**Experimental Section**

***C4β-Amido-azido-podophyllotoxin* (8):**

To a solution of azido acetic acid (245 mg, 2.42 mmol) and C4β-aminopodophyllotoxin (1 g, 2.42 mmol) in 10 mL of DCM was added 150 mg of EDCI and catalytic amount of HOBT at 0°C. The mixture was stirred overnight at ambient temperature followed by the addition of saturated aqueous sodium bicarbonate solution (30 mL). The organic layer was washed with water (2 x 50 mL) and dried over anhydrous $Na_2SO_4$. After the solvent was removed, the crude product was subjected to silica gel column chromatographic purification using hexane-ethyl acetate (90:10) to give 1.1 g (89%) of 4β-amidopodophyllotoxin as a syrup. Physical state: White Solid; $^1$H NMR (200 MHz, $CDCl_3$): δ 6.81 (1H, s), 6.55 (1H, s), 6.30 (2H, s), 6.02 (2H, d, *J* = 5.3Hz), 4.95 (1H, d, *J* = 7.8 Hz), 4.73 (1H, d, *J* = 2.6 Hz), 4.31 (2H, m), 3.9 (9H, s), 3.18 (1H, m), 2.83 (1H, m), 2.51 (2H, s); IR (KBr): 3435, 2910, 1765, 1715, 1510, 1456, 1395, 1055 cm$^{-1}$; Mass (ESI-MS): 519 $[M+Na]^+$.

***4β-[(4-substituted)-1,2,3-triazol-1-yl]Podophyllotoxins:***

***General procedure Click Reaction*:**

To a solution of acetylene (1.0 mmol) in t-butyl alcohol and water (1:2, 8 mL) was added $CuSO_4.5H_2O$ (1 mmol), sodium ascorbate (2 mmol) followed by 4β-azido-podophyllotoxin (44 mg, 0.1 mmol). The reaction mixture was stirred at room temperature for 8 hours. After completion that revealed by TLC, reaction mixture was diluted with 80 mL of water and extracted with ethyl acetate (2 × 20 mL). The combined extracts were washed with brine, dried over anhydrous $Na_2SO_4$ and evaporated in *vacuo*. The crude product obtained was precipitated in diethyl ether to yield the pure product **9**.

***4β-[2-(4-Phenyl-1H-1,2,3-triazol-1-yl)]-Amidopdophyllotoxin* (9a):**

Physical state: Brown Solid; $[\alpha]_D^{30}$: –172.1 (*c* = 1.0, $CHCl_3$); MP: 161–163°C; $^1$H NMR ($CDCl_3$, 300 MHz): *δ* 7.92 (1H, s), 7.71 (2H, d, *J* = 6.8Hz), 7.44 (2H, t, *J* = 8.0Hz), 7.35 (1H, d, *J* = 6.4Hz), 7.21 (1H, s), 7.05 (1H, d, *J* = 8.3Hz), 6.62 (1H, s), 6.4 (1H, s), 6.25 (2H, s), 5.98 (2H, d, *J* = 10.2Hz), 5.22 (1H, q, *J* = 4.2Hz), 5.15 (2H, s), 4.40 (1H, d, *J* = 5.2Hz), 4.32 (1H, t, *J* = 6.4 Hz),

3.91 (3H, s), 3.78 (6H, s), 2.91 (2H, m); $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ 174.3, 165.2, 152.4, 148.2, 147.4, 137.0, 134.8, 132.2, 129.6, 128.8, 128.0, 125.6, 121.5, 110.0, 108.8, 108, 101.5, 68.6, 60.6, 56.1, 52.5, 48.3, 43.5, 41.9, 37.0; MS (ESI): m/z 621 $[M+Na]^+$; HRMS (ESI m/z) for $C_{32}H_{31}O_8N_4$ calcd: 599.21419, observed: 599.21490 $[M+ H]^+$.

