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DESIGN, SYNTHESIS AND MOLECULAR DOCKING STUDIES OF 2-STYRYLCHROMONE DERIVATIVES AS NOVEL ANTIOXIDANT AGENTS

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ABSTRACT

In this present study of the Design, Synthesis and molecular docking studies of 2-styrylchromone derivatives as novel antioxidant agents was considered chromone as basic fundamental pharmacophore in order to show antioxidant properties. We have performed molecular docking studies of synthesized compounds to check the ligand interactions with target protein. In addition, ADMET studies and molecular simulations studies also performed to know the toxicity and other parameters of synthesized molecules. Finally, through molecular modelling studies it is concluded that the synthesized molecules follows Lipinski rule of five.

KEYWORDS

2-styrylchromone, Design, Synthesis and Antioxidant agents.

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INTRODUCTON

Naturally occurring chromones (1-benzopyran-4-ones) are widely distributed throughout the plant kingdom. These compounds have attracted a great deal of attention due to their substantial activities, including antioxidative and anticancer effects. Accordingly, many synthesized chromone derivatives have been extensively studied for the development of novel anticancer agents. Molecular mechanisms of anticancer effects mediated by chromones such as flavonoids could be attributed to antiproliferation, induction of apoptosis, cycle arrest, promotion of differentiation, inhibition

of angiogenesis, and modulation of multidrug resistance. Among these chromone derivatives, flavopiridol has been identified as a cyclin-dependent kinase (CDK) inhibitor and it has entered in Phase II clinical trial. 2-Styrylchromones are a small group of chromones with only two natural 2-styrylchromones hormothamnione (II) and 6-desmethoxyhormothamnione (III) are known.

Hormothamnione was isolated in 1986 from the marine cryptophyte Crysophaeumtaylor. Its 6-desmethoxy analog was characterized in 1989 from the extracts of the same blue-green algae. Hormothamnione demonstrated potent cytotoxicity against P388 lymphocytic leukemia and HL 60 human promyelotic leukemia cell lines, while 6-desmethoxyhormothamnione exhibited antitumor activity against 9 kb and colon 38 tumor cells, respectively. A number of synthesized 2-styrylchromone derivatives have shown to exhibit antiallergic, antiviral, antitumor, anticancer, and antioxidant activities, and to serve as antagonism of A3 adenosine receptor, and xanthine oxidase inhibitors. Among all biological activities, the anticancer effect is of particular interest that we decided to synthesize and evaluate the antiproliferation of a series of 2-styrylchromones against a panel of carcinoma cell lines. Herein, we report the synthesis of 2-styrylchromones based on the modifications of ring-B and ring-A as shown in Figure No.1. Mechanistic study of antiproliferative effect mediated by the representative compound 4q is examined in this paper. Moreover, 3D-QSAR model established by CoMFA analysis on BT483 cell line is studied as well.

Chromone derivatives are abundant in nature and exhibit a wide range of pharmacological activity like anti-bacterial, anti-funga, anti-cancer, anti-oxidant, anti-HIV, anti-ulcers, immuno stimulators, biocidal, wound healing, anti-inflammatory, and immune-stimulatory. Many chromone derivatives are also photoactive and can be used easily in various photo induced reactions affording diverse heterocyclic compounds. Chromone derivatives are also active at benzodiazepine receptors and on lipoxygenase and cyclooxygenase. In addition to this, they have been shown to be possessing antimutagenic properties as well as the ability to inhibit electron transport through inhibition at NADH: ubiquinone oxidoreductase and phorbol ester-induced ornithine decarboxylase. Chromones may also have application in cystic fibrosis treatment, as they activate the cystic fibrosis transmembrane conductance regulator. These compounds also possess low mammalian toxicity and are present in large amounts in the diet of humans due to their origin in plants. To list a few chromone derivatives, which are actively used in pharmacological field are given below. Although there are a large number of chromone derivatives known for their pharmacological properties there are only a few examples that have been or that are used as therapeutic agents today. Cromolyn or cromoglicate (Cromoglicic acid) is used as a mast cell stabilizer in allergic rhinitis, asthma and allergic conjunctivitis. Nedocromil (Alocril) is used to prevent wheezing, shortness of breath, and other breathing problems caused by asthma. Apigenin (40, 5, 7-trihydroxyflavone) and used as a potent inhibitor of Cytochrome P450 2C9 (CYP2C9). Diosmin used in the treatment of venous disease, i.e., chronic venous insufficiency (CVI) and hemorrhoidal disease (HD), in acute or chronic haemorrhoids. Flavoxate (2-(1-piperidyl) ethyl 3-methyl-4- oxo-2-phenylchromene-8-carboxylate) is an anticholinergic with antimuscarinic effects. Furthermore, around the 1950s, khellin was used as a smooth muscle relaxant in the treatment of angina pectoris and asthma. Therefore, the vast range of biological effects associated with this scaffold has resulted in the chromone ring system being considered as a privileged structure. The main objectives of chromones syntheses are not only for the development of more diverse and complex bioactive compounds for biological activity and structure activity relationship (SAR) and other applications in medicinal chemistry, such as preparation of fluorescence probes, due to photochemical properties of chromones. Some reviews on involvement of chromone nucleus in anticancer activity and synthesis part are available in literature. Some compilations of reports on all activities associated with chromone nucleus are also

reported. Sharma *et al,* have reviewed on the natural occurrence and biological activity of chromones. Khadem and Marles have reviewed on occurrence and bioactivity of chromone. Cazarolli *et al*, have published review on therapeutic potential of chromone nucleus for some activities but no comprehensive report on varied activities of chromone based compounds is available in literature till date. Hence, the present review gives a comprehensive insight into the current applications of chromone nucleus in varied therapeutic fields. In addition to various therapeutic uses chromone have been found as important intermediates in many organic reactions.

MATERIAL AND METHODS

Experimental Procedure

Chemistry

Chemical reagents and organic solvents were purchased from TCI and Alfa Aesar unless otherwise mentioned. Melting points were determined by Fargo MP-2D. Nuclear magnetic resonance spectra (1H NMR) were measured on a Bruker AC-300 instrument. Chemical shifts (δ) are reported in parts per million relative to the TMS peak. Mass spectra were obtained by FAB on a Jeol JMS-700 instrument. Flash column chromatography was performed with silica gel (230–400 mesh). Elemental Analysis was carried out on a Heraeus Vario EL-III C, H, N analyzer.

General procedure

1-(2-Hydroxy-4, 6-dimethoxy phenyl) ethanone (2a)

To a solution of 2′, 4′, 6′-trihydroxyacetophenone (1a, 5.0 g, 30.0mmol), Me2SO4 (5.3 ml, 56mmol), and anhydrous K2CO3 (8.2 g, 56mmol) in acetone (90ml) was stirred at room temperature for 18 h. The reaction mixture was filtered and evaporated in vacuo, followed by recrystallization from ether–hexane to afford 2a (4.9 g, 83%) as a yellowish solid. M.p. 78–80°C (lit [32] 78.5-79.5°C). 1H NMR (300 MHz, CDCl3) d 3.96 (s, 3H), 3.941 (s, 3H), 6.896 (s, 3H), 6.924 (d, J = 2.4 Hz, 1H), 7.245 (d, J = 2.3 Hz, 1H), 9.538 (s, 1H) ppm. 13C NMR (75MHz, CDCl3) d32.9, 56.0, 111.5, 111.9, 115.5, 50.4, 172.9ppm, MASS (311.1550, 415.2176) FTIR (3325.77, 2920.22, 1611.84, 1376.36, 1168.10, 801.60, 619.08, 515.82) HRMS (M) + calcd for C14H14O4 291.3319; found 291.1039. Anal. Calcd for C14H14O4: C, 69.01; H, 3.23. Found: C, 69.89; H, 3.23.

5, 7-Dimethoxy-2-methyl-4H-chromen-4-one (3a)

A solution of 2a (3.92 g, 20.0mmol) in dry ethyl acetate (30ml) was added sodium (2.76 g, 120mmol), the reaction mixture was stirred at room temperature for 18 h. Cold 0.5 N HCl (30 ml) was added and the aqueous layer was separated, the remained organic layer was dried and evaporated in vacuo to obtain the crude diketone. A solution of the crude diketone with couple drops of concentrated HCl in methanol (50ml) was stirred at room temperature for 4 h. The methanol was removed in vacuo to get the residue, followed by the addition of ethyl acetate (50ml) and washed with brine (50ml). The organic layer was dried, evaporated in vacuo and purified with silica gel chromatography to obtain 3a (2.95 g, 67% in two steps). M.p. 120-121°C. 1H NMR (300 MHz, CDCl3) d 3.944 (s, 3H), 3.96 (s, 3H), 5.14 (s, 3H), 5.19 (s, 1H), 6.51 (d, J = 2.3 Hz, 1H), 6.54, 7.29, 7.45 (d, J = 2.3 Hz, 1H) ppm. 13CNMR (125MHz, CDCl3) δ74.7, 111.2, 128.1, 128.2, 128.6, 136.0, 192.4ppm. MASS (545.00, 375.049, 297.138, 143.00, 84.9. FTIR (3465.25, 2918.92, 1735.09, 1629.38, 1436.10, 1198.26, 836.30, 587.01) HRMS (M) + calcd for C17H15O4 302.294; found 302.289. Anal. Calcd for C17H15O4: C, 53.01; H, 4.12. Found: C, 73.89; H, 4.12.

(E)-5, 7-Dimethoxy-2-styryl-4H-chromen-4-one (4a)

Sodium (0.69 g, 30.0mmol) was gradually added to dry methanol (30ml) and the mixture was stirred until the solution reached room temperature. 3a (1.1 g, 5.0mmol) and benzaldehyde (0.64 g, 6.0mmol) were added and the resulting mixture was allowed to stir at reflux for 18 h. After this period, the solution was poured into iced water and the pH was adjusted to 4 with HCl. The yellow solid was removed by filtration, taken up in DCM and purified with silica gel chromatography (eluent DCM: ethyl acetate = 4:1) to give 4a (1.1 g, 71%) as a white solid. M.p. 186-188°C. 1H NMR (300

MHz, CDCl3) δ 3.91 (s, 3H), 3.95 (s, 3H), 5.2 (s, 1H), 6.52 (d, J = 2.3 Hz, 1H), 6.94 (d, J = 2.3 Hz, 1H), 6.96 (d, J = 16.2 Hz, 1H), 7.19 (m, 3H), 7.21 (d, J = 16.2 Hz, 1H), 7.25 (m, 2H) ppm. 13C NMR (125.7MHz, CDCl3) δ 56.1, 60.7, 70.9, 71.6, 102.7, 128.0, 128.6, 136.6, 136.7, 136.9ppm. MASS (507.2288, 357.1609, 297.1391) FTIR (2920.3, 1737.61, 1632.53, 1441.47, 1161.32, 830.01, 644.29) HRMS (M) + calcd for C19H16O4 308.3279; found 308.1039. Anal. Calcd for C19H16O4: C, 74.01; H, 5.23. Found: C, 73.89; H, 5.32.

(E)-5, 7-Dimethoxy-2-(2-pyridin-4-yl-vinyl)-chromen-4-one (4b)

Compound 4b was synthesized from the procedure described for compound 4a. M.p. 212-213°C. 1H NMR (300 MHz, CDCl3)d 3.78 (s, 3H), 3.96 (s, 3H), 5.22 (s, 1H),5.27 (d, J = 16.0 Hz, 1H), 6.9 (d, J = 2.3 Hz, 1H), 7.10 (d, J = 2.3 Hz, 1H), 7.29 (d, J = 16.0 Hz, 1H), 7.47 (m, 2H), 7.9 (m, 2H) ppm. 13C NMR (75 MHz, CDCl3) d 55.8, 56.0, 71.4, 75.7, 100.3, 100.9, 115.9, 120.8, 121.6, 124.0, 127.4, 128.3, 144.7, 148.9, 150.0, 172.8ppm. MASS (419.176, 335.11, 313.135, 230.117, 143.0018) FTIR (3326.77, 2920.22, 1611.84, 1376.36, 1201.00, 1168.0, 831.46, 515.82) HRMS (M) + calcd for C18H15NO4 309.1001; found 309.0994. Anal. Calcd for C18H15NO4: C, 69.89; H, 4.89. Found: C, 69.76; H, 4.81.

