Pharmaceutical Regulatory Affairs 2012: The role of hydrophilic porphyrin-[C60] fulleropyrrolidine dyads as nano-assisted photosensitizers towards cancer photo dynamic therapy (PDT) - University of Sydney, Australia

Devashish Sengupta

University of Sydney, Australia , E-mail: devashish.sengupta@uni.sydney.edu.au

Abstract

Nanoparticles are non-immunogenic and fail to elicit any immune response when introduced into the body's circulatory system, which could otherwise lead to severe consequences like shutting off or blockage of the circulatory system. However, strong functionalization of nanoparticles like fullerenes with supramolecular photosensitizers (PS) can solve the problem and help develop nano-assisted PS with efficient applications in cancer photodynamic therapy (PDT). Hydrophilic porphyrinfulleropyrrolidine dyads of various topologies, consisting of meso- substituted pyridinium derivatives, covalently-linked to a fulleropyrrolidine, have shown selective cytotoxic action towards ovarian cancer cells. Since the discovery of C_{60} fullerene in 1985, scientists have been searching for biomedical applications of this most fascinating of molecules. The unique photophysical and photochemical properties of C_{60} suggested that the molecule would function well as a photosensitizer in photodynamic therapy (PDT). PDT uses the combination of non-toxic dyes and harmless visible light to produce reactive oxygen species that kill unwanted cells. However the extreme insolubility and hydrophobicity of pristine C_{60}, mandated that the cage be functionalized with chemical groups that provided water solubility and biological targeting ability. It has been found that cationic quaternary ammonium groups provide both these features, and this review covers work on the use of cationic fullerenes to mediate destruction of cancer cells and pathogenic microorganisms *in vitro* and describes the treatment of tumors and microbial infections in mouse models. The design, synthesis, and use of simple pyrrolidinium salts, more complex decacationic chains, and light-harvesting antennae that can be attached to C_{60}, C_{70} and C_{84} cages are covered. In the case of bacterial wound infections mice can be saved from certain death by fullerene-mediated PDT. These compounds are expected to be produced in an optically transparent form. Thus, light activation and optical probing can readily be accomplished for efficient generation of Reactive Oxygen Species (ROS). This is expected to enhance their role as anti-cancer agents. Depending upon their subcellular and submicron size, the C60 or C70 particles present in these PS can penetrate deep into tissues through fine capillaries and are able to pass through the fenestrate into the endothelial cells lining the blood vessels. The gel electrophoresis results indicated efficient cleavage of pUC DNA under light irradiated conditions. In the in vitro MTT cancer cell assays, the dyads inhibited the growth of ovarian cancer cells more significantly than it did the other adenocarcinoma epithelial cell lines like stomach, liver, lung etc. The most interesting outcomes of the study revealed that their biological activities with respect to cytotoxicity and DNA cleavage was higher and specific for dyads that experienced lower π-π interactions and showed higher fluorescence quantum yields. These results indicate great promise for the possible replacement of the controversial yet commercially available PS like photofrin, vasudyne etc with such dyads.