UNIVERSITY TEKNOLOGI MARA

INVESTIGATION OF *IN VITRO* METABOLISM OF CARBAMAZEPINE USING CYP2C9 ENZYMES THROUGH ^{1}H-NMR SPECTROSCOPIC METHOD

RAUDHATUN SA'ADIAH ITHNIN

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ABSTRACT

The main objective of this *in vitro* study were plan to identify major Carbamazepine metabolites formed in association with CYP2C9 enzymes respectively using variable such as different concentration of Carbamazepine, pH of medium and concentration of CYP2C9 enzymes. Other goals were to identify the structural changes during metabolism of Carbamazepine compound. There are several techniques involved in order to achieve the goals of this project. The first process involves enzymatic reactions of Carbamazepine. The reaction samples were subjected to extract and evaporate to get pure extract. Obtained extract were further subjected to Thin Layer Chromatographic (TLC) techniques in order to identify transformed metabolites. The suspected metabolites detected on TLC plates were sent for characterization as long as identification using ^{1}H-NMR spectrometer. Two compounds were detected namely, compound (**2**) and (**3**) respective to pH 5.8 and 7.4. Concisely, even though the compounds are not main metabolites in metabolism of Carbamazepine as stated in various literatures, we managed to identify new potential compounds that may have possible contribution in various toxicity problem of Carbamazepine.

CHAPTER 1

INTRODUCTION

Carbamazepine is now an established antiepileptic drug which classified under iminostilbene group. Nowadays Carbamazepine to be known first – line drug of choice in most types of epilepsy. However, it associated with variety of idiosyncratic adverse effects due to the formation of chemically reactive metabolite formed in the body. Thus, it may cause cardiovascular, dermatologic, immunologic and hematologic malfunction.

Cytochrome P450 enzymes found largely in liver are involved in the metabolism of most drugs include Carbamazepine. CYP2C9 enzymes belong to CYP450 subfamily which involved in mostly clinically important drug interaction. Genetic variation in CYP2C9 may either cause increase or decrease the interaction intensity of medications. During the research we would concentrate on CYP2C9 enzymatic reaction with Carbamazepine. Carbamazepine is demonstrated as mild inducer for CYP2C9 and this may reduce the efficiency of most of CYP2C9 substrate.

Few researches were published regarding the involvement of CYP2C9 enzymes responsible for formation of reactive Carbamazepine metabolites. The metabolites that may be formed from CYP2C9 enzymatic reactions may also associated with toxicity effects of Carbamazepine.