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RESEARCH

Efficacy of Novel L-Carnitine/PEG6000-Modified Exemestane Loaded Protein Nanoparticles Against Pre-neoplastic Mammary Damage

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Abstract
The objective of the study was to formulate a novel protein nanocarrier system for efficient oral delivery of exemestane. The outcomes of this study are promising and offer hope for the future of pharmaceuticals, nanotechnology and oncology. Whey protein concentrate (WPC) was selected as a protein excipient and processed with a naturally occurring crosslinker. The effect of various independent variables (i.e. WPC concentrations, ethanol concentrations and genipin concentration) was observed on hydrodynamic size (HD), zeta potential (ZP) and entrapment efficiency (EE). The optimised nanoparticles were further surface-modified with PEG6000/L-carnitine and characterised for their efficacy against DMBA-induced mammary damage. The optimised nanoparticles (WExe) had HD 410.32 ± 37.01 nm, ZP − 21.53 ± 2.35 mV and EE 82.7 ± 7.23%. SEM image revealed a much smaller size of these nanoparticles and an increased size of surface-modified nanoparticles (Car-WExe) over WExe. The optimised nanoparticles followed the Higuchi model. The modified nanoparticles exhibited good cytotoxicity against MCF7 cell lines. The uptake of L-carnitine modified whey nanoparticles was higher than non-modified whey nanoparticles in MCF7 cells. In vivo studies confirmed better efficacy of nanoparticles (as determined via proliferation assessment through carmine staining, histopathological studies and oxidative stress parameters) against DMBA-induced pre-neoplastic mammary damage. In conclusion, whey nanoparticles were promising nanocarriers for the oral delivery of exemestane.

Keywords Design of experiments · Box-Behnken design · Breast cancer · Carnitine/protein nanocarrier · Oxidative stress

1 Introduction

Protein-based nano-delivery systems have been extensively studied to improve the bioavailability and therapeutic outcome of anti-cancer drugs. Food proteins can also be utilised to prepare a wide range of matrices [1]. Proteins' unique functions offer several advantages, such as stability, ease of surface modification, fewer issues associated with toxicity and biodegradability. Thus, they are an attractive material in pharmaceutical research [2]. Whey protein is derived from cheese production as a by-product. Its low cost, high nutritional value and various other functionalities make it an attractive material for nano-research. Whey protein is not an individual protein but a mixture of several proteins. These proteins include α-lactalbumin, β-lactoglobulin, albumin and lactoferrin. Besides proteins, it contains other components, such as immunoglobulins, lactoperoxidase and glycomacropeptide. Whey protein concentrate (WPC) and isolate (WPI) are the two most widely produced whey protein products. The protein content in WPI exceeds 90%, while that of WPC is 50–80% [3, 4].

Whey protein can bind with hydrophobic drugs or other compounds. It holds gelling and emulsifying properties. It offers enhanced protection capability to the drug and may aid in its better delivery. Its uses can also be beneficial for the oral delivery of drugs [3]. WPC has been used before for oral delivery of atorvastatin, wherein its conjugate with soy protein acted as a good nanocarrier for atorvastatin [5]. Our current research is focused on applying WPC as a nanocarrier to encapsulate an oral anti-cancer drug,

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