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Brusatol Nanoparticles to Facilitate Clinical Translation for Chemotherapy

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Brusatol has been reported to possess a unique potential to target two distinct pathways that are important in the progression of cancers by its specific action on nuclear factor erythroid 2-related factor 2 (Nrf2) and as a global protein synthesis inhibitor. Due to its non-selective mechanisms of action, it is unlikely that brusatol can be administered as a therapeutic agent without substantial host toxicity. The oil-in-water emulsification solvent diffusion method was modified to prepare brusatol-loaded, polyethylene glycol-coated polylactide-*co*-glycolide nanoparticles. Scanning electron microscopy revealed the formation of nanoparticles and average size was determined by dynamic light scattering. Drug content of the nanoparticle formulation was determined by high performance liquid chromatography. The *in vitro* release isotherm showed a biphasic and sustained release of the encapsulated drug. Toxicity of the brusatol-loaded nanoparticles in prostate cancer cell lines was evaluated over 120 hours using the Cell Titer 96® Non-Radioactive Cell Proliferation Assay. *In vitro* cytotoxicity data revealed that both brusatol-loaded nanoparticles and the control brusatol solutions at the same concentrations exhibited dose-dependent toxicity to PC-3 and LNCaP prostate cancer cell lines at the concentrations used in this study with the nanoparticle formulation showing more toxicity to both cell lines. Cellular uptake of nanoparticles was evaluated using confocal microscopy after a 6-hour incubation of rhodamine-123-loaded nanoparticles with PC-3 cells. Data showed internalization of the nanoparticles. This study shows that the nanoparticle formulation of brusatol can overcome delivery challenges and facilitate the clinical translation of the compound for the treatment of cancers.

Biography:

Dr. Simeon K Adesina completed his Ph.D. at the Department of Pharmaceutical Sciences, Howard University. He has published several articles in peer reviewed journals and several abstracts and conference proceedings. He has a patent and another patent submission. He joined Howard University as Assistant Professor in 2012 and is currently an Associate Professor in the Department of Pharmaceutical Sciences, College of Pharmacy at Howard University.