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Design, docking and crystal structure determination of copper based chemotherapeutic as potential topoisomerase inhibitor: *In vitro* DNA binding, nuclease studies, *in vitro* and *in vivo* anticancer activity

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Small molecules that bind to DNA minor groove region which inhibit the expression of DNA-processing enzymes (topoisomerase I and II) and its delivery towards the targeted cell *via* binding to carrier protein represent an important class of anticancer drugs. In this point of view, a mononuclear and di nuclear Cu(II), Sn(IV), Ru(III) complexes were designed and synthesized and characterized by elemental analysis, spectroscopic and magnetic studies. The structure of complexes were solved by single crystal X-ray diffraction method which revealed that Cu(II) metal ion arranged in a N_4O coordination environment showing distorted square pyramidal geometry. The complexes were successively docked towards the molecular target DNA, HSA and topoisomerase in a site selective manner and further validated by *in vitro* DNA and employing different biophysical techniques. The pBR322 DNA cleavage and topoisomerase relaxation assay was investigated using concentration dependent agarose gel electrophoresis. *In vitro* and *in vivo* anticancer activity was performed.

Biography

Sartaj Tabassum is working as Professor in the Department of Chemistry, Aligarh Muslim University, Aligarh. He has published 86 papers in the journals of international repute. He is life member of ACS (USA) ICC, CRSI, ISCB, DNA Society of India and American Nano Society(USA). He has successfully completed many research schemes granted by TWAS, Italy, CSIR, New Delhi, DBT, Government of India. As a distinguished scientist, he was awarded Overseas Associateship award in 2005 by DBT, Goverment of India. He has signed several MoU and joint research collaboration with University of Camerino UNICAM, Italy, USM Malaysia and USTC, China.

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Grape seed proanthocyanidins inhibit the migration potential of human melanoma cells by targeting β-catenin

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Metastatic melanoma is a leading cause of death from skin diseases, and is often associated with activation of Wnt/β-catenin signaling pathway. To develop effective strategies against melanoma metastasis, we examined the inhibitory effect of grape seed proanthocyanidins (GSPs) on cell migration of metastasis-specific human melanoma cell lines (A375 and Hs294t) and assessed whether Wnt/β-catenin signaling is the target of GSPs. Using an *in vitro* invasion assay, we found that treatment of human melanoma cell lines with GSPs resulted in a dose-dependent inhibition of cell migration, which was associated with reduced levels of cytosolic and nuclear β-catenin and decreasing the expressions of matrix metalloproteinase (MMP)-2 and MMP-9 which are the down-stream targets of β-catenin. GSPs enhanced: (i) the levels of casein kinase1α, glycogen synthase kinase-3β and phosphorylated-β-catenin on critical residues Ser^{45}, $Ser^{33/37}$ and Thr^{41}, and (ii) the binding of β-transducin repeat-containing proteins (β-TrCP) with phospho forms of β-catenin in melanoma cells. Further to verify whether β-catenin is a potent molecular target of GSPs, the effect of GSPs was determined on β-catenin-activated (Mel1241) and β-catenin-inactivated (Mel1011) melanoma cells. Treatment of Mel1241 cells with GSPs or FH535, an inhibitor of Wnt/β-catenin pathway, significantly inhibited cell migration of Mel1241 cells, which was associated with the elevated levels of casein kinase1α and glycogen synthase kinase-3β, and decreased accumulation of nuclear β-catenin and inhibition of MMPs levels. However, this effect of GSPs and FH535 was not found in Mel1011 melanoma cells. These results indicate for the first time that GSPs inhibit melanoma cell migration by targeting β-catenin signaling pathway. This new insight into the anti-melanoma cell migration ability of GSPs may serve as a basis for chemoprevention or therapy of malignant melanoma, and it can be used either alone or in combination with other anti-metastatic drugs for the treatment of melanoma in humans.