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CAMPTOTECHIN LOADED SODIUM CASEIN NANOPARTICLES FOR TARGETED DRUG DELIVERY TO MULTI-DRUG RESISTANCE PROSTATE CANCER CELLS

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INTRODUCTION

1.1 Research background

Prostate cancer is the development of cancer cells in the prostate glands of the male reproductive system and the most commonly diagnosed cancer in male, especially in developed western countries (Dasgupta & Kirby, 2011). In Malaysia, prostate cancer is the fourth most common cancer diagnosed in men (Omar & Tamin, 2011). The mortality rate of cancer is reduced but therapy and surgery costs are expensive (Yallapu et al., 2014). Chemotherapy is not very effective because it causes undesirable side effects to the normal healthy cells which reduce the quality of life of cancer patients (Sowery, So, & Gleave, 2007). Moreover, after a period, the tumour cell becomes immune to chemotherapeutic drugs leading to multi-drug resistance (MDR).

MDR is defined as the development of resistances by cancer cells towards one chemotherapeutic drug followed by resistance to other chemotherapeutic drugs that may consists of unrelated structural and mechanisms of action (Fojo et al, 1987; Wu et al, 2014). Precisely, the cancer cells gain resistances towards drugs that not being exposed before, which are structurally and functionally unrelated with previous drug (Kaye, 1988). As a result, the therapeutic effects of chemotherapeutic drugs will decreased that causing cancer chemotherapeutics to be ineffective which encourage cancer cells to metastasize (Wu et al, 2014).

Prostate cancer usually transferred via blood circulation or lymphatic system and can metastasize at different part of the body such as bones, lungs, liver, lymph nodes and also brain, but it may affect other organs as well (Vinjamoori et al., 2012). MDR can be divided into 2 which are primary resistance that occurs before the exposure to chemotherapeutic drugs or acquired resistance that surface after the usage to chemotherapeutic drugs (Wu et al., 2014).

Camptothecin is a chemotherapeutic drugs that use in treatment of various kind of cancer such as ovarian, breast, prostate and lung cancer (Gaur et al., 2014). Unfortunately, the usage of CPT is restricted clinically due to it instability at physiological pH and insolubility, which lead to dose-limiting toxicity (Garcia-Carbonero & Supko, 2002). These are the reasons why combination of nanotechology and advanced therapeutic agents able to offer high potential to cope up with this problem (Steichen et al, 2013). Nanoparticles have a very small size enabling it to be taken into tumour cells more easily.

Meanwhile, the usage of polymer based nano formulations does not affect healthy body tissues, can be break down in times, and do not trigger immune reactions (Danhier et al, 2010). The example of drugs that currently marketed using nanotechnology is paclitaxel albumin-bound nanoparticle formulation with brand name Abraxane®, had been approved to treat metastasis cancer treatment(s) (Miele et al, 2009) and modified PLGA based docetaxel has currently completed Phase I clinical trials which specified for treatment of prostate cancer (Hrkach et al., 2012).