

UNIVERSITI TEKNOLOGI MARA (UiTM)

CYTOTOXICITY OF PACLITAXEL LOADED AND
SURFACE COATED POLYACRYLIC ACID-PEG-
CHITOSAN BASED NANOPARTICLES ON ER-
BREAST CANCER CELLS (MDA 231)

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ABSTRACT

Paclitaxel is an antineoplastic agent that is well-known for its poor aqueous solubility and a substrate for P-gp and CYP450 thus limiting the uptake whereby it mediates direct excretion of the drug in the intestinal lumen. This in turn causes paclitaxel to exhibit many side effects which includes acute hypersensitivity reaction, chest pain, hypotension, rashes, axonal degeneration and demyelination. Research on new formulations to improve the drug delivery system of paclitaxel is important to improve its efficacy and reduce the toxicity. The aim of this study is therefore to investigate the cytotoxicity of paclitaxel when compared to paclitaxel loaded with surface coated polyacrylic acid-PEG-chitosan-based-nanoparticles on ER- breast cancer cells (MDA 231). The polyacrylic acid-PEG-chitosan-based-nanoparticles is a new formulation. The Sulforhodamine B (SRB) assay was employed to determine the cytotoxicity of the newly formulated paclitaxel when compared to free paclitaxel. Polyacrylic acid based polymers are mainly used for oral and mucosal contact applications such as controlled released of tablets, oral suspensions and bioadhesives. The cytotoxicity of paclitaxel and paclitaxel loaded with surface coated polyacrylic acid-PEG-chitosan-based-nanoparticles were 0.03 $\mu\text{g/mL}$ and 16 $\mu\text{g/mL}$ respectively. In conclusion the study showed that the new formulation did not improve the anticancer effect of paclitaxel. The formulation needs further improvement and more studies need to be performed to understand the paclitaxel release.

CHAPTER 1

INTRODUCTION

Breast cancer is a major global health problem and a leading cause of death among women of all ethnic. Each year, an estimated 1,152,161 new cases is diagnosed worldwide. Breast cancer is the most common cancer in females and also the first common cancer among population regardless of sex in Malaysia (National Cancer Registry of Malaysia, 2011).

Unlike normal breast cells, cancer cells arising in the breast do not always have receptors for estrogen. Breast cancers that do have estrogen receptors are said to be estrogen receptor-positive (ER+) while those that do not possess estrogen receptors are estrogen receptor-negative (ER-). In women with ER+ cancers, cancer cell growth is under the control of estrogen. In contrast, the growth of ER- cancer cells is not governed by estrogen (National Cancer Institute, 2010).

Chemotherapy is the treatment of cancer with anticancer drugs. These drugs are used as pills, intravenous (i.v) injections, or topical applications. Chemotherapeutic drugs may destroy healthy tissue along with cancer cells. The cytotoxicity effect of chemotherapeutic drugs is highest in bone marrow, hair follicle