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Enhancement of taxane bioavailablility cum anticancer potential using engineered lipohybrid system

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Fabricated lipohybrid (FLH) systems have been developed with the purpose of improving bioavailability of paclitaxel combining concepts of thermoresponsive delivery and P-gp inhibition.

FLH systems were composed of DPPC (thermosensitive lipid), Brij78 and pluronic F68 (PF68, P-gp inhibitor) for thermosensitive delivery of paclitaxel (PTX) with sizes below 150 nm. The use of 2% (v/v) Tween 80 (P-gp inhibitor) in the hydration media was able to increase the solubility of drug (leading to increase in entrapment efficiency from 81 to 92%). The transition temperature of the FLH systems were ~41°C leading to enhanced bioavailability upon hyperthermia. *In vitro* drug release at 40±1°C was abrupt burst release (i.e., 100% within 5 min) whereas insignificant release at 37±0.5°C. Cytotoxicity in PTX-resistant human lung cancer cell line (A549/T cells) brought favorable results that DPPC/Brij78/PF68 FLH system being hydrated with Tween 80 was highly toxic in MTT assay, and it showed 3.5 fold enhancement of cytotoxicity as compared to DPPC/Brij78 FLH system. This was accounted to enhanced bioavailability of paclitaxel due to both high entrapment and least efflux (P-gp inhibition) from cancer cells.

Such FLH systems, possessing heralding features of thermo-sensitivity, high entrapment efficiency, that could not only enhance bioavailability but also anticancer potential, could serve as better alternative for the passive targeting of PTX-resistant human lung cancer.

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Thermal and dielectric studies of confined water in hydrated elastin and collagen

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In this work, we employ dielectric relaxation spectroscopy (DRS), thermally stimulated depolarization current technique (TSDC) and differential scanning calorimetry (DSC) in order to study water dynamics in the case of two hydrated fibrous proteins, elastin and collagen. The samples are hydrated over a wide range of compositions, from dry protein to swollen samples up to 60 wt% in water. The crystallization and melting events of water are studied by DSC. No crystallization of water is detected for elastin samples up to 23 wt% in water. Further addition of water results in the appearance of two distinct crystallization peaks during cooling. The peak recorded at lower temperatures, with a crystallization temperature T_m=-40°C, exhibits a crystallization enthalpy ΔH_m which is independent of hydration level. In the case of collagen, a similar crystallization peak is detected already for the dry sample and is maintained with further addition of water. The peak disappears after heating the dry sample above 100 °C. We assume that this peak corresponds to the crystallization of confined water molecules. In dielectric studies, we focus on the dielectric manifestation of water molecules confined within voids of the protein structure, which may obtain either uncrystallized or primary crystal forms, according to DSC. Dielectrically, the particular water population is manifested through a relaxation mode which exhibits lower relaxation times and more complex dynamical characteristics, when compared to the main secondary dielectric relaxation of uncrystallized water molecules participating in the water layer around the protein surface.

Biography

Anna Panagopoulou received a degree in applied mathematics and physics in 2006 and the M.Sc. degree in microsystems and nanodevices in 2008, both from the National Technical University of Athens, Athens, Greece. Currently, she is a member of the Dielectrics Group of the Physics Department of the National Technical University of Athens and a Ph.D. student, working on glass transition and dynamics in water and protein or molecule complex biopolymers. She has published 9 papers in peer reviewed journals and conference proceedings, has more than 25 presentations in international conferences and is a reviewer of international journals.

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