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Moringa oleifera gold nanoparticles modulate oncogenes, tumor suppressor genes and caspase-9 splice variants in A549 cells

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Gold nanoparticles (AuNP's) facilitate cancer cell recognition and can be manufactured by green synthesis using nutrient rich medicinal plants such as Moringa oleifera (MO). Targeting dysregulated oncogenes and tumor suppressor genes is crucial for cancer therapeutics. We investigated the antiproliferative effects of AuNP synthesized from MO aqueous leaf extracts (MLAuNP) in A549 lung and SNO oesophageal cancer cells. A one-pot green synthesis technique was used to synthesize MLAuNP. A549, SNO cancer cells and normal peripheral blood mononuclear cells (PBMCs) were exposed to MLAuNP and CAuNP to evaluate cytotoxicity (MTT assay); apoptosis was measured by phosphatidylserine (PS) externalization, mitochondrial depolarization ($\Delta\Psi_m$) (flow cytometry), caspase-3/7, -9 activity and ATP levels (luminometry). The mRNA expression of c-myc, p53, Skp2, Fbw7 α and caspase-9 splice variants was determined using qPCR, while relative protein expression of c-myc, p53, SRp30a, Bax, Bcl-2, Smac/DIABLO, Hsp70 and PARP-1 were determined by Western blotting. MLAuNP and CAuNP were not cytotoxic to PBMCs, whilst its pro-apoptotic properties were confirmed in A549 and SNO cells. MLAuNP significantly increased caspase activity in SNO cells while MLAuNP significantly increased PS externalization, $\Delta\Psi_m$, caspase-9, caspase-3/7 activities and decreased ATP levels in A549 cells. Also, p53 mRNA and protein levels, SRp30a ($p=0.428$), Bax, Smac/DIABLO and PARP-1 24 kDa fragment levels were significantly increased. Conversely, MLAuNP significantly decreased Bcl-2, Hsp70, Skp2, Fbw7 α , c-myc mRNA and protein levels and activated alternate splicing with caspase-9a splice variant being significantly increased. MLAuNP possesses antiproliferative properties and induced apoptosis in A549 cells by activating alternate splicing of caspase-9.

Biography

Charlette Tiloke has completed her PhD at the Department of Medical Biochemistry, University of KwaZulu-Natal and is currently a Postdoctoral Fellow. Her research interests include anticancer and antimicrobial activity of medicinal plants and their synthesized nanoparticles.

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