ABSTRACT

The role of *Leonotis nepetifolia* as a hepatoprotective agent against acetaminophen-induced toxicity *in vivo*.

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Shandilay (*Leonotis nepetifolia*) leaves have been used traditionally to treat ailments such as jaundice, coughs and colds. The animal model used in this study investigated whether extracts of *L. nepetifolia* prevented drug-induced liver damage. A single dose of acetaminophen was used as the non-lethal hepatotoxicant to evaluate probable hepatoprotective effects of methanolic and aqueous leaf extracts of *L. nepetifolia*.

Groups of mice (5 - 10) were given orally either methanolic or aqueous extracts at doses of 250 mg/kg, 500 mg/kg, 750 mg/kg and 1000 mg/kg as a pre- and post-treatment. In the pre-treatment model, animals were given a specified dose of the extract for three consecutive days, followed by either normal saline or toxic non-lethal acetaminophen (550 mg/kg) two hour after the last extract dose. In the post-treatment model animals received 550 mg/kg acetaminophen followed one hour later by the specified dose of either methanolic or aqueous extract.

Twenty-four hours following the final dosing; blood and liver were collected for antioxidant enzyme analysis and histological evaluation. Enzymes included alanine

aminotransaminase (ALT) and aspartate aminotransferase (AST), antioxidant enzyme; glutathione reductase (GR) and glutathione peroxidase (GPx), superoxide dismutase (SOD) and catalase (CAT).

Toxic non-lethal acetaminophen caused hepatic damage with statistically significant increases in serum ALT and AST levels, $p < 0.05$. High dose acetaminophen also caused statistically significant increases in both SOD and GR activities and a significant reduction in GPx activity, with no significant decrease in CAT activity. Acetaminophen produced significant hepatic necrosis, as observed by histopathological assessment.

In mice treated with extracts alone there were no significant changes in serum liver enzymes, antioxidant enzyme activities or histological architecture, being similar to saline controls, suggesting that extracts on their own had no effect on liver function.

Both extracts, as pre- and post-treatments, produced statistically significant reductions in the acetaminophen-induced increase in serum ALT and AST levels, $p < 0.05$. The extracts (at all doses) also prevented the acetaminophen-induced hepatic necrosis as evidenced by histopathological evaluation and the histological grades were significantly reduced, $p < 0.05$. Compared to the acetaminophen-treated animals SOD, GR and GPx enzyme activities were significantly lower ($p < 0.05$), whereas CAT activity was not significantly reduced. Effect of enzyme activity by both extracts suggests a stabilization of cellular status. Reduction in SOD activity and the stabilization of CAT activity observed both pre- and post- treatments suggests a reduction in free radical and ion formation in the presence of *L. nepetifolia*. In

addition the overall reduction of GPx and GR activities in both pre- and post-treatments together with the reverse in both enzymes' activities with extracts suggest the availability of glutathione to neutralize or abrogate NAPQI.

In conclusion both pre- and post-treatment with *L. nepetifolia* provided protection against acetaminophen-induced hepatic damage in this animal model with maintained liver enzyme and architecture. These findings suggest probable utility of *L. nepetifolia* as prophylaxis and therapeutic interventions in acetaminophen-induced hepatotoxicity. Further studies warrant identification and quantification of compounds responsible for protection and the precise mechanism of action.

KEYWORDS

Leonotis nepetifolia; hepatoprotective; acetaminophen; antioxidant enzyme activities