***4β-[2-(4-P-tolyl-1H-1,2,3-triazol-1-yl)]-Amidopdophyllotoxin* (9b):**

Physical state: Light yellow Solid; $[\alpha]_D^{30}$: –161.5 (*c* = 1.0, $CHCl_3$); MP: 160–162 °C; $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ 7.95 (1H, s), 7.76 (2H, d, *J* = 8.3Hz), 7.65 (1H, d, *J* = 8.2Hz), 7.24 (3H, t, *J* = 14.2Hz), 6.62 (1H, s), 6.35 (1H, s), 6.24 (2H, s), 5.97 (2H, d, *J* = 4.5Hz), 5.21–5.18 (1H, m), 5.12 (2H, s), 4.33–4.24 (2H, m), 3.79 (3H, s), 3.71 (6H, s), 2.94 (2H, m), 2.3 (3H, s); $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ 174.2, 165.2, 153.4, 152.5, 148.3, 147.4, 138.5, 137.3, 134.7, 132.3, 129.5, 125.6, 121.1, 110.0, 108.1, 101.5, 68.5, 60.6, 56.1, 52.6, 48.4, 43.5, 41.5, 37.0, 29.6, 21.2; MS (ESI): m/z 635 $[M+Na]^+$; HRMS (ESI m/z) for $C_{33}H_{33}O_8N_4$ calcd: 613.22984, observed: 613.22961 $[M+ H]^+$.

***4β-[2-(4-(4-Tert-butylphenyl)-1H-1,2,3-triazol-1-yl)]-Amidopdophyllotoxin* (9c):**

Physical state: Light Yellow Solid; $[\alpha]_D^{30}$ : –197.4 (*c* = 1.0, $CHCl_3$); MP: 169–170 °C; $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ 7.98 (1H, s), 7.61 (2H, d, *J* = 8.2Hz), 7.46 (2H, d, *J* = 8.5Hz), 7.28 (1H, s), 6.62 (2H, s), 6.2 (2H, s), 5.95 (1H, s), 5.93 (2H, s), 5.2 (1H, q, *J* = 4.4Hz), 5.12 (2H, s), 4.45 (1H, d, *J* = 2.4Hz), 4.3 (1H, t, *J* = 8.8Hz), 3.78 (3H, s), 3,72 (6H, s), 2.91 (2H, m), 1.3 (9H, s); $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ 174.3, 165.3, 152.4, 151.7, 148.2, 147.4, 138.8, 137.0, 134.8, 132.3, 128.0, 126.8, 125.8, 125.3, 121.1, 110.0, 108.7, 108.0, 101.5, 68.5, 60.6, 56.1, 48.3, 43.5, 41.4, 36.9, 34.6, 31.2; MS (ESI): m/z 613 $[M+Na]^+$; HRMS (ESI m/z) for $C_{36}H_{39}O_8N_4$ calcd: 655.27679, observed 655.27598 $[M+ H]^+$.

***4β-[2-(4-(3,4-Dimethoxyphenyl)-1H-1,2,3-triazol-1-yl)]-Amidopdophyllotoxin* (9d):**

Physical state: Yellow Solid; $[\alpha]_D^{30}$: –178.1 (*c* = 1.0, $CHCl_3$); MP: 154–155 °C; $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ 7.88 (1H, s), 7.4 (1H, s), 7.23 (2H, s), 6.96 (2H, s), 6.65 (1H, s), 6.44 (1H, s), 6.21 (2H, s), 5.97 (2H, d, *J* = 4.5Hz), 5.22 (1H, q, *J* = 4.5Hz), 5.08 (2H, s), 4.39 (1H, d, *J* = 5.4Hz), 4.28 (1H, t, *J* = 10.2Hz), 3.96 (3H, s), 3.92 (3H, s), 3.78 (3H, s), 3.72 (6H, s), 2.92 (2H,

m); $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ 174.3, 165.2, 152.4, 149.2, 148.1, 147.4, 137.0,134.7, 132.2, 134.0, 127.9, 122.6, 120.8, 118.2, 111.2, 109.9, 108.7, 107.9, 101.5, 68.5, 60.6, 56.1, 52.5, 48.3, 43.5, 41.4, 36.8, 30.9; MS (ESI): m/z 681 $[M+Na]^+$; HRMS (ESI m/z) for $C_{34}H_{35}O_{10}N_4$ calcd: 659.23532, observed: 659.23511 $[M+ H]^+$.

