UNIVERSITI TEKNOLOGI MARA

DEVELOPMENT OF A PCR METHOD TO DETECT POLYMORPHISM OF ACE IN OPTIMISATION OF HMG-CoA REDUCTASE INHIBITOR

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Dissertation submitted in partial fulfillment of the requirement for the

Bachelor Pharmacy (Honours)

Faculty of Pharmacy

November 2009

ACKNOWLEDGEMENT

In the name of Allah, the most Beneficent, the most Merciful, Salam to our Prophet Muhammad S.A.W., His companion and friends as well as to all people who follow his path.

First and foremost, I would like to express my earnest appreciation to my supervisor, Prof. Dr. Mohd Zaki Salleh for his interest, support, understanding, motivation and guidance throughout this research study period.

Special thanks are dedicated to Prof Madya Dr. Teh Lay Kek, Dr.Rosmadi and Ms Fazleen for helping me during my experiment and also for their ideas and guidance. I also would like to thank to the staff of pharmacogenomics laboratory and the all postgraduates student for their cooperation and kindness to teach and help me in all aspects along the study period.

Last but not least, I convey my thanks to my family and my colleagues who gave me a lot of moral support in completing this thesis.

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ABSTRACT

Angiotensin-converting enzyme (ACE) is a major component in the renin-angiotension-aldosterone system (RAAS) and has been studied as a candidate for development of some disease. Polymorphism of angiotensin-converting enzyme (ACE) means that there is variation in the nucleotide sequence of the ACE's gene due to insertion (I) or deletion (D). The aim of this study is to develop and validate a PCR based genetic test for identification of genetic variants of ACE. The primers were designed according to the gene and followed by reconstitution of primer working stock. The blood samples were already set up at the lab for this study but the samples collection of buccal and hair must be done. The samples were important as a template even different template have different amount of DNA. The Polymerase Chain Reaction (PCR) using the primers and different samples was done to amplify the sequence of ACE. The PCR component such as annealing temperature, magnesium concentration and primer concentration has been changed in order to get the desired product that amplified the ACE gene. The PCR method has been optimized to get the clear band in order to detect and identify the insertion (I) and deletion (D) of ACE gene. Based on the result of this study, it can be concluded that I/D polymorphism of ACE gene was successfully amplified by using the PCR. However, for further confirmation, the product that was obtained in this study would be sent for sequencing to compare it with the published sequences. The finding of this study can be used as a marker for optimization usage of drugs for example HMG-CoA reductase inhibitor (statins) for different individuals.

CHAPTER 1

INTRODUCTION

1.0   Background of study

Angiotensin converting enzyme (ACE) is an important component of the renin-angiotensin aldosterone system (RAAS). The common isoform of ACE is also present in other vascular tissue including heart, brain, striated muscle and kidney and not restricted to endothelial cells (Rang *et al.*, 1999). ACE will hydrolyze angiotensin I to angiotensin II (potent vasoconstrictor) and catabolyze bradykinin (potent vasodilator). Polymorphism of ACE means that there is variation in the nucleotide sequence of the ACE's gene due to insertion (I) or deletion (D). HMG-CoA reductase inhibitor or statins is a lipid-lowering drug. HMG-CoA reductase or 3-hydroxy-3-methylglutaryl-coenzyme A reductase is an enzyme that catalyses the conversion of HMG-CoA to mevalonic acid (MVA). Statins administration will lead to increase synthesis of LDL (low density lipoprotein) receptor and increased clearance of LDL and reduced concentration of LDL-cholesterol in plasma.