Supporting documents

Low toxic synthetic dendrimer conjugated podophyllotoxin nanodevice with potent antitumor activity against DMBA/TPA induced mouse skin carcinogenesis model

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**Figure S1:** $^1$H-NMR of the compound PODO-linker in CDCl$_3$. 
Figure S2: $^{13}$C-NMR of the compound PODO-linker in CDCl$_3$
**Figure S3:** $^1$H-NMR of the compound D-PODO-linker in DMSO

$^1$H-NMR (600 MHz, DMSO-$d_6$): 7.81-8.05 (m, amide –NH from D), 6.89 (s, 1H, Ar-H8), 6.59 (s, 1H, Ar-H5), 6.30 (s, 2H, Ar-H-2’ & 6’), 6.00 (m, 2H, H-13), 5.89 (m, 1H, H-4), 4.54 (CH$_2$-O from D), 4.27 (m, 1H, H-1), 4.12 (m, 1H, H-11), 3.98 (m, 1H, H-11), 3.61 (s, 3H, -OCH$_3$ –H), 3.63 (s, 6H, -OCH$_3$ –H), 3.25-2.20 (m, H-2, H-3, and proton from PODO-linker (a & b), and internal D-proton).

**Figure S4.** MALDI-TOF-MS showing increase in the molecular weight of the dendrimer conjugates. The relative change in molecular weight upon conjugation of linker attached PODO to the dendrimer (D). D (13573) and D-PODO (17464) conjugate; also previous generation D (6853) and conjugate D-PODO (8950)
Figure S5: Histopathological data for toxicity evaluation

Histopathological analysis (20x) of liver (up) and kidney (down) after 14 week of treatment schedule alone with concomitant topical application of carcinogen. (a and d: carcinogen control; b and e: 4 mg/kg D-PODO treatment group; c and f: 8 mg/kg treatment of D-PODO. Observation indicates there were not much change of hepatocytes and kidney cell after long term treatment with D-PODO.
Figure 6: Graphical representation of apoptotic cells of DMBA-TPA (carcinogen control), 4 mg/kg and 8 mg/kg treatment groups. (*): The compares made between the control and 4 mg group and the significance level is p<0.05 and (#): 8 mg group compared in between 4 mg as well as with control group, level of significance is p<0.05.

Figure S7. D-PODO induced expression of Bax (a); Bcl2(b), NFκB(c) and Bax/Bcl2 (d) ratio: graphical representation of the active area and their statistical significance; mean± SEM compares made between DMBA/TPA and the treatment group, data were significance upto *p> 0.05, whereas # indicated data were significance in compares to DMBA/TPA and 4 mg treatment group.