***4β-[4-(1-Methyl-1H-imidazole))-1,2,3-triazol-1-yl)]-Amidopdophyllotoxin* (9e):**

Physical State: Light Brown Solid; $[\alpha]_D^{30}$: –129.29 (*c* 1.0, $CHCl_3$); MP: 157–159 $^oC$;$^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ 7.76 (1H, s), 7.61 (2H, d, *J* = 7.5Hz), 7.32 (2H, s), 7.22 (1H, s), 6.63 (2H, s), 6.36 (2H, s), 6.16 (2H, s), 5.78 (2H, s), 5.19 (1H, s), 5.06 (2H, s), 4.32 (2H, m), 3.72 (3H, s), 3.65 (6H, s), 2.92 (2H, s); $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ 171.8, 152.6, 148.8, 148.2, 138.1, 133.9, 133.2, 131.0, 126.8, 125.1, 124.1, 122.1, 119.5, 111.5, 108.6, 108.5, 102.1, 95.9, 66.9, 60.8, 58.4, 56.2, 43.3, 42.1, 30.8, 29.3 MS (ESI): m/z 625 $[M+Na]^+$; HRMS (ESI m/z) for $C_{30}H_{31}O_8N_6$ calcd: 603.22033, observed: 603.22012 $[M+ H]^+$.

***4β-[-(4-(3-Aminophenyl)-1H-1,2,3-triazol-1-yl)]-Amidopdophyllotoxin* (9f):**

Physical state: Brown Solid; $[\alpha]_D^{30}$: –154.3 (*c* = 1.0, $CHCl_3$); MP: 155–156 $^oC$; $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ 7.89 (1H, s), 7.48 (1H, s), 7.21 (1H, s), 7.19–7.11 (3H, m), 7.03 (1H, s), 6.59 (2H, s), 6.28 (1H, s), 6.17 (1H, s), 5.91 (2H, s), 5.28–5.22 (1H, m), 5.12 (1H, d, *J* = 6.7Hz), 4.39–4.28 (2H, m), 4.13 (2H, d, *J* = 21.1Hz), 3.68 (3H, s), 3.6 (6H, s), 3.31 (1H, t, *J* = 14.3Hz), 3.01 (1H, d, *J* = 4.5 Hz), 2.79 (1H, s); $^{13}$C NMR ($CDCl_3$, 75 MHz): δ 174.4, 165.3, 152.5, 148.1, 147.1, 137.1, 134.8, 132.3, 130.5, 129.8, 128.0, 121.5, 115.7, 115.2, 112.0, 110.0, 108.1, 101.5, 60.6, 56.1, 52.9, 48.3, 43.5. 41.4, 37.0, 30.6; MS (ESI): m/z 636 $[M+Na]^+$; HRMS (ESI m/z) for $C_{32}H_{32}O_8N_5$ calcd: 614.22509, observed: 614.22489 $[M+ H]^+$.

***4β-[-(4-(3-Chlorophenyl)-1H-1,2,3-triazol-1-yl)]-Amidopdophyllotoxin* (9g):**

Physical state: Brown Solid; $[\alpha]_D^{30}$: –162.5 (*c* = 1.0, $CHCl_3$); MP: 159–1619$^oC$; $^1$H NMR ($CDCl_3$, 300 MHz): $\delta$ 8.09 (1H, s), 7.78 (1H, s), 7.72 (1H, d, *J* = 8.2Hz), 7.4–7.2 (2H, m), 7.08–6.9 (2H, m), 6.71 (1H, s), 6.47 (1H, s), 6.32 (2H, s), 6.03 (2H, d, *J* = 8.7Hz), 5.38–5.32 (1H, m), 5.19 (2H, s), 4.63 (1H, s), 4.37 (1H, t, *J* = 15.2Hz), 3.88 (3H, s), 3.83 (6H, s), 2.94 (2H, m); $^{13}$C NMR ($CDCl_3$, 75 MHz): $\delta$ 174.3, 165.0, 152.4, 148.2, 146.7, 136.9, 134.8, 132.2, 131.4, 130.1,

128.4, 127.9, 125.5, 123.6, 122.0, 109.9, 108.7, 108.0, 101.5, 60.6, 56.1, 52.5, 48.4, 43.5, 41.4, 36.9; MS (ESI): m/z 655 $[M+Na]^+$; HRMS (ESI m/z) for $C_{32}H_{30}O_8N_4Cl$ calcd: 633.17521, observed: 633.17592 $[M+ H]^+$.

