Thesis Title: Studies on the Effect of *Andrographis paniculata* on Hepatic Drug Metabolism in Rats

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ABSTRACT

Andrographis paniculata is a medicinal herb widely used in Asian countries such as China, India and Thailand for the treatment of fever, pharyngitis, tonsillitis and urinary tract infection. The use of this herbal drug has been promoted by the Ministry of Public Health of Thailand as one of the five plants in the primary health care program. Since patients receiving this drug may concomitantly take modern medicine for the treatment of other diseases or symptoms, pharmacokinetic drug interaction may occur and result in alterations of efficacy of other drugs. The objectives of this study were, therefore, to investigate effects of administration of *Andrographis paniculata* (AP), containing 11.89% total lactone content, on hepatic drug metabolism, liver function and liver morphology in adult male Wistar rats. The drug was prepared in the form of leaf powder suspension in agar (100 mg/ml). At 12 hours after a single oral administration of AP at the dose equivalent to lactone content of 38, 120 or 240 mg/kg, no significant change in hexobarbital sleeping time (CYP2B & 2C probe) elicited by an intraperitoneal injection of 120 mg/kg of hexobarbital was observed. Repeated oral administration of AP at the same dosages for 5 or 7 consecutive days did not cause statistically significant alterations in the response to this hypnotic drug. No statistically significant alterations in the liver weight, hepatic microsomal protein content and activities of aniline hydroxylase (CYP2E probe), aminopyrine N-demethylase (CYP2B, 2C11 & 3A probe) and erythromycin

demethylase (CYP3A probe) were observed in the animals receiving either single or repeated administration of AP at any doses. AP administration did not seem to have an antiandrogenic effect or affect sex hormone in male rats since there was no change in the rate of enzymatic reaction mediated by a male specific CYP2C11. Administration of AP at the dose equivalent to lactone content of 240 mg/kg/day or 20 fold of human dose for 7 days did not cause any alterations in the liver function as determined by serum alanine aminotransferase, blood urea nitrogen, albumin and bilirubin. No change in the morphology of hepatocytes of rats treated with this dosage regimen was observed. The effect of AP on hepatic mixed-function oxidase, if there was any, was thought to partially be due to its antiinflammatory effect via an intact adrenal gland and its ability to depress vascular type acute inflammation. It was, therefore, concluded that AP administration even at high doses for up to 1 week did not cause clinically significant hepatic drug-metabolizing enzyme inhibition or induction and the drug was not hepatotoxic. Administration of AP concomitantly with modern medicines undergoing metabolism by various forms of cytochrome P-450, especially CYP2B, 2E and 3A should not result in alteration in drug response due to pharmacokinetic drug interaction at the biotransformation level.