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DOCKING OF MOUSE P-GLYCOPROTEIN (ABCB1a/MDR3) WITH VERAPAMIL AND CYCLOSPORINE A

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APPROVAL SHEET

I hereby recommend that the thesis prepared under my supervision by Zakiah Binti Salleh entitle "Docking of mouse P-glycoprotein (ABCB1a/MDR3) with verapamil and cyclosporine A" accepted in partial fulfilment of the requirements for Degree of Pharmacy from Faculty of Pharmacy, UiTM.

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TABLE OF CONTENTS

ABSTRACT

Background: Nowadays, P-glycoprotein becomes the main focus of research interest since its discovery in 1976 by Juliano and Ling in Chinese hamster ovary cells. P-Glycoprotein (Pgp) is identified from adenosine triphosphate (ATP)-binding cassette (ABC) superfamily that encoding for gene in human of ABCB1. It can be identified as 3G5U from *Mus musculus* (mouse).

Result: The amino acid residues that having high binding affinity toward Pgp are Leu335 and Ala338 at TM 6. At TM 12, the amino acid residues like Val981, Val978 and Gly980 are consider the success amino acid that bind to Pgp. Then, the Pgp was docked using cyclosporine A as a ligand and was finding that the amino acid residue that binds to Pgp is only Ala338. Meanwhile, at TM 12, the amino acid residues that success binds to Pgp are Phe974 and Val978. Meanwhile, at TM 7, there is one amino acid residue success bind to Pgp which is Phe728 and Phe724.

Conclusion: The active binding sites of Pgp are at TM 6, TM 7 and TM 12. AutoDock software can be responsible for *in silico* method in designing the drug specificity in order to prevent multi drug resistance (MDR) especially in cancer cell.

Keywords: Pgp, P-glycoprotein, MDR, multidrug resistance, TM, transmembrane, ATP, adenosine triphosphate.