***4β-[-(4-(pyridin2-yl)-1H-1,2,3-triazol-1-yl)]-Amidopdophyllotoxin* (9h):**

Physical state: Brown Solid; $[\alpha]_D^{30}$: –165.5 (*c* = 1.0, $CHCl_3$); MP: 150–152 °C; $^1H$ NMR ($CDCl_3$, 300 MHz): *δ* 8.08-7.81 (3H, m), 7.23 (1H, s), 6.67 (2H, s), 6.48 (2H, s), 6.41 (1H, d, *J* = 4.2Hz), 6.19 (2H, s), 6.02 (2H, d, *J* = 6.7Hz), 5.22 (1H, d, *J* = 5.0Hz), 4.55 (1H, d, *J* = 4.7Hz), 4.31 (1H, t, *J* = 7.0 Hz), 4.02 (2H, s), 3.13 (3H, s), 3.73 (6H, s), 2.95 (2H, m); $^{13}C$ NMR ($CDCl_3$, 75 MHz):*δ* 174.0, 166.7, 152.5, 148.5, 147.7, 147.4,137.8, 137.1, 134.5, 132.3, 130.7, 128.0, 124.8, 124.5, 124.1,129.5, 110.1, 108.8, 108.0, 101.6, 68.7, 60.6, 56.1, 52.2, 48.1, 43.6, 41.6, 37.1, 31.5; MS (ESI): m/z 622 $[M+Na]^+$; HRMS (ESI m/z) for $C_{31}H_{30}O_8N_5$ calcd: 600.20944, observed: 600.20916 $[M+ H]^+$.

***4β-[2-(4-(Thiophen-2-yl)-1H-1,2,3-triazol-1-yl)]-Amidopdophyllotoxin* (9i):**

Physical State: Light Yellow Solid; $[\alpha]_D^{30}$: –109.29 (*c* 1.0, $CHCl_3$); MP: 149–150 °C; $^1H$ NMR ($CDCl_3$, 300 MHz): *δ* 7.78 (1H, s), 7.51 (2H, d, *J* = 7.5Hz), 7.29 (2H, s), 7.24 (1H, s), 6.6 (1H, s), 6.3 (1H, s), 6.11 (2H, s), 5.8 (2H, s), 5.2 (1H, s), 5.0 (2H, s), 4.33-4.31 (2H, m), 3.69 (3H, s), 3.64 (6H, s), 2.89 (2H, s); $^{13}C$ NMR ($CDCl_3$, 100 MHz): *δ* 172.8, 152.8, 149.4, 148.1, 137.7, 134.1, 133.3, 131.1, 126.4, 125.6, 124.7, 121.6, 119.5, 110.5, 108.9, 108.3, 101.9, 96.1, 67.3, 60.6, 58.6, 56.3, 43.7, 41.7, 31.1, 29.7; MS (ESI): m/z 627 $[M+Na]^+$; HRMS (ESI m/z) for $C_{30}H_{29}O_8N_4S$ calcd: 605.17061, observed: 605.17112 $[M+ H]^+$.

***4β-[2-(4-(4-Bromophenyl)-1H-1,2,3-triazol-1-yl)]-Amidopdophyllotoxin* (9j):**

Physical state: Dirty white Solid; $[\alpha]_D^{30}$: –164.4 (*c* = 1.0, $CHCl_3$); MP: 209–211 °C; $^1H$ NMR ($CDCl_3$, 300 MHz): δ 8.01 (1H, s), 7.78 (1H, s), 7.68 (1H, d, *J* =7.2Hz),7.44–7.23 (3H, m), 7.02 (1H, s), 6.67 (1H, s), 6.48 (1H, s), 6.27 (2H, s), 6.05 (2H, s), 5.32–5.38 (1H, m), 5.19 (2H, s), 4.47 (1H, d, *J* = 4.4Hz), 4.38 (1H, t, *J* = 7.0Hz), 3.88 (3H, s), 3.82 (6H, s), 2.93 (2H, m); $^{13}C$ NMR ($CDCl_3$, 75 MHz): *δ* 174.3, 166.8, 152.6, 148.2, 147.4, 147.0, 136.6, 134.7, 131.9, 128.7, 128.0, 127.0, 122.3, 121.6, 110.0, 108.8, 108.0, 101.5, 60.6, 56.1, 52.1, 48.0, 43.5, 41.5, 36.3, 30.8; MS

(ESI): m/z 699 $[M+Na]^+$; HRMS (ESI m/z) for $C_{32}H_{30}BrO_8N_4$ calcd: 677.12470, observed: 677.12439 $[M+ H]^+$.

