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METHOD DEVELOPMENT USING HIGH PERFORMANCE LIQUID CHROMATOGRAPHY TO ASSESS THE EFFECT OF *EURYCOMA LONGIFOLIA* ON CYP2D6 BY USING BUFURALOL AS A PROBE

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TABLE OF CONTENTS

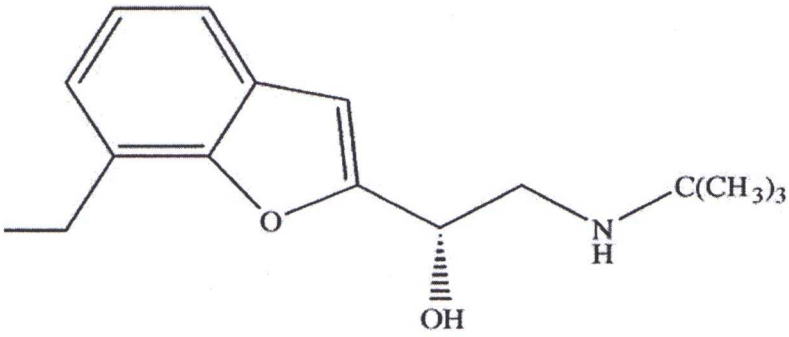
ABSTRACT

Nowadays, the use of *Eurycoma longifolia* (Tongkat ali) is increasing rapidly. The belief that the herbs' component can treat or prevent disease has encouraged the new generation to trust on the beneficial effects of the active components contained within nature's packages. However,the public are not aware of the possible interactions that might occur when the herbs is taken concomitantly with conventional medicine. Therefore, research is carried out to assess the effect of *Eurycoma longifolia* on CYP2D6 which is one of the main enzymes in human that is involved in metabolizing drug. This research involves the use of bufuralol as a CYP2D6 substrate. Metabolism of bufuralol is mainly governed by CYP2D6 enzyme and producing its major metabolite which is 1-hydroxybufuralol. The study involved the use of HPLC to detect the amount of metabolite; 1-hydroxybufuralol produced when *Eurycoma longifolia* reacts with bufuralol and CYP2D6 enzyme. The best HPLC conditions that is developed by this research involve the use of Luna 5u CN column, mobile phase (70% Ammonium acetate pH 3 and 30% methanol), flow rate of 1 ml/min, temperature of 40^0C with fluorescence as detector. After few variables are changed and modified such as the incubation time, type of vial use for incubation, concentration of the CYP2D6 enzyme and other samples of CYP2D6 enzyme, it is found that the major possibility that might prevent the interaction between the drug and the enzyme from occurring is due to the degeneration of CYP2D6 enzyme. Therefore, the effect of *Eurycoma longifolia* on CYP2D6 cannot be further proceeding and concluded.

CHAPTER 1

INTRODUCTION

Drug metabolism is a major factor governing the efficacy, duration of action and toxicity of drugs. Most beta-adrenoceptor antagonists (beta-blockers) are extensively metabolised via oxidative routes (M.S. Lennard, 1985). Bufuralol is a non- selective ß-adrenoceptor antagonist with a moderate degree of intrinsic sympathomimetic activity (ISA). The drug is racemic and the biological activity is confined to the (-) isomer. The beta-blocking agent bufuralol is subject to first-pass metabolism and is eliminated from the body almost entirely by biotransformation. Its major metabolite in plasma (1-hydroxy-bufuralol) is biologically active and may contribute to the pharmacological effect of the drug (Balant *et.al.*, 1980). The side effects of bufuralol are flushing, headache, restlessness, orthostatic hypotension and tingling in the extremities (T.H Pringle *et al.,* 1986).



Chemical structure of bufuralol (M.M. Hefnawy *et al.,* 2007)