SHORT COMMUNICATION

Guggulu (Commiphora mukul) Potentially Ameliorates Hypothyroidism in Female Mice

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The efficacy of guggulu, the gum resin of Commiphora mukul in regulating hypothyroidism was evaluated in female mice. In addition to estimating serum levels of thyroxine and triiodothyronine, hepatic 5′ monodeiodinase, hepatic glucose-6-phosphatase and lipid-peroxidation (LPO), the activities of the anti-oxidative enzymes, superoxide dismutase (SOD) and catalase (CAT), were investigated. While 6-n-propyl-2-thiouracil (PTU, 10.00 mg/kg/d for 30 days) induced hypothyroidism in mice, as evidenced by a decrease in thyroid hormone concentration and in hepatic 5′D-I activity, simultaneous administration of guggulu (200 mg/kg/d for 30 days) reversed this effect, indicating its potential to stimulate thyroid function. Although in PTU treated animals a marginal increase in hepatic LPO was observed, when simultaneously treated with guggulu, it was decreased. A parallel increase in the activity of endogenous antioxidants, SOD and CAT, in the latter group indicated the safe and antiperoxidative nature of the drug. These findings suggest the possible use of guggulu in the amelioration of hypothyroidism. Copyright © 2005 John Wiley & Sons, Ltd.

Keywords: Commiphora mukul; guggulu; thyroid hormones; 5′ monodeiodinase; lipid peroxidation.

INTRODUCTION

Inadequate thyroid hormone synthesis and secretion lead to hypothyroidism, which, if not treated over time results in a generalized slowing down of metabolic processes, a condition known as myxoedema. The literature available on the role of plant extracts in the stimulation of thyroid function is meagre (Kar and Panda, 2003), and in particular, systematic scientific investigations are negligible.

Commiphora mukul (Balsamodendron mukul Hook family Burseraceae) is attributed with several medicinal properties, particularly regarding the gum resin, guggulu (Dwivedi, 1996). In our preliminary studies guggulu appeared to be stimulatory to thyroid function in mice (Panda and Kar, 1999b). However, it was not known if this showed potential for use in hypothyroidism. Therefore, in this investigation the effect of guggulu in the regulation of 6-n-propyl-2-thiouracil (PTU) induced hypothyroidism has been evaluated.

Changes in tissue lipid peroxidation (LPO), and the associated defensive enzymes such as superoxide dismutase (SOD) and catalase (CAT), are commonly investigated for tissue toxicity studies (Halliwell and Gutteridge, 1989). Since most of the thyroid hormones are metabolized in the liver, hepatic LPO, SOD and CAT activities were also evaluated in order to reveal any toxic effects of the drug. The female mouse was used as a working model because females are known to suffer more frequently from hypothyroidism (Fry, 1993).

MATERIALS AND METHODS

Plant material. Gum extract of Commiphora mukul containing guggulu sterones (3.8% by HPLC) was obtained from Kisalaya Herbas Ltd, Indore, India.

Animals. Adult female Swiss albino mice (28–30 g) were used. The animals were housed in polypropylene cages with the provision of food and water ad libitum.

Experimental design. Twenty eight mice were acclimatized for 7 days in a temperature (27°± 1°C) and light controlled (14 h light: 10 h dark) room with the provision of food and water ad libitum. Mice were divided randomly into four groups of seven each. While group I, receiving 0.1 mL of normal saline (the vehicle) served as a control, animals of groups II and III were treated with 10 mg/kg/day of PTU (i.p.) for the first 15 days. From day 16 onwards, group II continued to receive only PTU, while group III received an equivalent amount of PTU and 200 mg/kg/day of guggulu (Panda and Kar, 1999b). Group IV received only an equivalent amount of guggulu from day 16 onward. Normal saline and guggulu were administered by gastric intubations. Every day vehicle/drug administration was performed between 1000 and 1100 h to avoid any circadian interference. The experiment was continued for a total period of 30 days.

Twenty-four hours after the last dose, the overnight fasted animals were killed under anaesthesia and the blood was collected by cardiac puncture. Serum samples were stored at −20 °C for further use. After exsanguination, the liver was removed, cleaned twice in phosphate buffered saline (pH 7.4) and immediately processed for biochemical estimations.

