Increased cytotoxic efficacy of protocatechuic acid in A549 human lung cancer delivered via hydrophobically modified-chitosan nanoparticles as an anticancer modality

ABSTRACT

The growing incidence of global lung cancer cases against successful treatment modalities has increased the demand for the development of innovative strategies to complement conventional chemotherapy, radiation, and surgery. The substitution of chemotherapeutics by naturally occurring phenolic compounds has been touted as a promising research endeavor, as they sideline the side effects of current chemotherapy drugs. However, the therapeutic efficacy of these compounds is conventionally lower than that of chemotherapeutic agents due to their lower solubility and consequently poor intracellular uptake. Therefore, we report herein a hydrophobically modified chitosan nanoparticle (pCNP) system for the encapsulation of protocatechuic acid (PCA), a naturally occurring but poorly soluble phenolic compound, for increased efficacy and improved intracellular uptake in A549 lung cancer cells. The pCNP system was modified by the inclusion of a palmitoyl group and physico-chemically characterized to assess its particle size, Polydispersity Index (PDI) value, amine group quantification, functional group profiling, and morphological properties. The inclusion of hydrophobic palmitoyl in pCNP-PCA was found to increase the encapsulation of PCA by 54.5% compared to unmodified CNP-PCA samples whilst it only conferred a 23.4% larger particle size. The single-spherical like particles with uniformed dispersity pCNP-PCA exhibited IR bands, suggesting the successful incorporation of PCA within its core, and a hydrophobic layer was elucidated via electron micrographs. The cytotoxic efficacy was then assessed by using an MTT cytotoxicity assay towards A549 human lung cancer cell line and was compared with traditional chitosan nanoparticle system. Fascinatingly, a controlled release delivery and enhanced therapeutic efficacy were observed in pCNP-PCA compared to CNP, which is ascribed to lower IC50 values in the 72-h treatment in the pCNP system. Using the hydrophobic system, efficacy of PCA was significantly increased in 24-, 48-, and 72-h treatments compared to a single administration of the compound, and via the unmodified CNP system. Findings arising from this study exhibit the potential of using such modified nanoparticulate systems in increasing the efficacy of natural phenolic compounds by augmenting their delivery potential for better anti-cancer responses.

Keyword: Hydrophobically modified-chitosan nanoparticle; Nanobiotechnology; Protocatechuic acid