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Cytotoxic, apoptotic and tumor regressive efficacy of polylactic-co-glycolic acid encapsulated diosgenin nanoparticles in cancer cell lines

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Nancer is a universal public health problem as it is one of the main causes of morbidity and mortality worldwide. Polylactic-✓ co-glycolic acid (PLGA) nanoparticles, one of the most effective biodegradable polymeric nanoparticles, are approved by the US FDA to use for the encapsulation of various cancer-related drugs and their successful delivery in vivo due to its controlled and sustained release properties, low toxicity, and biocompatibility. Diosgenin (DGN), a steroidal saponin phytocompound, plays a predominant role in decreasing cell malignancy and inhibits tumor promotion reducing matrix metalloproteinases expression and inducing apoptosis through cell cycle arrest, activation of p53 and caspase-3 but DGN has many limitations in clinical application due to its poor solubility and low bioavailability. The present study was designed to synthesize PLGA encapsulated diosgenin nanoparticles (PLGA-DGN NPs) and to evaluate its anticancer efficacy. The PLGA-DGN nanoparticles exhibited high entrapment efficacy (73.8%), and a higher blood circulation half-time as well as sustained release kinetics, better bioavailability, and rapid intracellular uptake capability. PI and DAPI staining, cell cycle study by flow cytometry, DNA laddering, measurement of generation of reactive oxygen species using H2DCFDA stain, mitochondrial membrane potential by rhodamine 123 and Western blot analysis were performed to explore the pathways involved in the apoptosis. PLGA-DGN NPs showed cytotoxicity to MCF-7 and Ehrlich ascites carcinoma (EAC) cells without producing no toxicity to human and mouse lymphocytes. PLGA-DGN NPs induced apoptosis by elevating ROS, chromatin condensation, DNA fragmentation, cell cycle arrest, expression of proapoptotic proteins and mitochondrial dysfunction in MCF-7. The immunofluorescence studies of cytoskeletal and nuclear morphology revealed that after PLGA-DGN NPs treatment, the regular reorganization of actin filaments in MCF-7 cells became disrupted. In EAC-induced mouse solid tumor model, PLGA-DGN NPs significantly decreased cell proliferation, angiogenesis by reducing Ki-67 and CD-31 expression and the solid tumor were regressed and increased mean survival time of EAC-bearing mice was seen through the restoration of antioxidant status of the host mice. The findings confirm that PLGA-DGN NPs induced an antineoplastic effect that led to cell cycle arrest and apoptosis through the mitochondria-mediated intrinsic pathway and it is a promising anticancer nano-drug candidate for breast carcinoma.

Biography

Sujata Maiti Choudhury is a Professor and In-charge of Biochemistry, Molecular Endocrinology and Reproductive Physiology Laboratory in the postgraduate Department of Human Physiology with Community Health of Vidyasagar University, West Bengal, India. She completed her M.Sc. in Physiology in 1986 and M.Phil. Degree in Environmental Science in 1988 from University of Calcutta, Kolkata. She was awarded Doctor of Philosophy in 1995 from Jadavpur University, Kolkata. She was also graced as the Founder Director of Women's Studies Centre, of Vidyasagar University (2010-2015). She is a Life member of Indian Science Congress of India, Indian Association of Cancer Research (IACR), Physiological Society of India, Kolkata, and South Asian Association of Physiologists. She is acting as a reviewer for many journals including Nanotoxicology (Taylor & Francis), Food and Chemical Toxicology (Elsevier), Journal of Basic Microbiology (Wiley-VCH), Drug and Chemical toxicology (Taylor & Francis) etc.

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