Graphene oxide loaded with protocatechuic acid and chlorogenic acid dual drug nanodelivery system for human hepatocellular carcinoma therapeutic application

ABSTRACT

Hepatocellular carcinoma or hepatoma is a primary malignant neoplasm that responsible for 75–90% of all liver cancer in humans. Nanotechnology introduced the dual drug nanodelivery method as one of the initiatives in nanomedicine for cancer therapy. Graphene oxide (GO) loaded with protocatechuic acid (PCA) and chlorogenic acid (CA) have shown some anticancer activities in both passive and active targeting. The physicochemical characterizations for nanocomposites were conducted. Cell cytotoxicity assay and lactate dehydrogenase were conducted to estimate cell cytotoxicity and the severity of cell damage. Next, nanocomposite intracellular drug uptake was analyzed using a transmission electron microscope. The accumulation and localization of fluorescent-labelled nanocomposite in the human hepatocellular carcinoma (HepG2) cells were analyzed using a fluorescent microscope. Subsequently, Annexin V- fluorescein isothiocyanate (FITC)/propidium iodide analysis showed that nanocomposites induced late apoptosis in HepG2 cells. Cell cycle arrest was ascertained at the G2/M phase. There was the depolarization of mitochondrial membrane potential and an upregulation of reactive oxygen species when HepG2 cells were induced by nanocomposites. In conclusion, HepG2 cells treated with a graphene oxide–polyethylene glycol (GOP)–PCA/CA–FA dual drug nanocomposite exhibited significant anticancer activities with less toxicity compared to pristine protocatechuic acid, chlorogenic acid and GOP–PCA/CA nanocomposite, may be due to the utilization of a folic acid-targeting nanodrug delivery system.

Keyword: Graphene oxide; Dual drug; Nanodrug delivery; Cancer therapy