

## HEPATOPROTECTIVE EFFECTS OF *Curcuma longa* RHIZOMES IN PARACETAMOL-INDUCED LIVER DAMAGE IN RATS.

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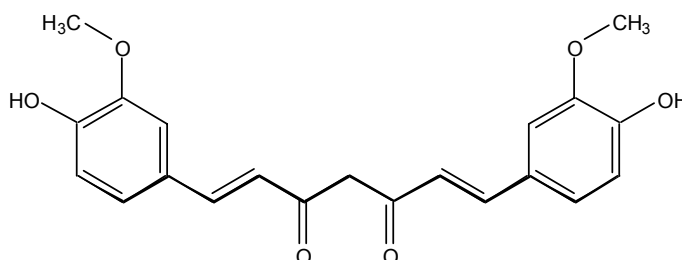
### ABSTRACT

The hepatoprotective activity of the ethanol extract of *Curcuma longa* was investigated against paracetamol-induced liver damage in rats. At the dose of 600 mg/kg, paracetamol induced liver damage in rats as manifested by statistically significant increase in serum alanine aminotransferase (ALT) and Aspartate aminotransferase (AST) and alkaline phosphatase (ALP). Pretreatment of rats with the ethanolic extract of *Curcuma longa* (100 mg/kg) prior to paracetamol dosing at 600 mg/kg statistically lowered the three serum liver enzyme activities. Moreover, treatment of rats with only the ethanolic extract of *Curcuma longa* (100 mg/kg) had no effects on the liver enzymes. This current results suggest that ethanolic extract of *Curcuma longa* has potent hepatoprotective effect against paracetamol-induced liver damage in rats.

### INTRODUCTION

*Curcuma longa* or tumeric is a member of Zingiberaceae family which is a perennial herb with short and thick rhizomes. It is known as kunyit in Malaysia and Indonesia (Abdul Rahman Md. Derus 1996). Tumeric has been used extensively in traditional Chinese medicine and Ayurvedic medical system (Kapoor 1990).

*Curcuma longa* contains approximately 2% volatile oil, composed mainly of  $\alpha$ - and  $\beta$ -turmerone, monoterpenes (Leung and Foster 1996), 5% curcuminoids, mainly curcumin (Budavari 1996), minerals, carotene and vitamin C (Kaapor 1990). The active constituent of *Curcuma longa* is Curcumin, which is the yellow pigment of tumeric (Figure 1).



**Figure 1:** Chemical structure of Curcumin

Curcumin has been shown to have a wide range of therapeutic actions such as anti-inflammatory (Rao *et al.* 1995), anti-tumour (Shukla *et al.* 2002), antioxidant (Miquel *et al.* 2002), anti-fungal (Wuthi-udomler *et al.* 2000), anti-parasitic and antispasmodic (Araújo *et al.* 2001). Kiso *et al.* (1983) had reported that tumeric has anti-hepatotoxic and

anti-bacterial effects and Luper (2000) reviewed tumeric as a potential agent for the treatment of liver diseases. In continuation of this work, we undertook investigation the ethanolic extract of *Curcuma longa* rhizomes as a hepatoprotective agent against paracetamol-induced liver damage in rats.

## MATERIALS AND METHODS

### Plant and Extraction

*Curcuma longa* rhizomes were purchased from local wet market. The rhizomes were powdered and macerated in 95% (v/v) ethanol for 48 hours using Soxhlet apparatus. The extract was filtered using Whatman No 1 filter and concentrated to dark yellow residue on a rotary evaporator.

### Materials and Animals

Paracetamol and other chemicals were obtained from Sigma Chemicals (USA) and palm oil was purchase from local market. Paracetamol was suspended in 1% dimethyl sulfoxide in palm oil (150 mg/mL). Male Sprague Dawley rats (180-200g, n=6/group) from Institute for Medical Research (IMR), Kuala Lumpur were housed at the Animal House, Faculty of Medicine and Health Sciences, Universiti Putra Malaysia. Animals were divided randomly into four groups of six rats each. Pre-treatment was given orally daily for 7 days of either the plant extract (100mg/kg) or normal saline. The animals were then treated with either paracetamol (600mg/kg) or dosed vehicle (1% v/v DMSO in Palm oil) (Table 1).

**Table 1:** Treatment groups of rats

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Group	Pre-treatment	Treatment
1	Normal Saline	1% DMSO/Palm oil
2	Normal Saline	600 mg/kg Paracetamol in 1% DMSO/Palm oil
3	100 mg/kg <i>Curcuma longa</i> extract	1% DMSO/Palm oil
4	100 mg/kg <i>Curcuma longa</i> extract	600 mg/kg Paracetamol in 1% DMSO/Palm oil