2-[2-(4-Fluoro-phenyl)-vinyl]-5, 7-dimethoxy-chromen-4-one (4c)

Compound 4c was synthesized from the procedure described for compound 4a. M.p. 169-171°C. 1H NMR (300 MHz, CDCl3)d 3.9 (s, 3H), 4.0 (s, 3H), 5.27 (s, 1H), 5.28 (d, J = 2.3 Hz, 1H), 6.92 (d, J = 2.3 Hz, 1H), 7.04 (d, J = 16.0 Hz, 1H), 7.05 (m, 2H), 7.07 (d, J = 16.0 Hz, 1H), 7.08 (m, 2H) ppm. 13C NMR (75 MHz, CDCl3) d 56.5, 61.5, 70.8, 71.1, 110.0, 113.9, 114.1, 115.6, 120.8ppm. MASS (497.16, 399.0987, 303.0957, 201.0429) FTIR (2930.05, 1686.22, 1611.83, 1454.32, 1359.94, 1035.31, 758.10. HRMS (M+1) + calcd for C19H15FO4 326.0954; found 326.0952. Anal. Calcd for C19H15FO4: C, 69.93; H, 4.63. Found: C, 69.04; H, 4.58.

2-[2-(4-Chloro-phenyl)-vinyl]-5, 7-dimethoxy-chromen-4-one (4d)

Compound 4d was synthesized from the procedure described for compound 4a. M.p. 171-172°C. 1H NMR (300 MHz, CDCl3)d 3.84 (s, 3H), 3.85 (s, 3H), 6.93 (s, 1H), 6.96 (d, J = 2.3 Hz, 1H), 7.14 (d, J = 2.3 Hz, 1H), 7.17 (d, J = 16.0 Hz, 1H), 7.44 (d, J = 8.5 Hz, 2H), 7.46 (d, J = 16.0 Hz, 1H), 7.87 (d, J = 8.5 Hz, 2H) ppm. 13C NMR (75 MHz, CDCl3) d56.0, 111.5, 111.9, 114.4, 115.5, 121.8, 124.5, 133.0, 137.8, 144.8, 146.4, 150.4ppm, MASS (945.534, 473.271, 340.1819, 134.0965, FTIR (2924.08, 1614.12, 1515.37, 1452.23, 1153.73, 1074.91, 831.34, 527.04 HRMS (M) + calcd for C19H15ClO4 342.0659; found 342.0660. Anal. Calcd for C19H15ClO4: C, 66.58; H, 4.41. Found: C, 65.95; H, 4.52.

2-[2-(4-Bromo-phenyl)-vinyl]-5, 7-dimethoxy-chromen-4-one (4e)

Compound 4e was synthesized from the procedure described for compound 4a. M.p. 172-173°C. 1H NMR (300 MHz, CDCl3)d 3.941 (s, 3H), 3.962 (s, 3H), 6.8963 (s, 1H), 6.924 (d, J = 2.3 Hz, 1H), 7.245 (d, J = 2.3 Hz, 1H), 7.275 (d, J = 16.0 Hz, 1H), 7.587 (d, J = 8.5 Hz, 2H), 7.595 (d, J = 16.0 Hz, 1H), 7.616 (d, J = 8.5 Hz, 2H) ppm. 13CNMR (75MHz, CDCl3) d56.5, 61.1, 110.5, 114.8, 115.6, 116.2, 119.8, 120.1, 122.5, 130.1, 136.1, 137.2, 145.1, 145.5, 147.5, 148.6, 155.8ppm, FTIR (3326.77, 3202.20, 2920.22, 1659.01, 1611.84, 1376.36, 1201.00, 1168.0, 515.82, 419.19, MASS (311.1550, 415.2176, 445.2636, 519.2795, HRMS (M + 1) +calcd for C19H16BrO4 388.2314; found 388.0143. Anal. Calcd for C19H15BrO4: C, 58.93; H, 3.90. Found: C, 58.42; H, 3.92.

5, 7-Dimethoxy-2-[2-(4-methoxy-phenyl)-vinyl]-chromen-4-one (4f)

Compound 4f was synthesized from the procedure described for compound 4a. M.p. 175-176°C. 1H NMR (300 MHz, CDCl3)d 6.8825 (s, 3H), 6.8995 (s, 3H), 6.9287 (s, 3H), 6.9462 (s, 1H), 7.4227 (d, J = 2.3 Hz, 1H), 7.4401 (d, J = 2.3 Hz, 1H), 7.6324 (d, J = 16.0 Hz, 1H), 7.6366 (d, J = 8.5 Hz, 2H), 7.6494 (d, J = 16.0 Hz, 1H), 7.6535 (d, J = 8.5 Hz, 2H) ppm. 13CNMR (75MHz, CDCl3) d113.9, 114.4, 115.0, 115.1, 115.2, 115.5, 120.0, 122.8,

132.8, 136.9, 145.0, 145.8, 147.3, 149.6, 172.4ppm, MASS (134.0, 340.1, 430.22, 473.27, 945.5, 1006.5, FTIR (2920.33, 1737.61, 1632.53, 1441.47, 1252.30, 1161.2, 830.01, 644.29, 960.35, 527.88 HRMS (M) + calcd for C20H18O5 338.1154; found 338.1154. Anal. Calcd for C20H18O5: C, 70.99; H, 5.36. Found: C, 70.23; H, 5.29.

2-(2-Benzo [1, 3] dioxol-5-yl-vinyl)-5, 7-dimethoxy-chromen-4-one (4g)

Compound 4g was synthesized from the procedure described for compound 4a. M.p. 217-218°C. 1H NMR (300 MHz, CDCl3)d 5.1933 (s, 3H),5.2282 (s, 3H), 6.4828 (s, 2H), 6.5086 (s, 1H), 6.5355 (d, J = 3.8 Hz, 1H), 6.5613 (d, J = 15.9 Hz, 1H), 6.4828 (d, J = 2.2 Hz, 1H), 6.5086 (d, J = 7.9 Hz, 1H), 6.5355 (d, J = 7.9 Hz, 1H), 7.0939 (d, J = 3.8 Hz, 1H), 7.1006 (d, J = 15.9 Hz, 1H) ppm. 13C NMR (75 MHz, CDCl3) d 56.1, 60.7, 71.0, 71.5, 102.7, 113.4, 114.5, 115.7, 127.2, 127.4, 128.0, 128.6, 136.7, 136.8, 137.0, 142.5, 145.1, 149.1, 150.4, 158.3, 192.4ppm. MASS (84.9599, 143.0017, 201.0433, 297.1389, 375.0497, 545.0056, FTIR (3455.25, 2918.92, 1735.09, 1629.38, 1436.10, 1301.11, 1198.26, 1162.2, 1017.85, 836.30, 746.78, 549.5 HRMS (M) + calcd for C20H16O6 352.0947; found 352.0946. Anal. Calcd for C20H16O6: C, 68.18; H, 4.58. Found: C, 68.04; H, 4.44.

2-[2-(3, 5-Dimethoxy-phenyl)-vinyl]-5, 7-dimethoxy-chromen-4-one (4h)

Compound 4h was synthesized from the procedure described for compound 4a. M.p. 188-189°C. 1H NMR (300 MHz, CDCl3)d 3.9249, 3.9464 (s, 3H), (s, 3H), 5.1349 (s, 3H), 5.18 (s, 3H), 6.49 (s, 1H), 6.52 (d, J = 2.3 Hz, 1H), 6.86 (d, J = 2.3 Hz, 1H), 6.88 (s, 1H), 6.92 (d, J = 16.0 Hz, 1H), 6.95 (s, 2H), 7.03 (d, J = 16.0 Hz, 1H) ppm. 13C NMR (75MHz, CDCl3) d55.9, 56.0, 70.7, 74.7, 104.3, 109.1, 111.1, 115.7, 121.6, 122.5, 124.9, 125.7, 127.2, 128.1, 128.2, 128.6, 129.1, 136.2, 137.6ppm. MASS (121.064, 258.14, 327.149, 447.207, 521.22, 893.4077, FTIR (3326.77, 3202.20, 2920.22, 1744.65, 1611.84, 1376.36, 1246.61, 1168.0, 1082.22, 831.46, 726.58, 619.08, 515.82, 419.19, HRMS (M) + calcd for C21H20O6 368.1260; found 368.1263. Anal. Calcd for C21H20O6: C, 68.18; H, 4.58. Found: C, 68.04; H, 4.44.

5, 7-Dimethoxy-2-[2-(4-trifluoromethyl-phenyl)-vinyl]-chromen-4-one (4i)

Compound 4i was synthesized from the procedure described for compound 4a. M.p. 201-202°C. 1H NMR (300 MHz, CDCl3) d 3.91 (s, 3H), 3.95 (s, 3H), 5.20 (s, 1H), 6.50 (d, J = 2.3 Hz, 1H), 6.53 (d, J = 2.3 Hz, 1H), 6.80 (d, J = 16.0 Hz, 1H), 6.84 (d, J = 16.0 Hz, 1H), 6.85 (m, 4H) ppm. 13C NMR (75MHz, CDCl3) d56.1, 60.7, 71.0, 71.5, 102.7, 113.4, 114.5, 115.7, 127.2, 127.4, 128.0, 128.6, 136.7, 137.8, 138.0ppm, MASS (235.1226, 331.0993, 365.0610, 491.2120, 695.1361, FTIR (2930.05, 2853.83, 1686.22, 1454.32, 1359.94, 1203.19, 1035.31, 1012.88, 831.77, 758.90, 742.31, 615.47, 520.68, 484.58, 434.00 HRMS (M)+ calcd for C20H15F3O4 376.0922; found 376.0921. Anal. Calcd for C20H15F3O4: C, 63.83; H, 4.02. Found: C, 63.75; H, 4.13.

RESULTS AND DISCUSSION

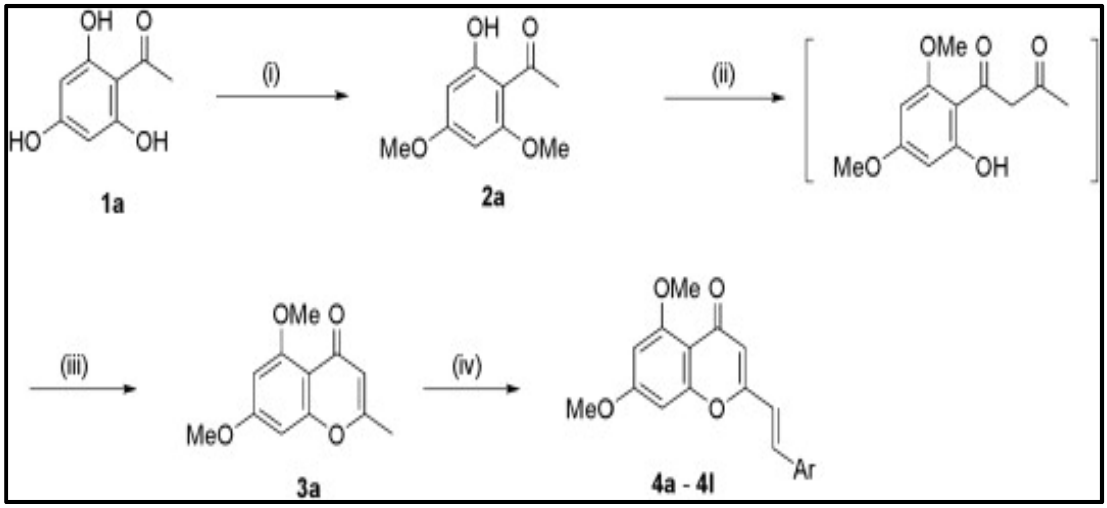
Chromone derivatives are abundant in nature and exhibit a wide range of pharmacological activity like anti-bacterial, anti-fungal, anti-cancer, anti-oxidant, anti-HIV, anti-ulcers, immunostimulators, biocidal, wound healing, anti-inflammatory, and immune-stimulatory. Hence we considered chromone as basic fundamental pharmacophore in order to show antioxidant properties.

