

UNIVERSITI TEKNOLOGI MARA

**CYTOTOXICITY OF PACLITAXEL LOADED AND
SURFACE COATED POLY METHACRYLIC ACID-PEG-
CHITOSAN BASED NANOPARTICLES ON OESTROGEN
POSITIVE BREAST CANCER CELLS (MCF7)**

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ABSTRACT

Cancer is a class of diseases which is characterized by uncontrolled division of abnormal cells in the body. It can be divided into two major types, which is benign and malignant tumour. Since conventional paclitaxel formulation using Cremophor-ethanol (CrEL) is associated with adverse effects, new formulations in the form of paclitaxel nanoparticles are recently developed so as to improve the therapeutic effectiveness and reduce the toxicity arisen from CrEL. This study compared the cytotoxicity of conventional paclitaxel and the new formulation which containing polymethacrylic acid. This can be done by using cell culture technique. Cell culture is a complex process by which cells are grown under controlled conditions, generally outside of their natural environment. Cells were grown and maintained at an appropriate temperature and gas mixture (typically, 37°C, 5% CO₂ for mammalian cells) in a cell incubator. Cells were then plated and treated with the formulation and incubated for 72 hour. After that, the cells is were fix with trichloro acetate and dried overnight. The sulforhodamine B (SRB) assay is used for cell density determination, based on the measurement of cellular protein content. In this study we found that polymethacrylic acid loaded with paclitaxel did not result in improved antitumor activity. The IC₅₀ of paclitaxel alone remains low which is 0.8%. Besides, the result also shows that paclitaxel alone is more potent than the new formulation. Therefore, more extensive investigation of polymethacrylic acid-paclitaxel formulation should be carried out in the future.

CHAPTER 1

INTRODUCTION

Cancer is a class of diseases which is characterized by uncontrolled division of abnormal cells in the body. There was an estimated 12.7 million cancer cases around the world in 2008 and of these, 6.6 million cases were in men and 6.0 million in women (Jemal et al., 2011). In Malaysia, the most common and number one cause of cancer deaths among women is breast cancer (Hisham & Yip, 2003).

In recent years, there are several means of therapy that can be used against breast cancer and one of the most common treatments is chemotherapy. Chemotherapy involves the use of medicine to destroy cancer cells in the body. Over the past three decades, taxanes represent one of the most important new classes of drugs approved in oncology (Win, 2005). The prototype of this class, paclitaxel (PTX) is an antineoplastic agent initially extracted from the bark of the Pacific Yew Tree (*Taxus brevifolia*). It has powerful antitumour ability against a wide spectrum of cancers such as metastatic breast, refractory ovarian and colon cancers (Mo et al., 2011). PTX acts as a microtubule stabilizer and interfere with the normal breakdown of microtubules during cell division.

One of the major problems in the management of breast cancer is resistance to chemotherapy. This phenomenon is also known as multidrug resistance (MDR) and it is associated with over-expression of P-glycoprotein, which results in increased