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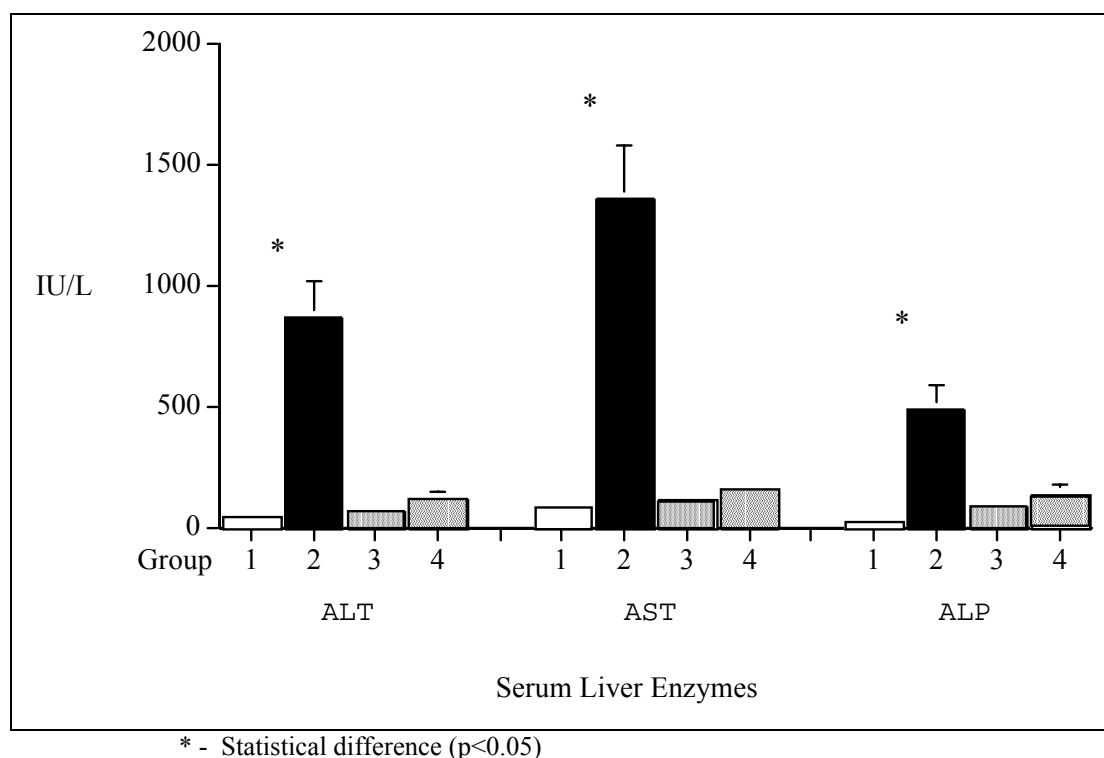
Animals were anaesthetized with pentobarbitone (70 mg/kg, ip) 24 hours after the treatment and blood (3.0 mL) was collected by cardiac puncture using sterile disposable syringes. Serum was obtained by centrifugation (5000 rpm for 10 min) and stored at – 20oC prior to analysis. Serum alanine aminotransferase (ALT) and Aspartate aminotransferase (AST) and alkaline phosphatase (ALP) were assayed spectrophotometrically using Sigma Diagnostic kits (USA).

## Statistical analysis

The results are expressed as mean  $\pm$  sd. One-way analysis of variance was performed and sequential differences among the means were calculated at the level of  $p < 0.05$  using Tukey-Kramer post test analysis.

## RESULTS

Paracetamol at the dose of 600 mg/kg p.o. induced significant increase in serum liver enzymes. Control (Group 1) which received normal saline and dosed vehicle serum value of ALT, AST and ALP in rats were found to be  $89.3 \pm 10.5$ ,  $47.2 \pm 15.9$  and  $25.4 \pm 12.4$  respectively (Figure 2). In Group 2, which received normal saline and paracetamol had significant increased ( $P < 0.05$ ) of the respective liver enzyme activities values to  $1354.6 \pm 217.3$ ,  $862.4 \pm 157.3$  and  $487.3 \pm 98.6$ . Group 3 which received the plant extract and dosed vehicle had similar values ( $P > 0.05$ ) of serum liver enzymes to the controls (Group 1) (Figure 2). In group 4, which received the plant extract (100 mg/kg orally, daily for 7 days) and 600 mg/kg paracetamol were found to be  $156.7 \pm 23.5$  (ALT),  $112.4 \pm 35.2$  (AST) and  $135.5 \pm 38.8$  (ALP). These values are significantly lower ( $P < 0.05$ ) than the values of the toxic control group (Group 2) and were similar ( $P > 0.05$ ) to the control values (Group 1).



**Figure 2:** Effects of ethanolic extract of *Curcuma longa* rhizomes on paracetamol-induced rise in serum liver enzymes in rats.

## DISCUSSION

Paracetamol-induced liver injury is commonly used as models for investigation into the efficacy of hepatoprotective drugs (Plaa and Hewitt 1982). The raised serum liver enzymes such as ALT, AST and ALP in intoxicated rats can be attributed to the damage in the histostructural integrity of the liver cells (hepatocytes) (Kaplowitz 2001). The crude extract of *Curcuma longa* rhizomes used in this study preserve the structural integrity of hepatocytes membrane. This was evident from the hepatoprotection provided by *Curcuma longa* rhizomes to rats given paracetamol, which inhibited the rise in serum liver enzymes.

Paracetamol is mainly metabolized in the liver by glucuronidation and sulfation (Smith *et al.* 1986). However, hepatotoxicity of paracetamol has been attributed to the formation of a toxic reactive metabolite where a part of paracetamol is activated by the hepatic Cytochrome P450 (Kitteringham *et al.* 1988). This highly reactive metabolite, N-acetyl-p-benzoquinoneimine (Vermeulen *et al.* 1992) capable of biding covalently to cellular macromolecules (proteins, DNA) to produce protein adducts. It is still unknown what is the exact hepatoprotective mechanism of *Curcuma longa* extract. However, the extract may either inhibit the formation of the toxic paracetamol metabolite or stimulate the hepatic regeneration. This type of stimulation is known to cause the liver to become more resistant to damage by toxins (Lesch *et al.* 1970).

Hepatoprotective effects of *Curcuma longa* rhizomes was observed in paracetamol-induced liver damage in rats. This investigation validate the use of *Curcuma longa* in traditional medicine as a hepatoprotectant agent.

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