We have performed molecular docking studies of synthesized compounds to check the ligand interactions with target protein. In addition, ADMET studies and molecular simulations studies also performed to know the toxicity and other parameters of synthesized molecules. Finally, through molecular modeling studies it is concluded that the synthesized molecules follows Lipinski rule of five.

Table No.1: DPPH Assay

S.No	Synthesized Compound (s)	% DPPH Scavenging
1	4a	41.16 ± 0.28
2	4b	38.67 ± 0.37
3	4c	53.31 ± 0.46
4	4d	37.62 ± 0.51
5	4e	45.83 ± 0.48
6	4f	74.29 ± 0.53
7	4g	62.63 ± 0.64
8	4h	48.91 ± 0.38
9	4i	52.48 ± 0.67

Synthetic Scheme



Scheme No.1: Reagents and conditions: (i) Me2SO4/K2CO3, acetone; (ii) Na/EtOAc; (iii) conc. HCl/MeOH; (iv) MeONa/ArCHO/MeOH

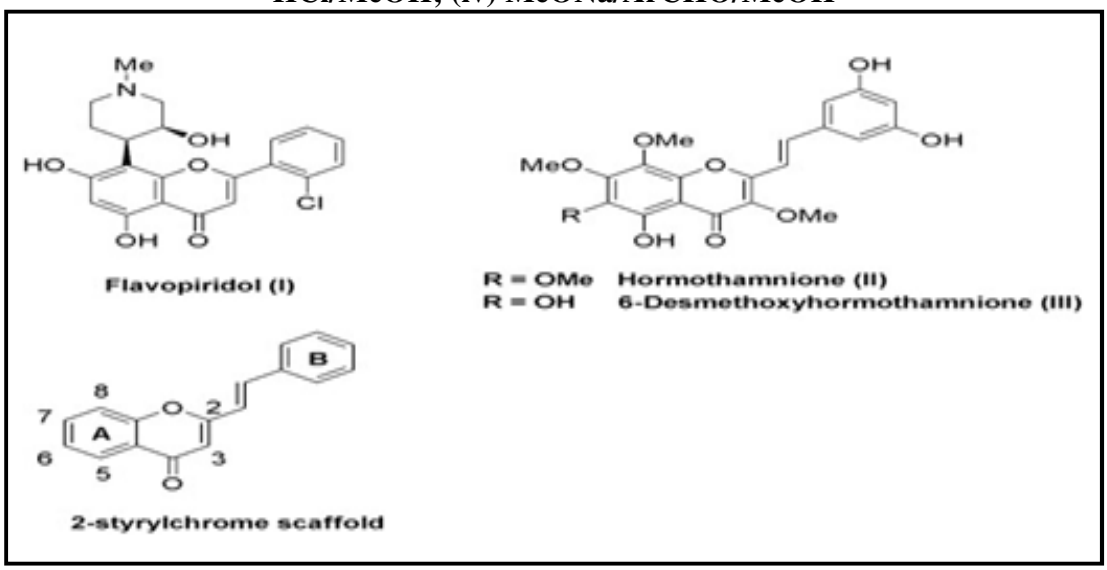
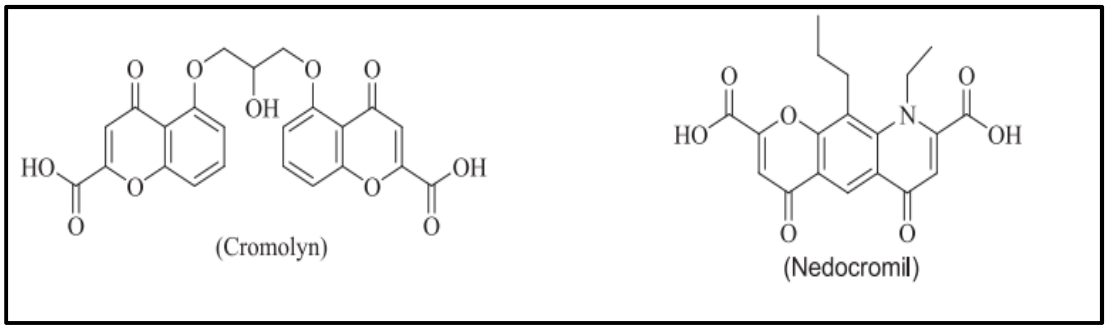
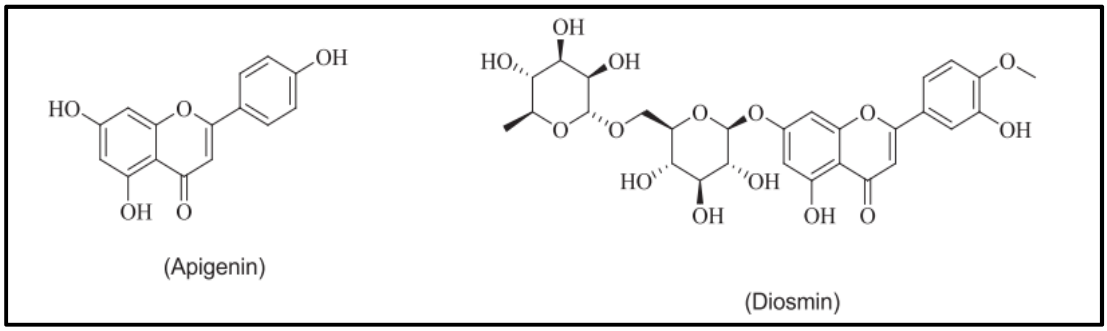
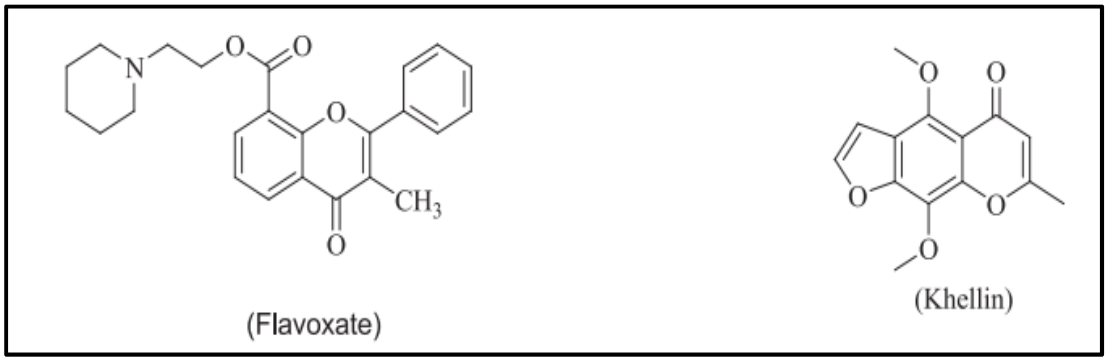


Figure No.1: Chemical structures of Chromone derivatives







Supporting Information

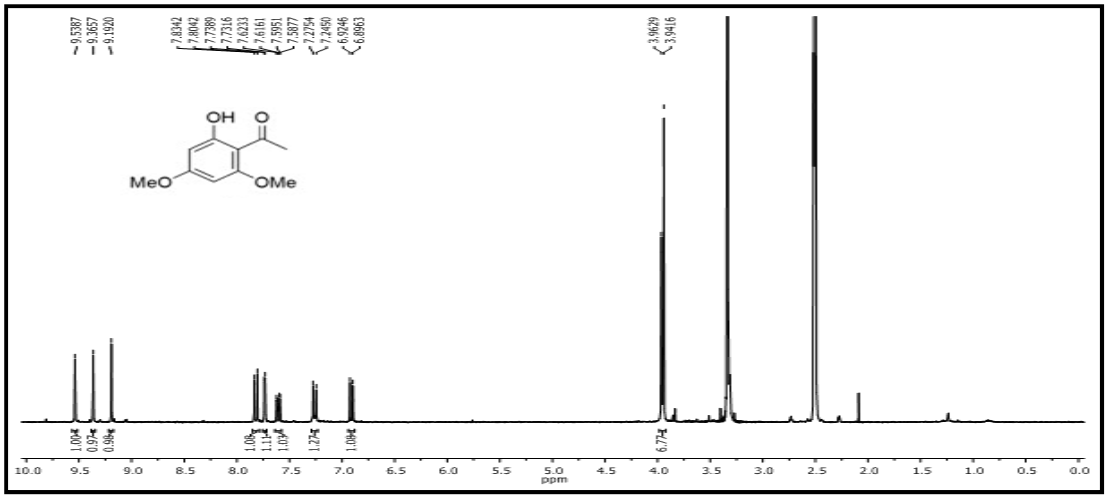
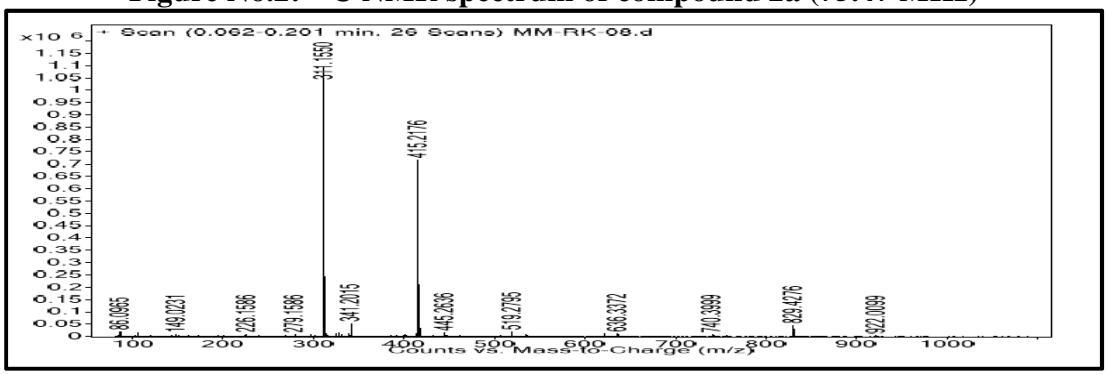
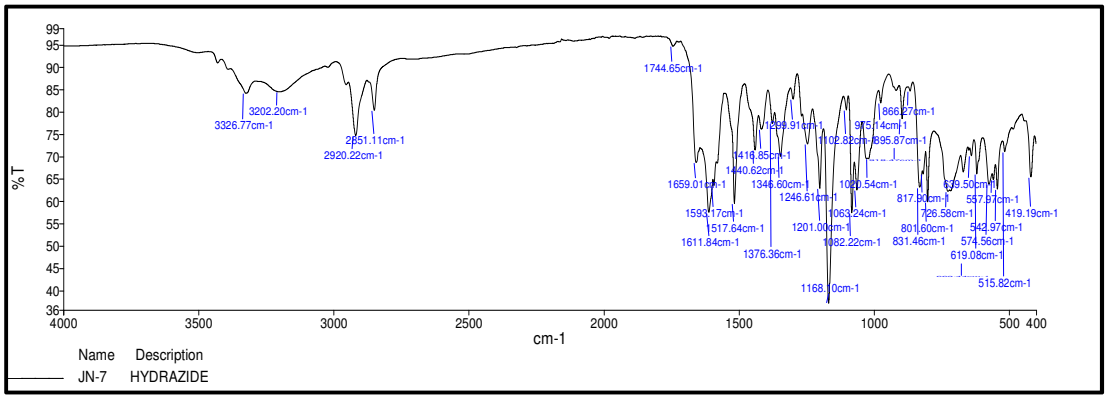


Figure No.1: ^{1}H NMR spectrum of compound 2a (300.13 MHz)

Figure No.2: ^{13}C NMR spectrum of compound 2a (75.47 MHz)





