UNIVERSITI TEKNOLOGI MARA

DEVELOPEMENT OF RAPID PCR METHOD FOR THE DETECTION OF GENETIC POLYMORPHISM OF CYP2C19

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ABSTRACT

Cytochrome P450 2C19 enzymes are predominantly found in the human liver, and have important functions in the metabolism of many different classes of commonly used drugs. Their genetic polymorphisms give rise to both important interethnic variability in metabolism and the risk of treatment failure or dose-dependent drug toxicity. The aim of this research is to develop a rapid PCR (polymerase chain reaction) based method to detect genetic polymorphism of *CYP2C19* and to validate the PCR method that has been developed. The primers were designed according to the gene and followed by reconstitution of primer working stock. This research has a clinical significance as *CYP2C19* polymorphism has been related to the usage of proton pump inhibitor drug that are usually used in the treatment of gastric or peptic ulcer patients. By getting the result from this research, we can know who is a poor metabolizer and who is rapid metabolizer and with this we can individualize each patient's own dosage regimen.

CHAPTER 1

INTRODUCTION

1.1 Introduction

Polymorphism is extremely common, it is a kind of variation related to biodiversity, genetic variation and adaptation. Polymorphism usually indicate presence of at least 1% of different forms in a population. Genetic polymorphism (Greek: poly = many, and morph = form) is often defined as the presence of more than one genetically distinct type in a single population (Ibeanu *et al.*, 1999). Polymorphism results from an evolutionary process, as does any aspect of a species. Polymorphism is heritable, and is modified by selection (either artificial or in the wild). In genetic polymorphism or balanced polymorphism, the genetic make-up determines the morph (Blaisdell *et al.*, 2002).

Genetic polymorphism of drug metabolizing enzymes have been implicated which cause large inter-individual variation in drug responce. The study on the relevence of genetic polymorphism in clinical implication has received much attention. It is hopeful that study on the influence of genetic variations on drug responses would materialized the dream of personalized medicine.

The major PPIs are Omeprazole (OPZ), lansoprazole (LPZ), pantoprazole (PPZ) and rabeprazole (RPZ). These are used for the treatment of non ulcer dyspepsia (NUD), reflux oesophagitis, gastroesophageal reflux disease (GERD), *Helicobacter pylori*