



Alexandria University
Institute of Graduate Studies and Research
Department of Biotechnology



Biopolymeric Nanovehicular Drug Delivery Systems for Targeted Cancer Therapy

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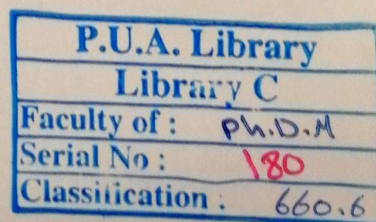
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1. ABSTRACT

Several data reveal the beneficial effect of co-administration of celecoxib (CXB) with aromatase inhibitors (AIs) in managing postmenopausal breast cancer. The purpose of this study is to elaborate novel natural protein nanocapsules based on protamine for tumor-targeted co-delivery of letrozole (LTZ) and celecoxib in breast cancer therapy. Polymer coating technique was employed for the preparation of dual drug-loaded protamine nanocapsules (DDLPCs). Moreover, PEGylated and non-PEGylated CXB-phospholipid complex bilayer enveloping protamine nanocapsules were designed as passive-targeted formulations whereas hyaluronic acid (HA)-coated protamine nanocapsules were prepared for active targeting. The optimal formulations showed high (% EE) of both drugs and sustained drug release. All formulations exhibited a nanometer size range (85–267 nm), spherical shape and were physically stable for three months. Pharmacokinetic studies demonstrated that DDLPCs exhibit a longer circulation time with markedly delayed blood clearance of both drugs, compared with free dual drug solution. Cytotoxicity studies and biological evaluations of the anti-tumor efficacy revealed the superiority of DDLPCs over the free dual drug solution. This superiority was manifested as a marked reduction of % cell viability and % change of tumor volume. Mechanistically, the anti-tumor properties were correlated to the ability to activate caspase 3 and marked inhibition of aromatase expression, NF- κ B, TNF- α and VEGF. These results were further augmented by the histopathological studies. Conclusively, these results offer a promising method for tailoring tumor-targeted protamine nanocapsules as parenteral, long-circulating nanovehicles of hydrophobic anti-cancer drugs in aqueous vehicles.