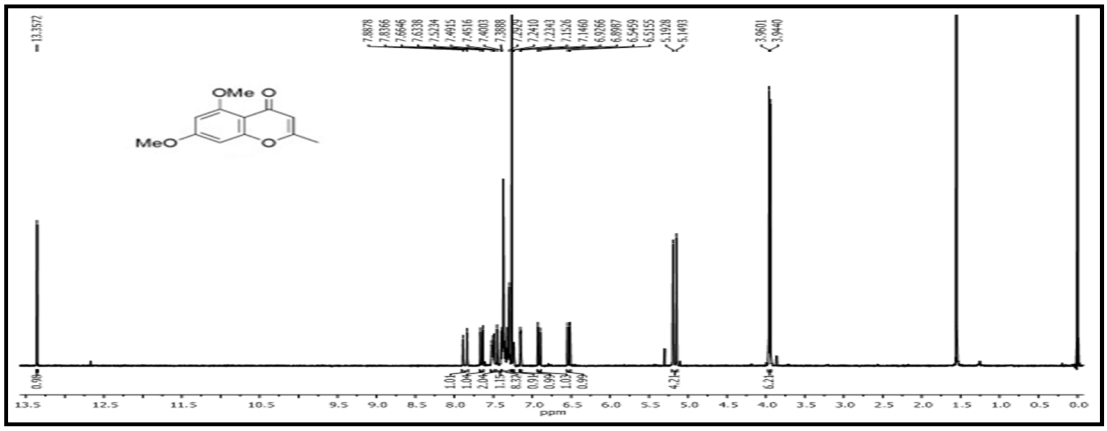


Figure No.3: ^{1}H NMR spectrum of compound3a (300.13 MHz, $CDCl_3$)

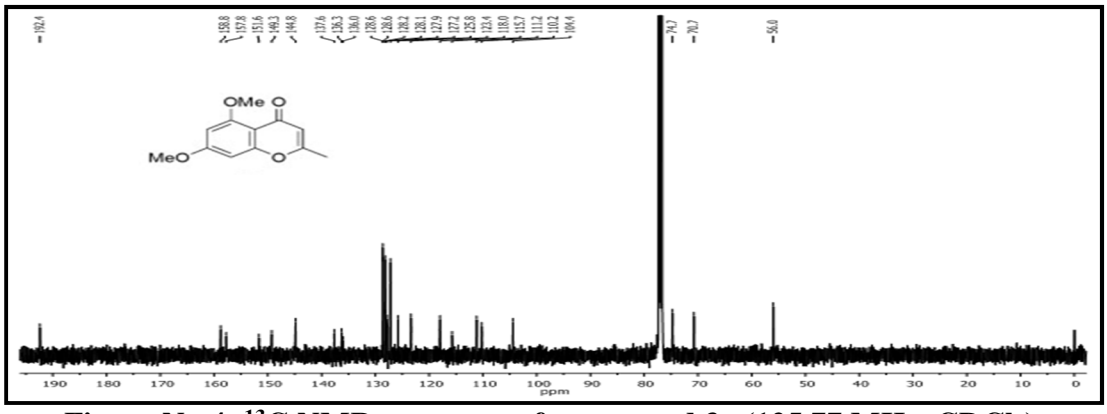
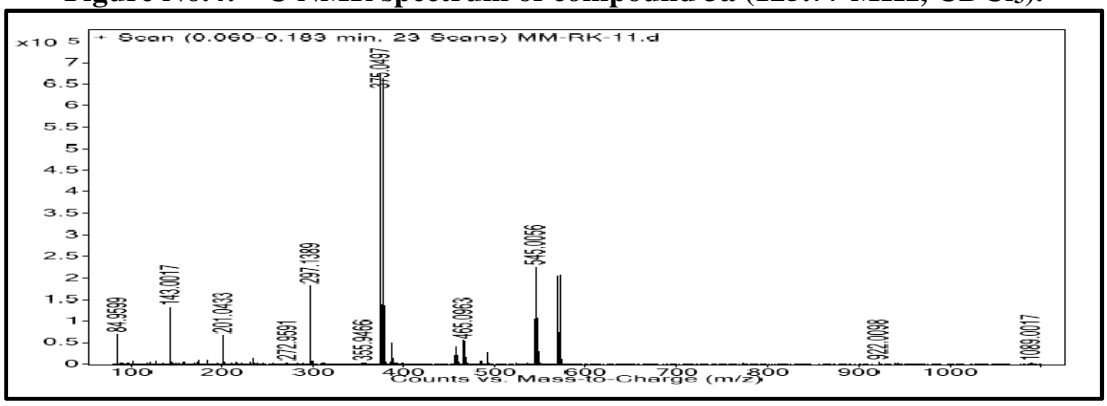
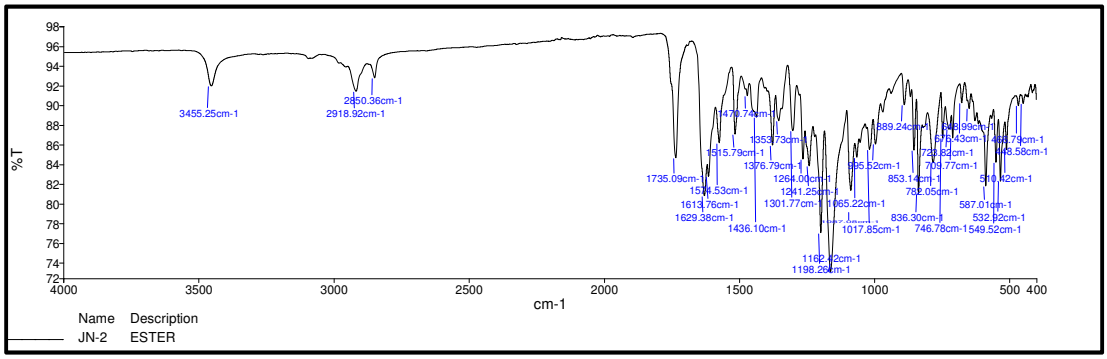


Figure No.4: ^{13}C NMR spectrum of compound 3a (125.77 MHz, $CDCl_3$).





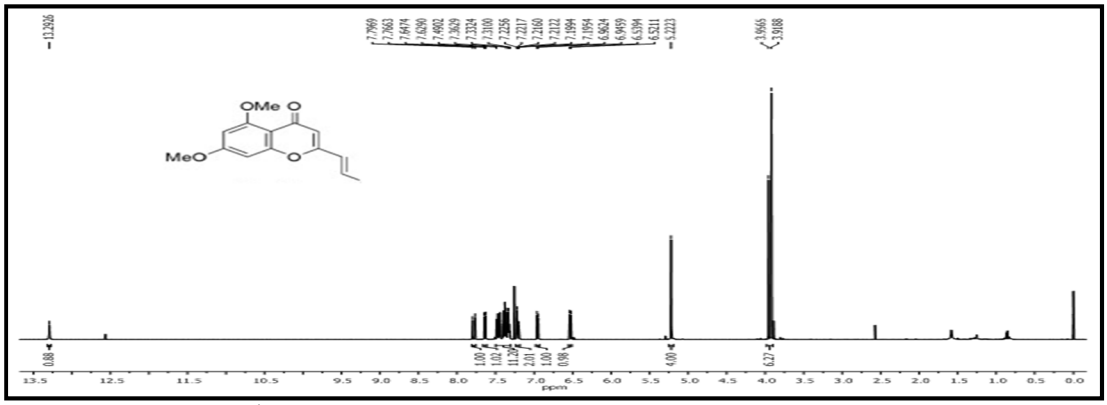


Figure No.5: ^{1}H NMR spectrum of compound 4a (500.13 MHz, $CDCl_3$)

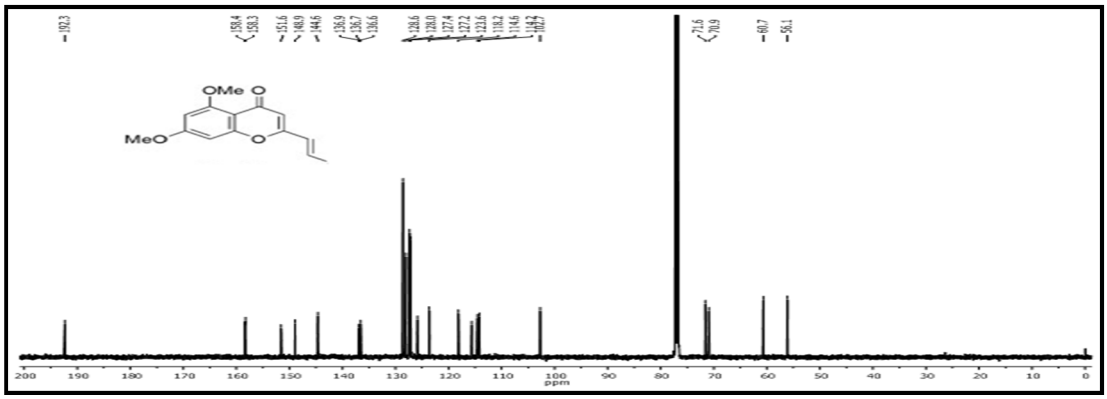
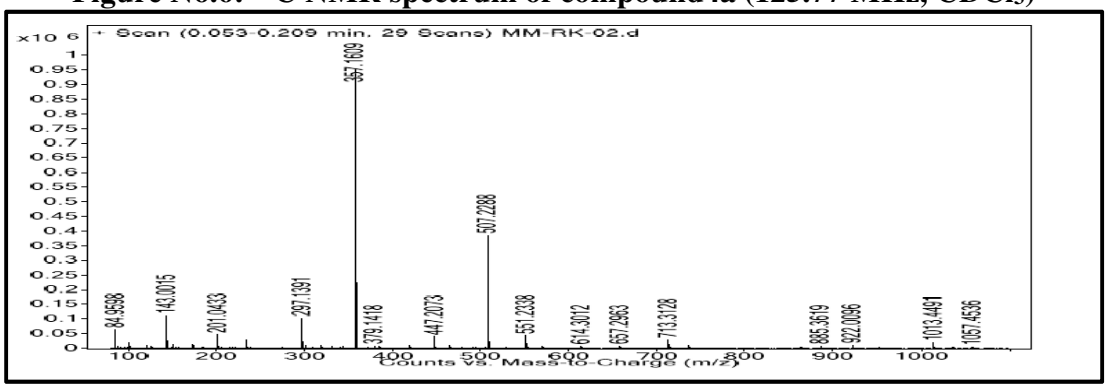
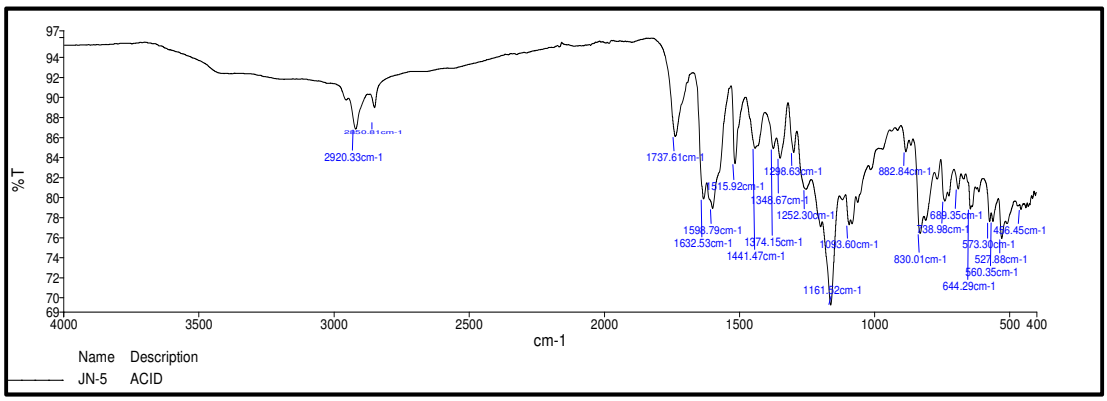


Figure No.6: ^{13}C NMR spectrum of compound4a (125.77 MHz, $CDCl_3$)