***4β-[2-(4-(2-(1,3-Dioxo-2,3-dihydro-1H-inden-2-yl)ethyl)-1H-1,2,3-triazol-1-yl)]-Amidopdophyllotoxin* (9k):**

Physical State : brown Solid; $[\alpha]_D^{30}$: –104.4 (*c* 1.0, $CHCl_3$); MP: 154–156 $^oC$; $^1H$ NMR ($CDCl_3$, 300 MHz): $\delta$ 7.61–7.42 (4H, m), 7.07 (2H, d, *J* = 6.2Hz), 6.69 (2H, s), 6.38 (1H, s), 6.15 (2H, s), 5.89 (2H, s), 5.19 (1H, t, *J* = 11.7Hz), 5.11 (2H, s), 4.42 (1H, d, *J* = 4.2Hz), 4.26 (1H, t, *J* = 8.2Hz), 4.08 (1H, d, *J* = 7.4Hz), 3.83 (3H, s), 3.72 (6H, s), 2.93 (2H, m), 2.43 (2H, t, *J* = 4.3Hz), 1.93 (2H, m), $^{13}C$ NMR ($CDCl_3$, 75 MHz): $\delta$ 174.3, 168.2, 165.6, 152.5, 148.3, 147.4, 145.4, 137.0, 134.7, 134.0, 132.5, 131.7, 128.2, 123.2, 110.0, 108.9, 108.0, 101.5, 68.6, 60.6, 56.1, 52.5, 48.2, 43.6, 41.3, 37.8, 36.9, 24.8; MS (ESI): m/z 717 $[M+Na]^+$; HRMS (ESI m/z) for $C_{37}H_{35}O_{10}N_4$ calcd: 695.23532, observed: 695.23491 $[M+ H]^+$.

***4β-[2-(4-(6-Methoxynaphthalen-2-yl)-1H-1,2,3-triazol-1-yl)]-Amidopdophyllotoxin* (9l):**

Physical state: Yellow Solid; $[\alpha]_D^{30}$: –152.2 (*c* = 1.0, $CHCl_3$); MP: 141–143 $^oC$; $^1H$ NMR ($CDCl_3$, 300 MHz): $\delta$ 8.08 (1H, s), 8.02 (1H, s), 7.68 (2H, s), 7.59 (2H, d, *J* =7.5Hz), 7.21–7.07 (2H, m), 6.73 (2H, s), 6.31 (2H, s), 6.07 (2H, s), 5.89 (2H, d, *J* = 9.8Hz), 5.21–5.15 (1H, m), 5.02 (1H, d, *J* = 9.2Hz), 4.33–4.22 (2H, m), 3.93 (3H, s), 3.76 (3H, s), 3.69 (6H, s), 2.93 (2H, m); $^{13}C$ NMR ($CDCl_3$, 75 MHz): $\delta$ 174.2, 165.2, 158.0, 152.5, 147.4, 148.3, 137.0, 134.7, 134.4, 132.3, 129.6, 128.7, 128.0, 127.4, 124.4, 124.0, 121.3, 119.4, 110.0, 108.7, 108.0, 105.6, 101.5, 68.6, 60.6, 56.1, 55.2, 52.6, 48.3, 43.5, 41.4, 36.9, 31.3 MS (ESI): m/z 701 $[M+Na]^+$; HRMS (ESI m/z) for $C_{37}H_{35}O_9N_4$ calcd: 679.24040, observed: 679.24071 $[M+ H]^+$.

**Biology**

**Cell lines**

MCF-7 cells (breast cancer), B-16 cells (oral cancer), HT-29 cells (colon cancer) and HeLa cells (cervical cancer) were obtained from National Centre for Cell Science (NCCS), Pune, India.

