr, Cm^{-1}): 3374 (O-H), 3063, (C-H aromatic), 2919 (C-Haliphatic), 1657 (C=O).

*3.3.3. Demethylation of **4a** (Preparation of 5,7-Dihydroxy-3-(4-hydroxyphenyl)-4H-chromen-4-one) (**4b**)*. 4a (0.26 gm, 0.91 mmol) suspended in toluene (10 ml) was added to anhydrous $AlCl_3$ and the mixture was refluxed with string to 160°C for 6 h; after completion of reaction (monitored by TLC), the reaction mixture was cooled and poured into water and acidified with HCl acid to break the $AlCl_3$; the solution was then filtered, dried, and washed with toluene and purified by column chromatography to yield 4b.

Yield: 84%, Mp: 292–294°C; Anal. Calcd for $C_{15}H_{10}O_5$: C, 66.67; H, 3.73; O, 29.60; found: C, 66.62; H, 3.76; O, 29.62; ^{1}H NMR (DMSO-d_6, 400 MHz): δ 12.94 (s, 1 H, 5-OH), 10.9 (s, 1H, 7-OH), 9.61 (s, 1H, 4′-OH), 8.31 (s, 1H, 2-H), 7.38 (d, J = 4.0 Hz, 2H, Ar-H), 6.82 (d, J = 4.0 Hz, 2H, Ar-H), 6.39 (s, 1H, Ar-H); ^{13}C NMR (DMSO-d_6, 100 MHz): δ 180.2, 164.2, 161.9, 157.5, 157.4, 153.9, 130.1, 122.2, 121.20, 115.0, 104.4, 98.9, 93.6; ESI-MS: m/z 271 $[M + H]^+$.; FT-IR (KBr, Cm^{-1}): 3412 (-OH), 3004, (C-H aromatic), 2933 (C-H aliphatic), 1652 (C=O).

*3.3.4. 3-(4-Bromophenyl)-5,7-dimethoxy-4H-chromen-4-one (**4h**) (Prepared by Methylation of **4g**).* To a solution of 4 g (6 mmol) in 10 mL acetone, potassium carbonate (18 mmol) was added and then DMS (15 mmol) was added dropwise and refluxed at 60°C for about 2 h. After completion of the reaction as indicated by TLC, the reaction mixture was filtered and concentrated and the crude product was purified by column chromatography (eluent hexane : ethylacetate, 8 : 2).

Yield: 80%, Mp: 174–176°C; Anal. Calcd for $C_{17}H_{13}BrO_4$: C, 56.53; H, 3.63; Br, 22.12; O, 17.72; found: C, 56.50; H, 3.64; O, 17.74; ^{1}H NMR (DMSO-d_6, 400 MHz): δ 7.78 (s, 1H, 2-H), 7.52 (d, J = 8.4 Hz, 2H, Ar-H) 7.43 (d, J = 8.4 Hz, 2H, Ar-H) 6.45 (d, J = 2.4 Hz, 1H, Ar-H), 6.38 (d, J = 2 Hz, 1H, Ar-H), 3.93 (s, 3H), 3.89 (s, 3H); ^{13}CNMR (DMSO-d_6, 100 MHz): δ 174.8, 164.1, 161.4, 159.8, 150.4, 130.9, 125.3, 122.1, 109,8, 96.3, 96.2, 92.6, 92.5, 56.0; ESI-MS: m/z 361 $[M + H]^+$; FT-IR (KBr, Cm^{-1}): 3002, (C-H aromatic), 2923 (C-H aliphatic), 1657 (C=O).

Conflicts of Interest

The authors declare that they have no conflicts of interest.

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