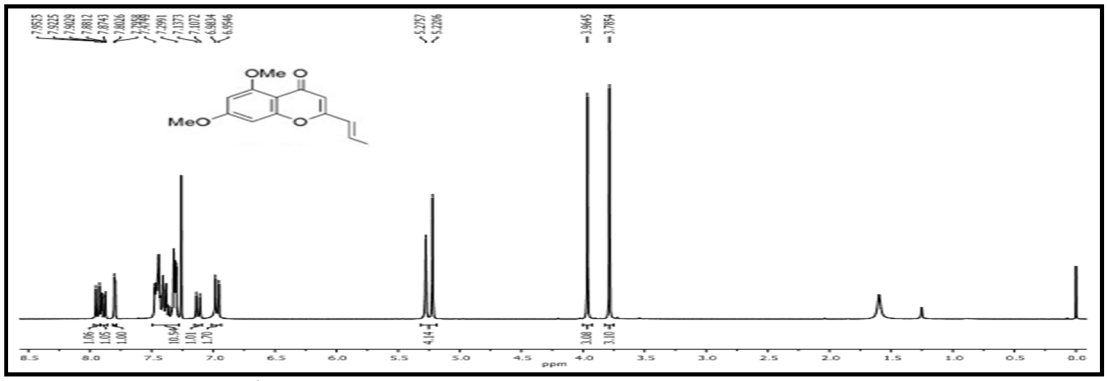


Figure No.7: ^{1}H NMR spectrum of compound 4b (300.13 MHz, $CDCl_3$)

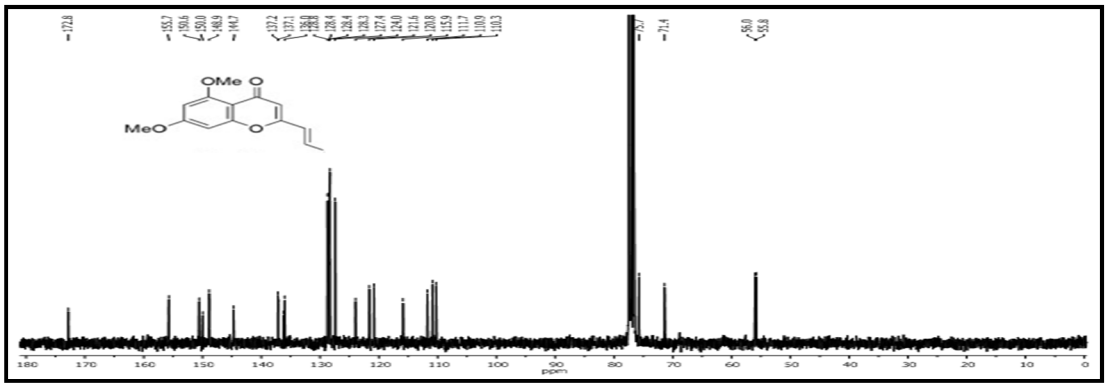
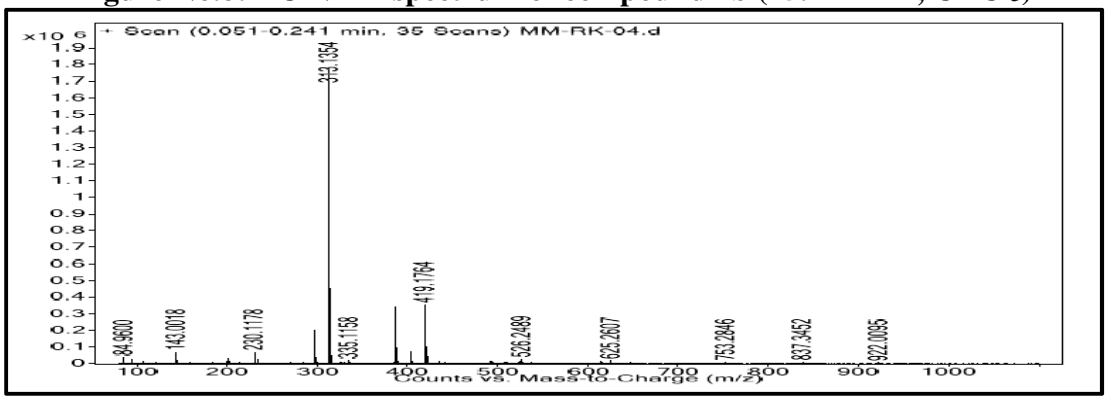
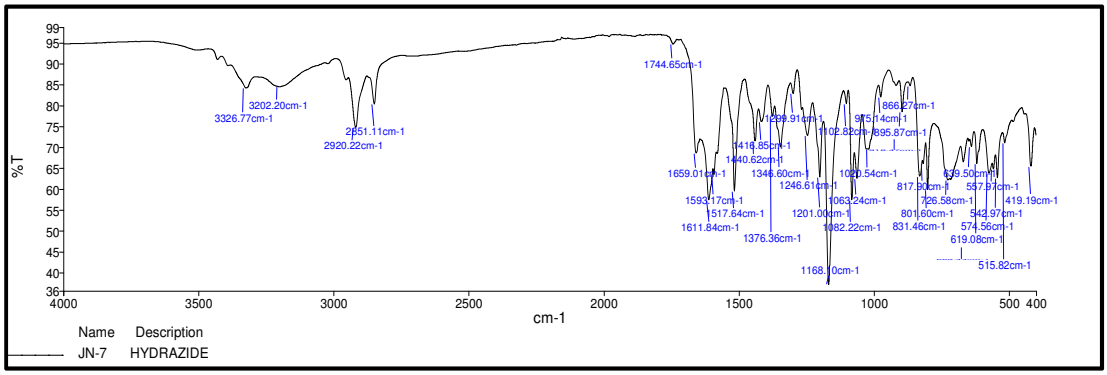


Figure No.8: ^{13}C NMR spectrum of compound 4b (75.47 MHz, $CDCl_3$)





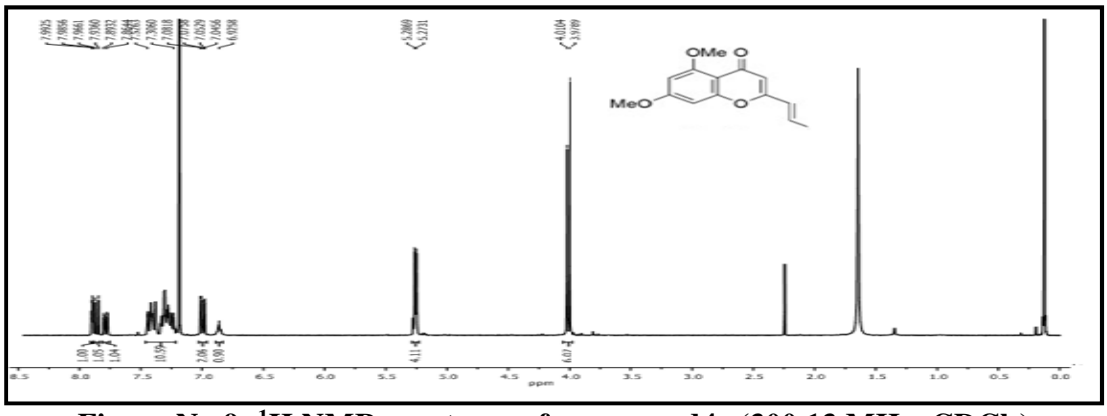


Figure No.9: ^{1}H NMR spectrum of compound4c (300.13 MHz, $CDCl_3$)

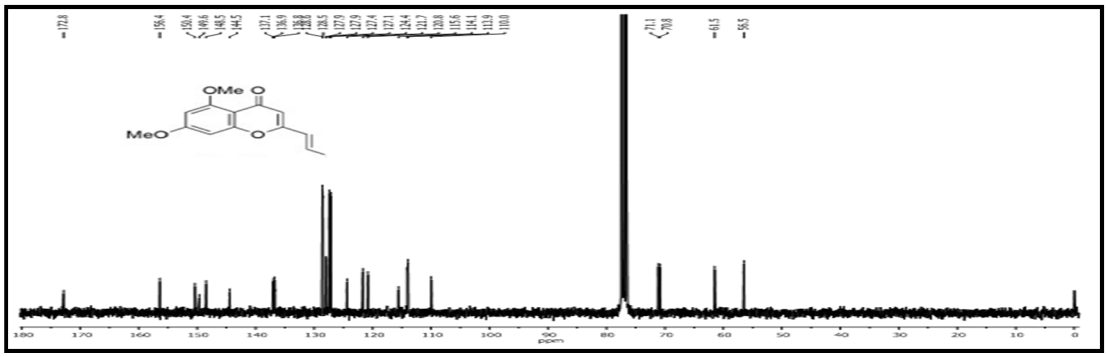
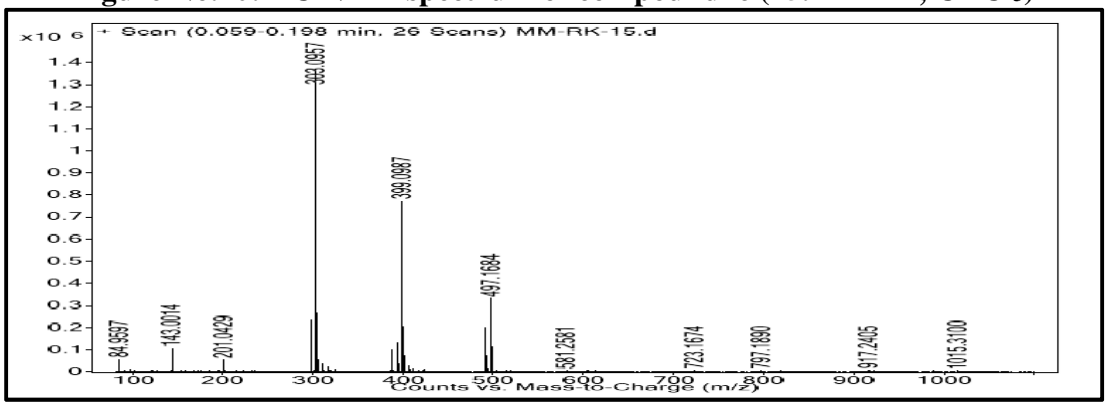
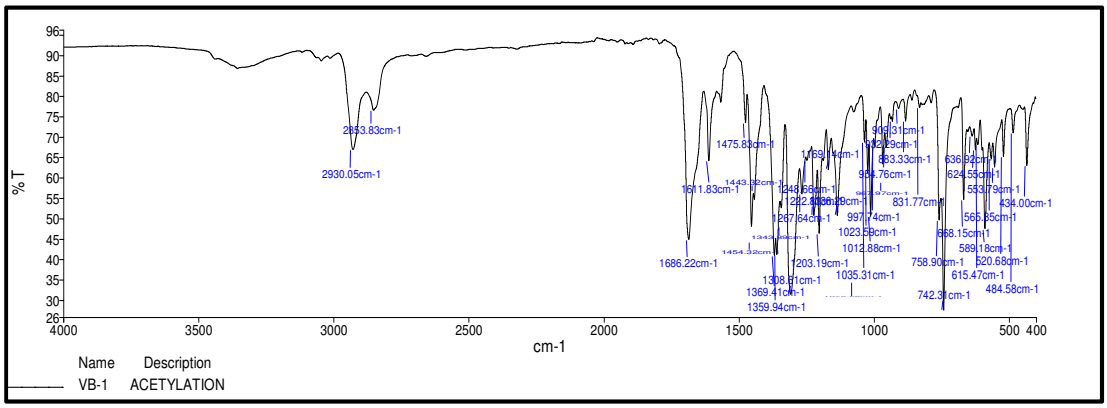


Figure No.10: ^{13}C NMR spectrum of compound4c (75.47 MHz, $CDCl_3$)