**Anticancer activity (MTT Assay)**

The cytotoxicity activity of the conjugates was determined using MTT assay. 10,000 cells/well were seeded in 200 µl DMEM, supplemented with 10% FBS in each well 96 well micro culture plates and incubated for 24h at 37 °C in a $CO_2$ incubator. Compounds diluted to the desired concentrations in culture medium, were added to the wells with respective vehicle control. After 48 h of incubation, 10µL of MTT (3-(4, 5-dimethylthiazol-2-yl)-2, 5-diphenyltetrazolium bromide) (5 mg/mL) was added to each well and the plates were further incubated for 4 h. Then the supernatant from each well was carefully removed and formazon crystals were dissolved in 100 µL of DMSO and absorbance at 540 nm wavelengths was recorded. [23]

**Cell cycle analysis**

HeLa cancer cells were seeded in 6 well plates and treated with conjugates **9c** and **9j** at concentrations of 0.5 µM for 48 h. After the treatment, both the floating as well as trypsinised adherent cells were collected, washed with phosphate buffer saline and fixed with 70% ethanol. After fixation the cells were washed with PBS and stained with 50 µg/mL propidium iodide in hypotonic lysis buffer (0.1% sodium citrate, 0.1% Triton X-100) containing DNase free RNase-A for about 20 min. Stained cells were analyzed then using fluorescence-activated cell sorter caliber (Becton Dickinson). [24]

**2.2.2 *Invitro* tubulin polymerization**

A fluorescence based tubulin polymerization inhibition assay was performed according to the manufacturers protocol (BK011, Cytoskeleton, Inc.). Briefly, the reaction mixture was taken within a total volume of 10 µL contained PEM buffer, GTP (1µM) in the presence or absence of test conjugates **9c** and **9j** at a final concentration of 3 µM. *Invitro* tubulin polymerization was followed by a time dependent increase in fluorescence due to the incorporation of a fluorescence reporter into microtubules as polymerization proceeds. Fluorescence emission at 420 nm (excitation wavelength is 360 nm) was measured by using a Biotek multimode plate reader. Polymerization was finally monitored by increase in the fluorescence mentioned above at 37 $^{o}$C .[25]

### 2.2.3 Immunohistochemistry of tubulin

Cervical cancer cells were seeded on glass cover slips, incubated for 48 hours in the presence or absence of test conjugates **9c** and **9j** and reference nocodazole at a concentration of 0.5 µM. Following the termination of incubation, cells were fixed with 3% formaldehyde, 0.02%glutaraldehyde in PBS and permeabilized by dipping the cells in100% methanol and kept overnight at $4^0$C. Later the cover slips were blocked with 1% BSA in phosphate buffered saline for 1 h followed by incubation with a primary antibody α-tubulin (mouse monoclonal) and later with FITC conjugated secondary mouse anti IgG antibody. Photographs were taken using the confocal microscope, equipped with FITC settings and the pictures were analyzed for the integrity of microtubule network. [26]

### 2.2.4 Hoechst staining

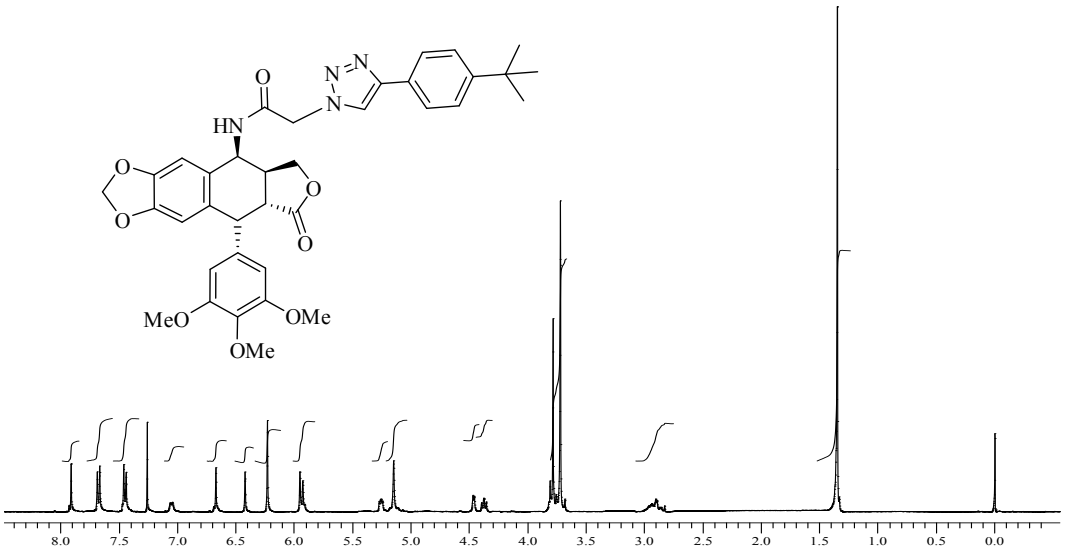
HeLa cancer cells were seeded at a density of 10,000 cells over 18-mm covers lips and incubated for a period of 48 h. Then, the medium was taken and again replaced, and cells were treated with 0.5 µM concentration of conjugates **9c** and **9j** for 48 h. Cells treated with vehicle(0.001% DMSO) were included as controls for all experiments. Cells were fixed with 4% paraformaldehyde and stained with solution of Hoechst 33342 (Sigma Aldrich) 5 µg/mL in PBS. After incubating for 30 min at 37 $^o$C, excess dye was washed with PBS and cells from each dish were captured from randomly selected fields under fluorescent microscope (Olympus) to qualitatively determine the proportion of viable and apoptotic cells based on their relative fluorescence and nuclear fragmentation. [27]

