# UNIVERSITI TEKNOLOGI MARA

# POTENTIAL INTERACTION OF TOCOTRIENOLS WITH P-GLYCOPROTEIN (MDR1/ABCB1a): A MOLECULAR DOCKING STUDY

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## ABSTRACT

Multi drug resistance (MDR) remains a significant obstruction to successful chemotherapy. Even though the number of new cancer drugs keep increasing, but its benefit cannot be fully utilized. The ability to predict drug resistance or overcome the MDR problem can be a huge success. P-glycoprotein (Pgp) which is associated with MDR caused the cancer drug to be less effective. Tocotrienols have gained attention as potentially therapeutics for various diseases. However, the efficacy of tocotrienols for the use of chemotherapy has not been fully explored. To clarify the potential of tocotrienols, molecular docking study has been used. Tocotrienols have four derivatives; alpha, beta, gamma and delta-tocotrienol. These derivatives have been docked with Pgp to determine the potential molecular interaction between them using software, AutoDock Vina. For most tocotrienol derivatives, the docking simulation clearly predicted a consistency of location of binding sites. The study of their interaction with Pgp shows gamma and delta-tocotrienol interact to the Gly721. For the beta-tocotrienol, it binds to Ser725.

# CHAPTER ONE

# INTRODUCTION

## 1.1 Introduction

Multidrug resistance (MDR) is a foremost challenge in a treatment of cancer treatment. Chemotherapy is highly limited by the MDR, leading to reduce the efficacy of the cancer drugs. The chemotherapy is not effective because tumor cells will try to evade the cytotoxic effects to the cells. It can occur in several ways involving the process of drug uptake, drug efflux, activation of detoxifying systems and DNA repair mechanisms and also evasion of drug-induced apoptosis (Gottesman, Fojo, & Bates, 2002). This will reduce in sensitivity of the tumor cells to the chemotherapy drugs and also to most of drugs with the common target.

One of the major problems involved in MDR is the overexpression of the ABC transporters; P-glycoprotein (Pgp), the multidrug resistance associated proteins and the ABCG2 protein (Pérez-Tomás, 2006). MDR is highly related to the Pgp which affect the effectiveness and concentration of drugs. Pgp is known as the energy-dependent efflux transporter which is used to reduce the harmful substances by decreasing the uptake into the human body. It shows that this transporter gives an