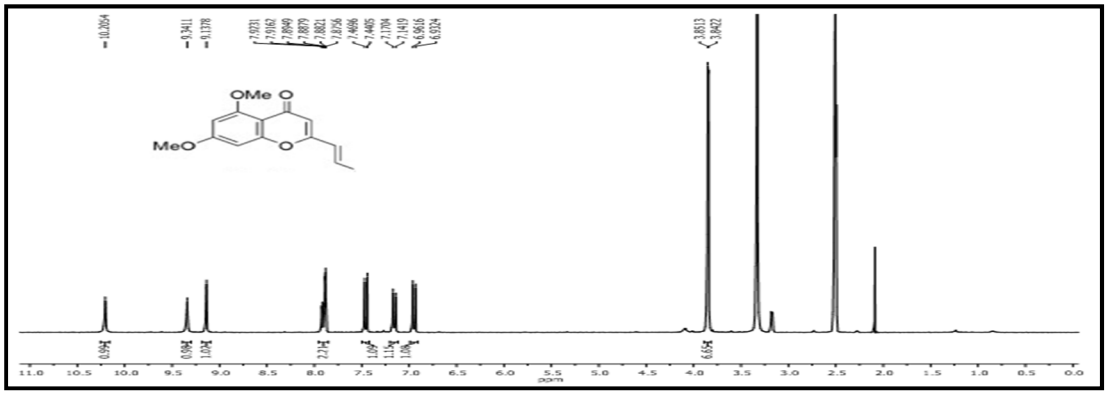


Figure No.11: ^{1}H NMR spectrum of compound4d (300.13 MHz, DMSO-d_6)

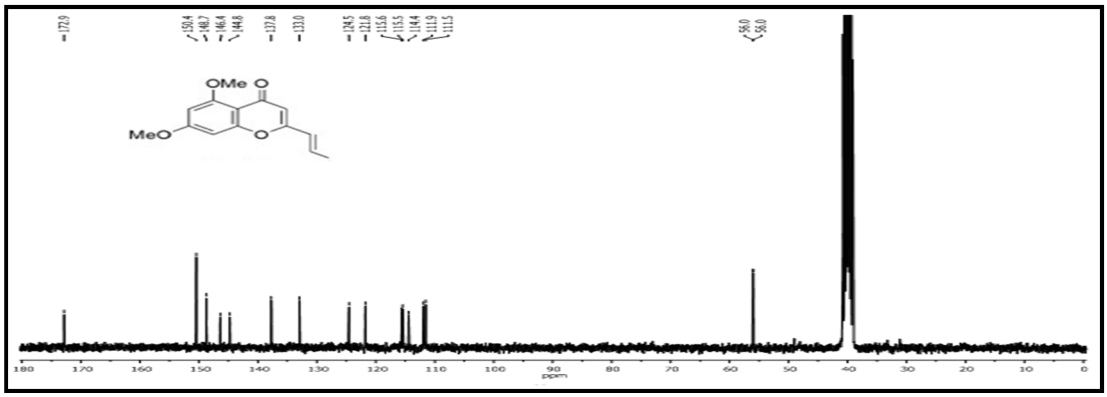
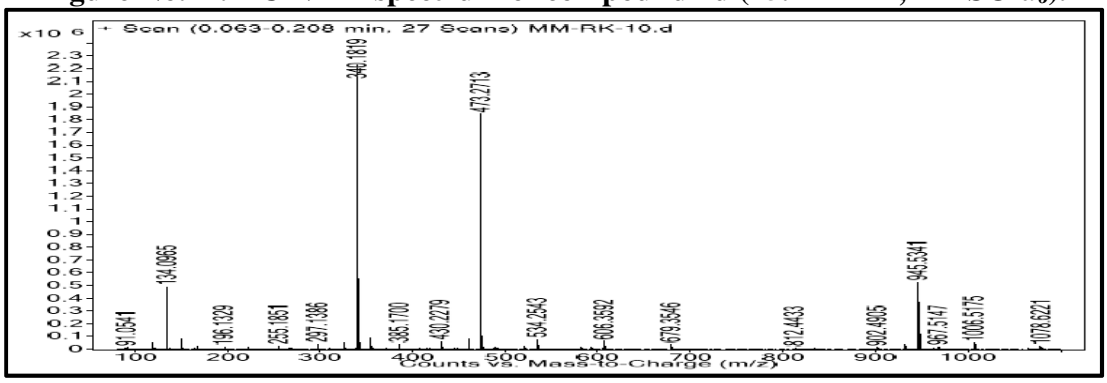
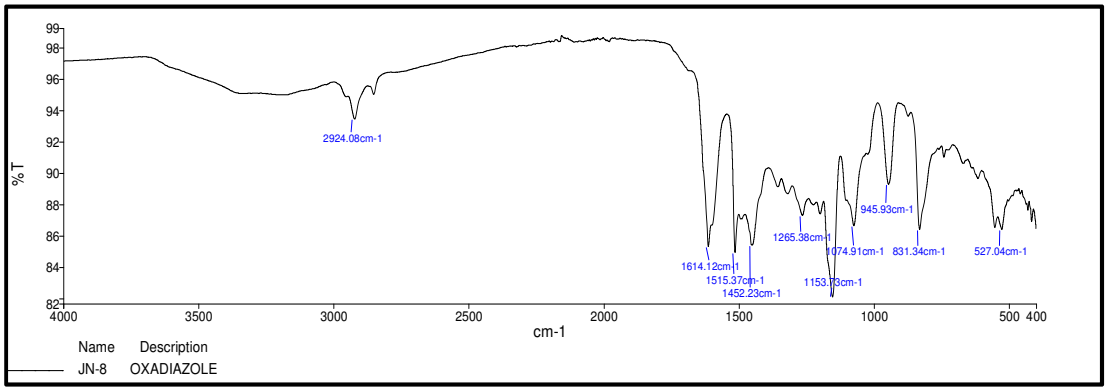


Figure No.12: ^{13}C NMR spectrum of compound 4d (75.47 MHz, DMSO-d_6).





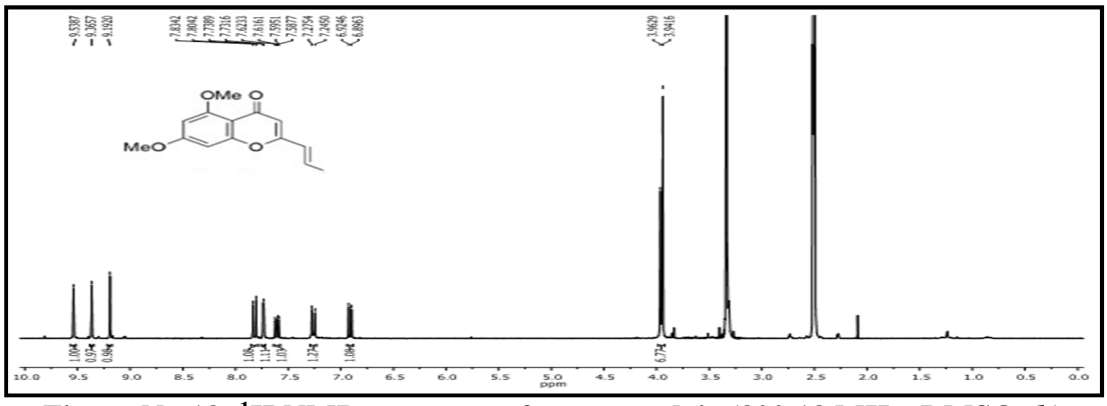


Figure No.13: ^{1}H NMR spectrum of compound 4e (300.13 MHz, DMSO-d_6)

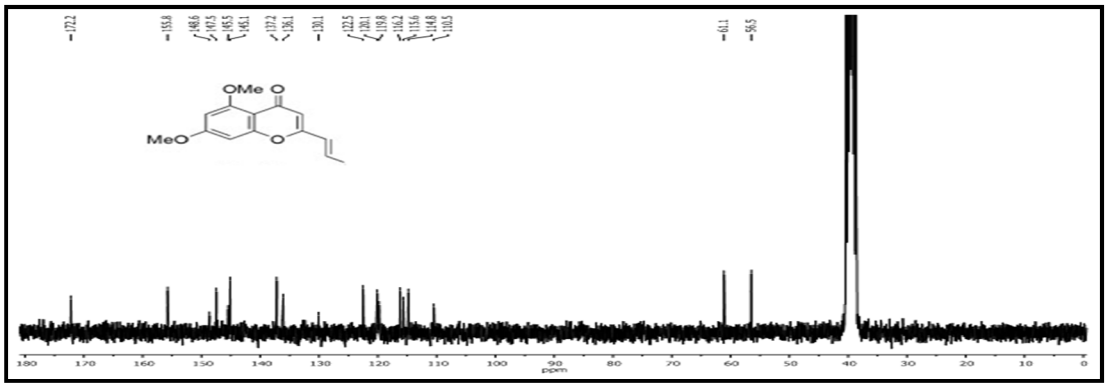
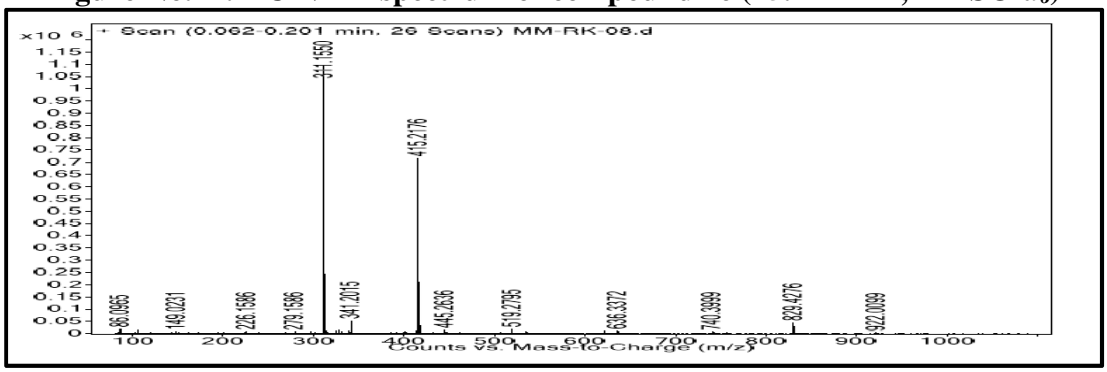
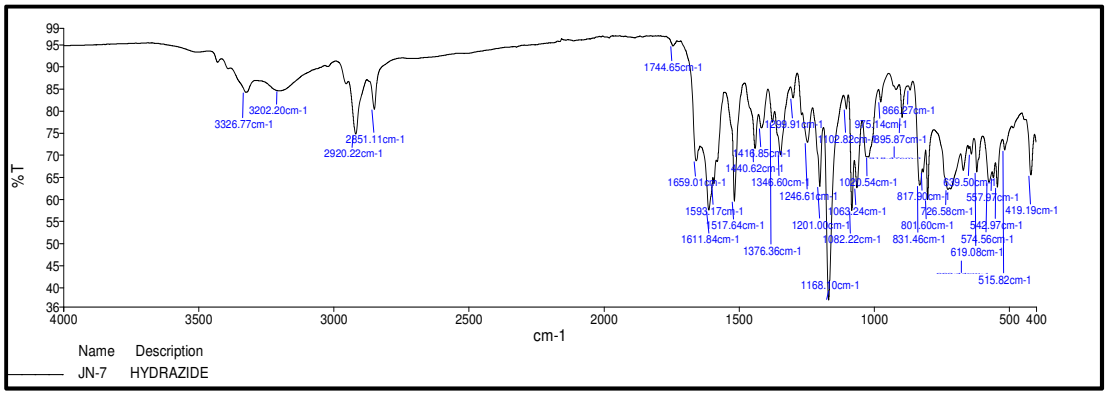


Figure No.14: ^{13}C NMR spectrum of compound 4e (75.47 MHz, DMSO-d_6)