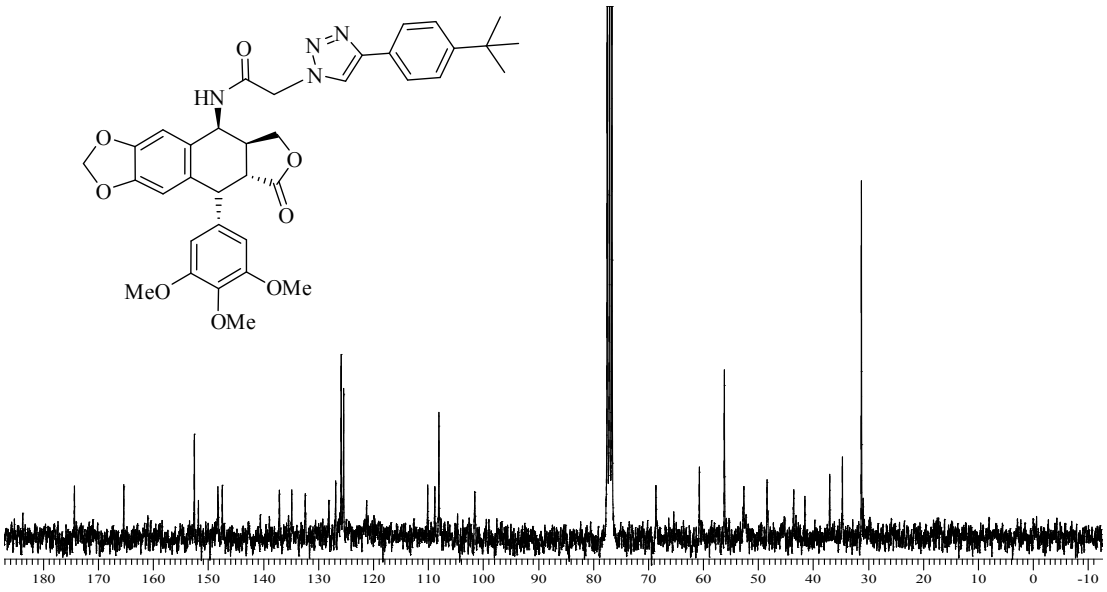
### 2.2.5 Caspase-3 activation

To find out the caspase-3 activity of the active compounds **9c** and **9j** AFC conjugated Ac-DEVD substrate was used. HeLa cancer cells were seeded in 6 well plates with the confluence of $2.5*10^{-5}$per well and are treated with the compounds at 0.5 µM concentration. After incubation for 48 h cell were washed with PBS and then cells were scraped in to the PBS and centrifuged at 2000 rpm for 10 min at 4 $^0$C. Pellet was resuspended in 80 µL of lysis buffer, pellet was passed through insulin syringe followed by incubation of suspension on ice for 20-30 min centrifuged the lysate at 13,200 rpm for 20 min at 4 $^o$C and transferred the supernatant to fresh tubes. In a 96 well black polystyrene plate, 50 µL of 2X assay buffer, 50 µl cell lysate and 2 µL of caspase-3 substrate were

taken. The reaction was allowed to take place for 1 h. The fluorescence generated by the release of the fluorogenic group AFC on cleavage by caspase-3 was measured by excitation at 400 nm and emission at 505 nm for every 5 min over 1 h. Protein was estimated by Bradford's method and normalized accordingly. [28]

# Proton and Carbon spectrum of compound 9c



# Proton and Carbon spectrum of compound 9j