UNIVERSITI TEKNOLOGI MARA

TOXICITY EVALUATION OF *Cosmos caudatus*, *Periskia bleo* AND *Averrhoa bilimbi* ON SPRAGUE DAWLEY RATS

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AUTHOR'S DECLARATION

I declare that the work in this thesis was carried out in accordance with the regulations of Universiti Teknologi MARA. It is original and is the result of my own work, unless otherwise indicated or acknowledged as referenced work. This topic has not been submitted to any other academic institution or non-academic institution for any other degree or qualification.

I, hereby, acknowledge that I have been supplied with the Academic Rules and Regulations for Post Graduate, Universiti Teknologi MARA, regulating the conduct of my study and research.

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ABSTRACT

Cosmos caudatus, *Periskia bleo* and *Averrhoa bilimbi* are among the common plants regularly consumed and used for the treatment of various ailments in Malaysia. The present study evaluated the acute and subacute toxicity of *C. caudatus*, *P. bleo* and *A. bilimbi in vivo,* which followed closely the Organization for Economic Co-operation and Development (OECD) Guidelines 423 and 407, respectively. Acute toxicity was tested on 3 groups, each with 6 female rats, at the doses of 2000 and 5000 mg/kg b.wt., respectively of each extract. Meanwhile, subacute toxicity tests involved 4 groups of rats, with 6 males and 6 females for each group. The doses used were 125, 250 and 500 mg/kg b.wt. of the extracts. The control groups in both toxicity studies received saline. The values of Lethal Dose (LD_{50}), haematological, biochemical as well as histopathological assessments were evaluated. Acute toxicity study revealed female rats could tolerate 5000 mg/kg b.wt. of *C. caudatus*, *P.bleo* and *A. bilimbi* ethanolic extracts. Neither mortality nor treatment related changes in their behaviour and external appearance were observed, which indicated that the LD_{50} of all the extracts were higher than the tested dosage. However, consideration should be taken with 5000 mg/kg b.wt. dose of *P. bleo*, since sign of dizziness was detected among experimental rats. Subacute toxicity study of *C. caudatus* showed that the extract caused slight decreased in red blood cell count (RBC) and packed cell volume (PCV) in all treated male rats, PCV value of 250 mg/kg b.wt of female rats, white blood cell count (WBC) of both 125 and 500 mg/kg b.wt. of male rats and in haemoglobin (Hb) level of 125 mg/kg b.wt. of both male and female treated rats. Slight increased in the value of mean corpuscular haemoglobin (MCH) was observed in groups of 250 and 500 mg/kg b.wt. of male rats. Similarly, mean corpuscular haemoglobin concentration (MCHC) also increased in all treated rats. In subacute toxicity study of *P. bleo*, slight decreased in the PCV values of 250 mg/kg b.wt. of female rats, MCH value of 125 mg/kg b.wt. of male rats and in MCHC value of 125 mg/kg b.wt. of female rats, along with an increased in the MCHC value of 250 mg/kg b.wt. of female rats. In addition, *A. bilimbi* showed a decreased in PCV value of 250 mg/kg b.wt. of male rats, and an increased in the MCHC value of 250 mg/kg b.wt. of male rats and in Hb value of 500 mg/kg b.wt. of female rats. Even though statistical differences were obtained among dosages, all values obtained were within the standard laboratory range. Histological assessment revealed normal cellular architectures in all selected organs among the treated rats. This study also revealed that the extract of *C. caudatus* and *P. bleo* both possessed hepatoprotective effects, which lowered the ALT levels in 5000 mg/kg b.wt. for *C. caudatus* extract, in 2000 mg/kg b.wt. and in all treated female rats of 125, 250 and 500 mg/kg b.wt. for *P. bleo* extract. AST levels of 500 mg/kg b.wt. of male rats for *C. caudatus* extract was also reduced. Increased RBC at higher dosages of 2000 mg/kg b.wt. for *C. caudatus* and *P. bleo*, and in 5000 mg/kg b.wt. of *A. bilimbi*, even though not significant, indicated that all of these extracts could possessed haematopoietic potential. The findings therefore, revealed that the ethanolic extract of *C. caudatus*, *P. bleo* and *A. bilimbi* were evaluated to be non toxic to the tested animals, hence, it is postulated that the extracts are safe for human consumption and to be used for further potential drug development.

TABLE OF CONTENTS

CHAPTER ONE
INTRODUCTION

1.1 BACKGROUND OF STUDY

Traditional uses of herbal remedies for the treatment of a variety of diseases are widely practised all over the world. It had been estimated that 60% of the world population, both in the developing and developed countries where modern medicines are predominantly used, opted for herbal remedies (Mythilypriya et al., 2007). The treatment for ailments using herbs and herbal formulations, continued to receive increased attention because of the strong belief that the products are safe, easy to access and primarily due to economic reasons (Said et al., 2002). Therefore, plants remain to be the main sources of the active drugs supplied by the nature and are crucially important in the traditional practises for treating a number of diseases (Ogbonnia et al., 2008).

In general, the practitioners prepared herbal remedies from a combination of two or more plant products, which could be used in the treatment of more than one disease conditions (Pieme et al., 2006). The administration of these remedies has been accepted over generations without a proper dosage monitoring and consideration of the negative effects that it might cause from such a prolonged usage. *Cosmos caudatus, Averrhoa bilimbi* and *Pereskia bleo,* each is traditionally claimed to provide a positive effect for treating various diseases ('O' Hara et al., 1998). However, there has been limited research conducted to evaluate the effects of daily consumption of these plants for the general body health. Therefore, it is very important to scientifically ascertain that these plants are safe and do not cause any harm to consumers, based on the dosages of intake.

Toxicology is the science of poisons which are known as toxins. This field of study deals with the nature and mechanism of toxicity and how a poisonous substance produces adverse effects on living organisms and other biological systems (Ramirez, 2007). Generally, a poison is defined as any chemical agent that has the capacity to produce abnormal, undesirable, or harmful changes to an organism exposed to it. Poisoning by a chemical agent is equivalent to chemically induced disease (Miami University, 2006). In humans, adverse effects of poisons on living organisms may