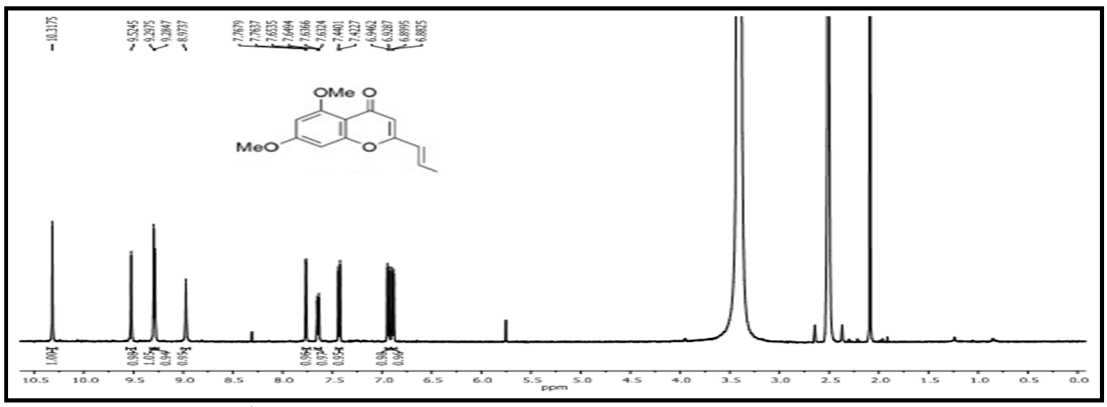


Figure No.15: ^{1}H NMR spectrum of compound4f (500.13 MHz, DMSO-d_6)

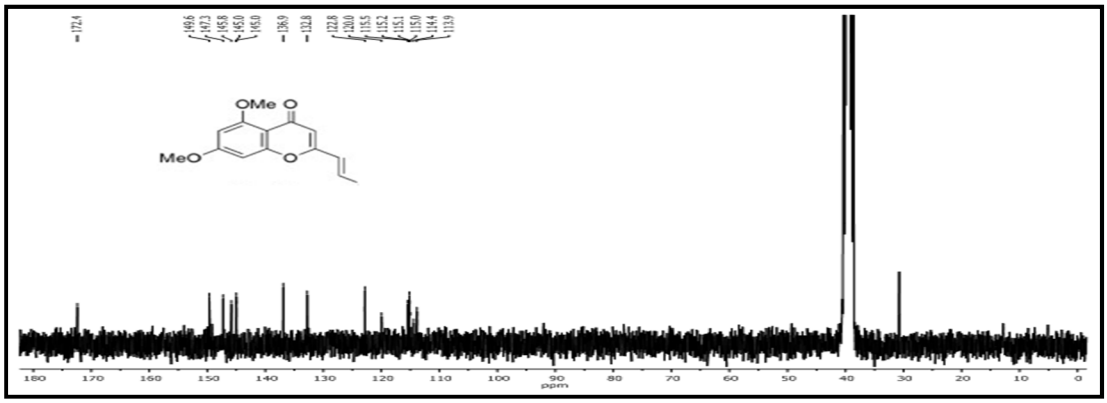
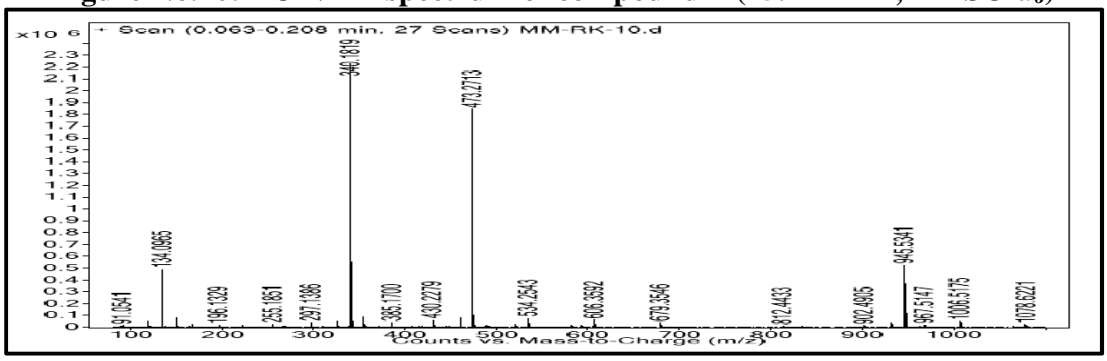
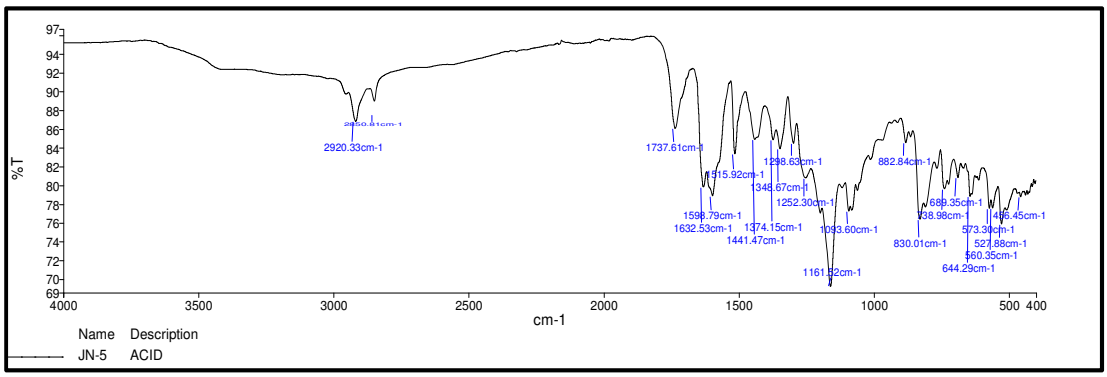


Figure No.16: ^{13}C NMR spectrum of compound4f (75.47 MHz, DMSO-d_6)





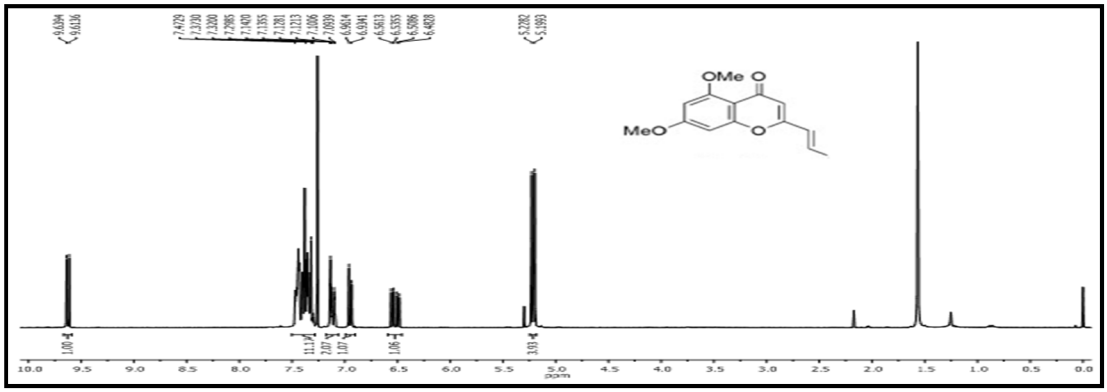


Figure No.17: ^{1}H NMR spectrum of (compound4g (300.13 MHz, $CDCl_3$)

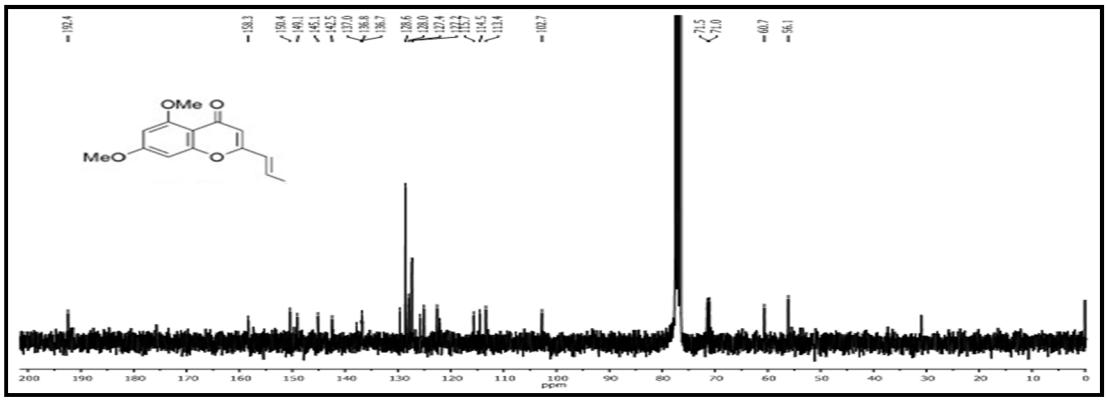
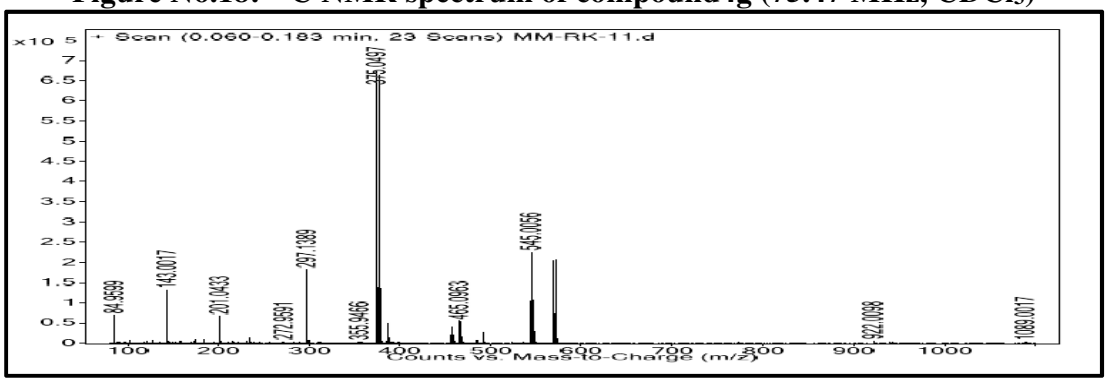
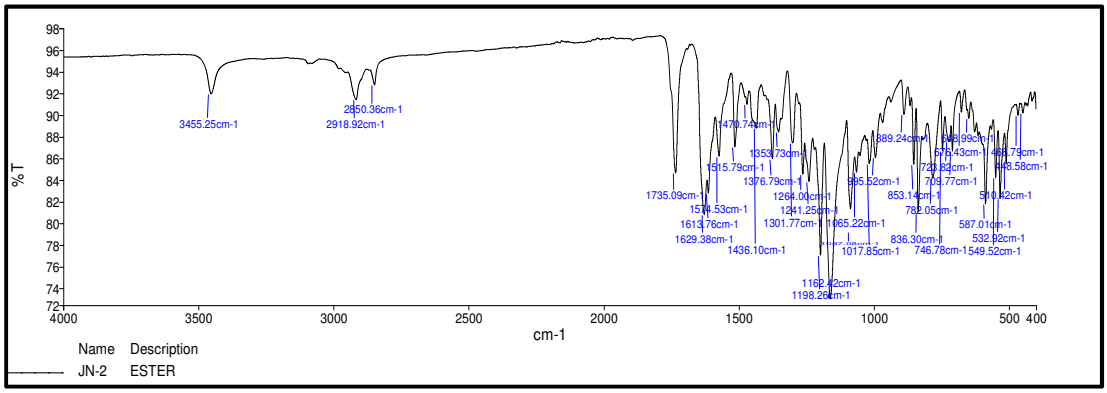


Figure No.18: ^{13}C NMR spectrum of compound4g (75.47 MHz, $CDCl_3$)





