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MOLECULAR DOCKING STUDY OF TRITERPENE GLYCOSIDES AND THE MOUSE P-GLYCOPROTEIN (MDR1/ABCB1) USING AUTODOCK VINA SOFTWARE

NURLIYANA BINTI RAMLI

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ABSTRACT

The phenomenon of multidrug resistance (MDR) is associated with the over expression of P-glycoprotein (P-gp) at the target cell. P-gp responsible to efflux drugs out of the cell and reduce the accumulation of drugs thus decrease the therapeutic effect of these chemotherapy drugs. Triterpene glycosides can be found mostly in sea cucumber and are shown to give cytotoxic activity against tumor and cancer cell. In this computational study, Autodock Vina was employed to study potential interactions between P-glycoprotein and triterpene glycosides. Two triterpene glycosides derivatives, Intercedenside A and Intercedenside B are found to form hydrogen bond with Tyr 303 of P-gp.

CHAPTER ONE

INTRODUCTION

Drug discovery is a process of discovering a new medication where it uses some compounds and most common organic compounds to bind to biomolecule target such as protein. The compounds that bind to the protein will activate or inhibit the target and produce therapeutic benefit to the body. Drug design is a process of designing a medication which requires the compound to complement either in shape or charge with the biomolecule target that the compound binds to. Commonly the drug design is based on computer modeling technique called computer- aided drug design. The drug design also involves the structure-based drug design where it relies on the knowledge of three-dimensional structure of a biological target. The process of a drug discovery takes a long period. Computational-aided drug design ease the process and also become more relevant when it improves the understanding of molecular activity (Finn & Kavraki, 1999).

P-glycoprotein (P-gp) is an ATP-binding cassette (ABC) subfamily. P-gp has seven distinct subfamilies including ABC1, MDR/TAP, MRP, ALD, OABP and GCN20. This protein belongs to the MDR/TAP family. It acts as an efflux pump which pumps out the drug out of the cell where it uses the ATP as a source of energy. By acting this particular way, it reduces the accumulation of drug in the body as well as protects the cell from harmful foreign substance. It is also responsible to transport substances across the extracellular and intracellular membrane. It has been studied that the Pgp has a