The design of sonoresponsive curcumin nanodroplets for anticancer therapy

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Background: Nanodroplets are novel phase-changing materials which undergo acoustic droplet vapuorization (ADV) and cavitate, forming gaseous microbubbles upon the exposure of ultrasound. Drugs are loaded into nanodroplets and delivered into deep tissues through sonoporation and propulsion induced by non-invasive focused ultrasound. The shell of nanodroplets is composed of lipids and/or polymers whereas the core consists of liquid perfluorocarbon. As liquid perfluorocabon vapourises during cavitation, both pressure and temperature within the core increases which potentially cause bubble implosions and the releases of drugs.

Methods: In this study, curcumin which has been reported to possess anticancer properties is loaded into nanodroplets and expected to be delivered into deep tumour tissues by ultrasound. Perfluorohexane (PFH) is loaded into the core while dipalmitoylphosphatidylcholine (DPPC) and 1,2-distearoyl-sn-glycero-3-phosphoethanolamine-N-[amino(polyethylene glycol)-2000] (DSPE-PEG_{2000}) are used to construct the shell. Curcumin nanodroplets (NDCur) are synthesized using thin-lipid film method and characterized by measuring diameter size and particle polydispersion, performing fluorescence spectrometry and differential scanning calorimetry (DSC) heat scans, determining gas expansion and cavitation profiles as well as evaluating reactive oxygen species (ROS) productions by using 1M potassium iodide to quantify ROS.

Results: According to results, the diameter size and polydispersity index (PDI) values of NDCur maintained between 100-200nm and indexed below 0.3, respectively for 13 days of storage in buffer at 4°C. Curcumin loaded in nanodroplets is identified in fluorescence analysis (Ex_{max}:430nm, Em_{max}:560nm). Based on the DSC heat scans, curcumin lowers down the transitional (T_m) temperature point of nanodroplets lipidic shell. NDCur expand with increasing thermal exposure up to 42°C to form bubbles in gas expansion analysis. This shows that droplet vapourisation may occur. Upon ultrasound irradiation, nanodroplets cavitate according to different acoustic pressures ranging from 250-500kPa at a frequency of 1MHz. ROS productions were obtained according to two different acoustic pressures i.e. 0.9 and 1.3MPa where almost four folds of ROS produced by NDCur compared to blank nanodroplets and liposomal curcumin.

Conclusions: NDCur has been shown to be synthesized and characterized, cavitate upon ultrasound exposure and produce ROS to potentially provide effective anticancer therapy.