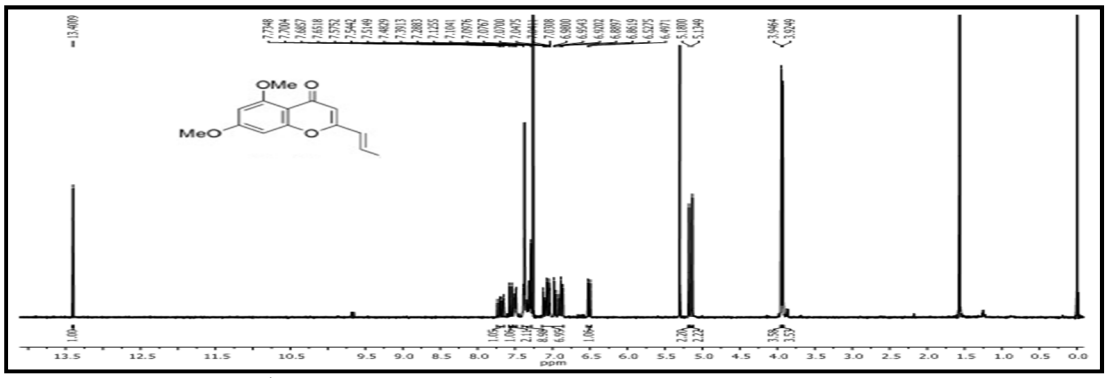


Figure No.19: ^{1}H NMR spectrum of compound4h (300.13 MHz, $CDCl_3$)

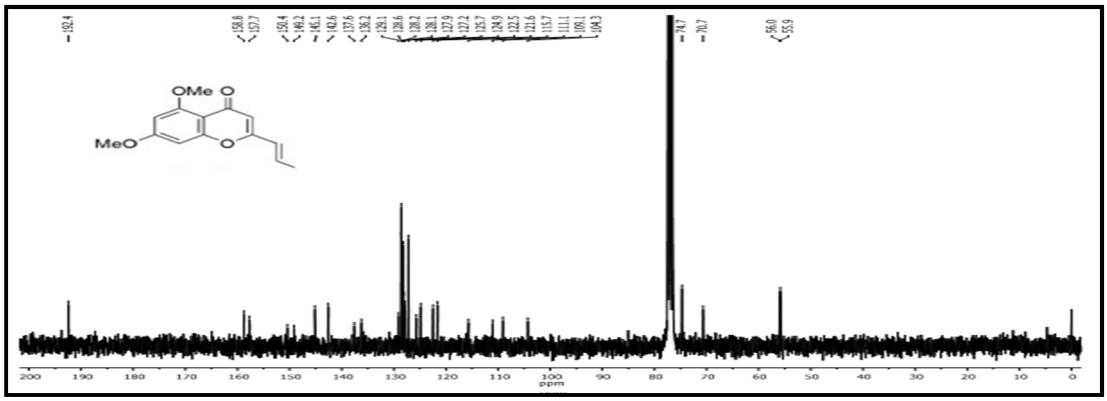
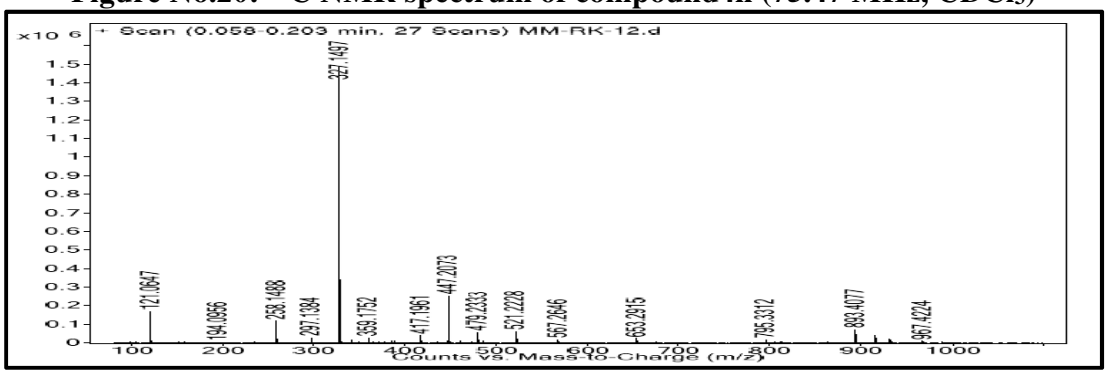
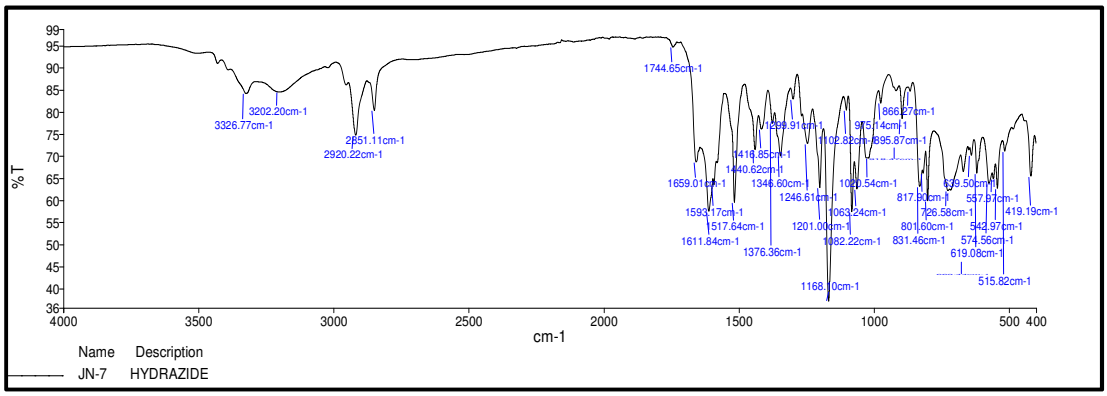


Figure No.20: ^{13}C NMR spectrum of compound4h (75.47 MHz, $CDCl_3$)





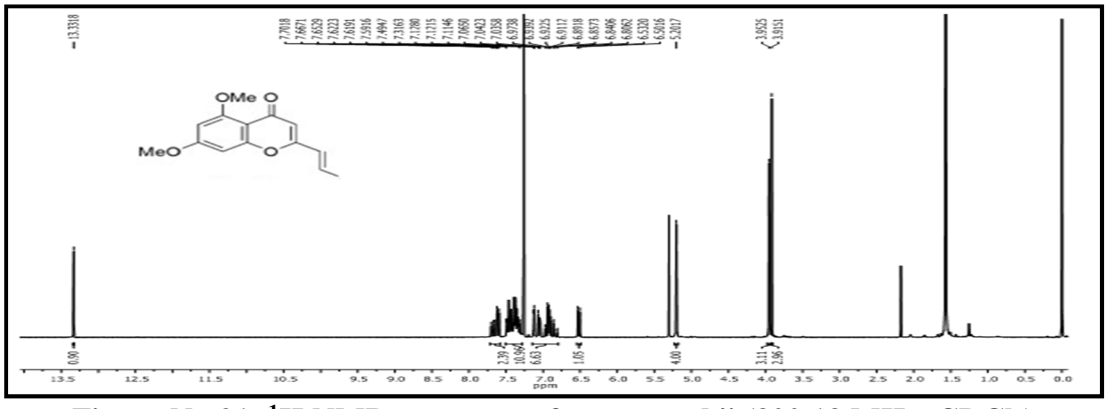


Figure No.21: ^{1}H NMR spectrum of compound4i (300.13 MHz, $CDCl_3$)

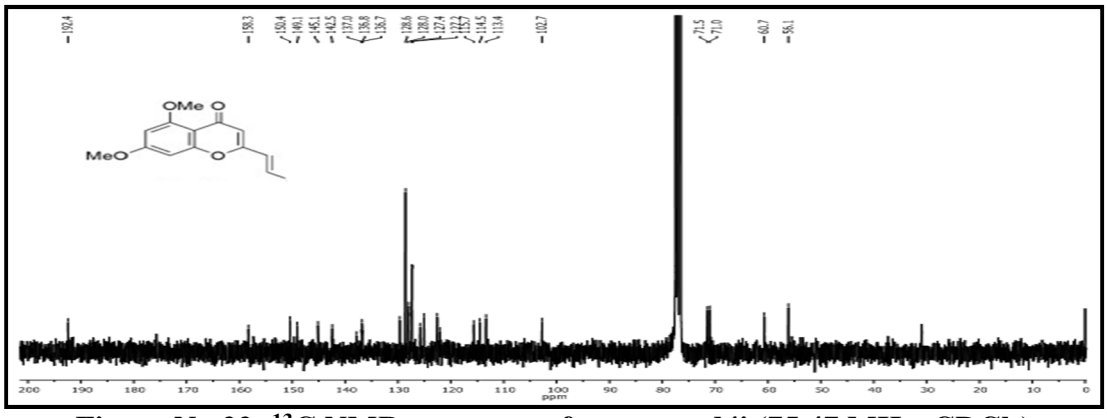
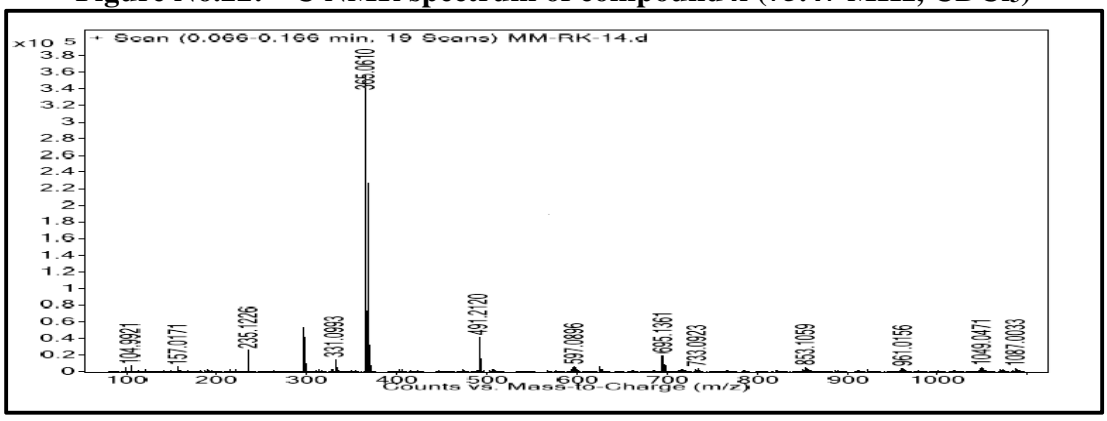
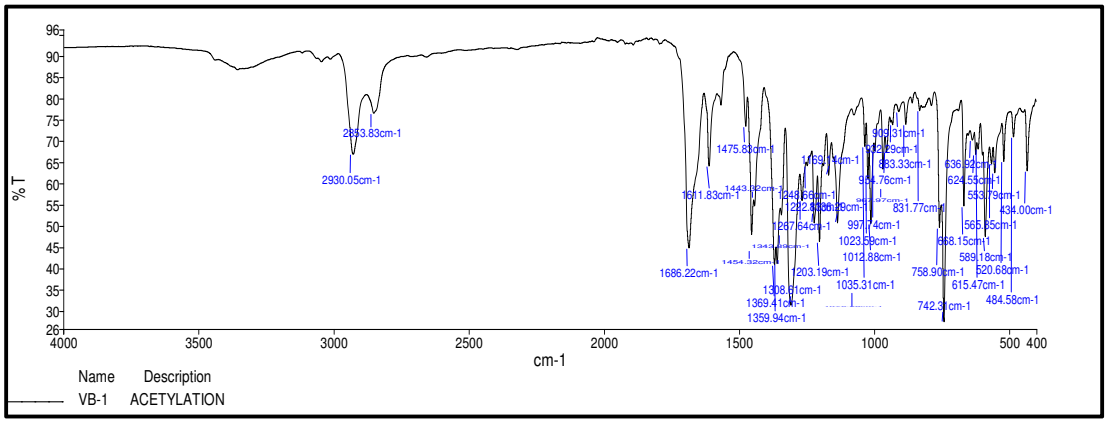


Figure No.22: ^{13}C NMR spectrum of compound4i (75.47 MHz, $CDCl_3$)





CONCLUSION

In this present study of the Design, Synthesis and molecular docking studies of 2-styrylchromone derivatives as novel antioxidant agents was considered chromone as basic fundamental pharmacophore in order to show antioxidant properties. Finally, through molecular modelling studies it is concluded that the synthesized molecules follows Lipinski rule of five.

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CONFLICT OF INTEREST

We declare that we have no conflict of interest.

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