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Biochemical estimations. For the evaluation of LPO, SOD and CAT activities, the liver was homogenized in 10% w/v ice cold phosphate buffer (0.1 M, pH 7.4) and the homogenate was centrifuged at 15,000 × g for 30 min. The activity of hepatic LPO, SOD, CAT and G-6-Pase was evaluated by our routine protocols (Panda and Kar, 1998, 1999a&b). Serum concentrations of total T₄ and T₃ were estimated by radioimmunoassay (RIA) following the protocols used earlier (Panda and Kar, 2003; Tahiliani and Kar, 2003).

Statistical analysis. Data are expressed as mean ± SE. Statistical analysis was done using analysis of variance (ANOVA), followed by Student’s t-test.

RESULTS AND DISCUSSION

Administration of guggulu increased the level of T₃ in euthyroid animals suggesting the efficacy of the drug in augmenting the thyroid function. This is in accordance with our earlier finding (Panda and Kar, 1999b). In the present study, while in PTU treated animals, a significant decrease in serum T₃ and T₄ concentration was observed (Fig. 1), administration of the drug in PTU induced hypothyroid animals nearly normalized the thyroid hormone levels, indicating clearly the effectiveness of the drug in counteracting the thyroid inhibitory effect of PTU. With respect to 5'D-I activity which reflects the rate of conversion of T₄ to T₃, the major source of T₃ generation, a similar effect was exhibited, as in the PTU treated group 5'D-I activity was significantly less, whereas, in the group that received both PTU and guggulu, it was more. This suggests that guggulu possibly enhances T₃ levels by stimulating the conversion of T₄ to T₃. A concomitant increase in hepatic glucose-6-phosphatase (a thyroid hormone dependent enzyme) activity further supports the stimulatory role of guggulu in T₃ production.

Although other plant extracts also have been found to exhibit thyroid stimulatory actions (Panda and Kar, 1998, 1999a), they were performed in euthyroid animals. The present finding is significant in that the guggulu was effective in hypothyroid animals.

With respect to lipid peroxidation, guggulu treatment significantly decreased the LPO and increased the SOD and CAT activities in euthyroid animals. While in PTU treated animals no significant change in hepatic LPO, SOD and CAT activities were observed (Table 1), administration of guggulu along with PTU decreased the values of LPO and increased SOD and CAT activities compared with the respective values of PTU treated hypothyroid animals, indicating the safe and antiperoxidative nature of the drug.

The present results thus clearly reveal that guggulu extract is stimulatory to thyroid function and may ameliorate hypothyroidism, as it was able to increase the concentration of the thyroid hormone, T₃, in PTU induced hypothyroid animals. Further more, it appears that the drug at its present dose is not hepatotoxic, rather antiperoxidative, in nature. Since a parallel increase in T₃ and 5'D activity was observed following drug administration, it may be suggested that the guggulu-induced increase in T₃ could be the result of enhanced conversion of T₄ to T₃, the major source of T₃ generation. Whatever the mechanism of action(s) in mice, it appears that guggulu therapy may ameliorate the hypothyroid condition without any hepatotoxic effects.

Table 1. Effects of guggulu (200 mg/kg) for 30 days on the changes in hepatic LPO (µM of MDA formed/h/mg protein), SOD (units/mg protein), CAT (µM of H₂O₂ decomposed/min/mg protein) and G-6-Pase (µM phosphate generated/min/mg protein) activities in female mice (n = 7 for each group)

<table>
<thead>
<tr>
<th>Treatment</th>
<th>LPO</th>
<th>SOD</th>
<th>CAT</th>
<th>G-6-Pase</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>0.881 ± 0.104</td>
<td>4.831 ± 0.219</td>
<td>54.24 ± 5.61</td>
<td>0.32 ± 0.02</td>
</tr>
<tr>
<td>PTU</td>
<td>0.981 ± 0.121</td>
<td>3.901 ± 0.141</td>
<td>49.09 ± 4.72</td>
<td>0.09* ± 0.02</td>
</tr>
<tr>
<td>PTU + Guggulu</td>
<td>0.614 ± 0.104</td>
<td>4.781 ± 0.182</td>
<td>69.48 ± 8.92</td>
<td>0.16* ± 0.01</td>
</tr>
<tr>
<td>Guggulu</td>
<td>0.560± 0.096</td>
<td>5.685± 0.288</td>
<td>71.22± 8.63</td>
<td>0.41± 0.03</td>
</tr>
</tbody>
</table>

Data are expressed as mean ± SEM. * p < 0.001;  † p < 0.01 and ‡ p < 0.05 compared with the respective control values. * p < 0.05, † p < 0.01, ‡ p < 0.001 compared with the respective value of PTU treated group.

REFERENCES