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Protective role of Murraya Koenigii and Citrus Medica leaf extract in Thyroxine treated Female Mice

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Abstract

The effects of Murraya koenigii and Citrus medica leaves extract were studied to understand the interaction between the two extract in female mice model by using L-thyroxine. The analysis was done by using similar dose but the comparison was made with the response of individual plant extract. Serum level of T_3 and T_4 was increased by the oral administration of L-thyroxine (0.5mg/kg b.w) in albino mice to make them hyperthyroidic. However simultaneous administration of Murraya koenigii (83% and 7.6%) and Citrus medica (73% and 54%) reduce serum T_3 and T_4 level suggested that Citrus medica strongly suppress the serum level of thyroid hormones. These observations explain the hidden potential of the leaves extract in the regulation of thyroid hormones.

Keywords: Hyperthyroidism, L- thyroxine, murraya koenigii, citrus medica.

Introduction

Thyroid disorders are studied as one of the important endocrinopathy in humans¹ and in animal science². Thyroid hormone malfunction occurs due to the imbalance of T_3 and T_4 hormones which are secreted by the thyroid gland. Conditions like hypertension and disturb BMR are some of the conditions caused by the imbalance of thyroid hormones. Thyroid disorders are mainly of two types- Hyperthyroidism and Hypothyroidism. Hyperthyroidism is the most common endocrine disease in women³: Women suffer from hyperthyroid are four times more than men and eight times more from hypothyroidism.

Murraya *koenigii* also known as kari patta in hindi is used as flavoring agent in many countries. In traditional medicine system, Murraya koenigii is used to cure many diseases like diarrhea, influenza, piles, vomiting dysentery etc.⁴⁻⁵. Studies also reveal that MK leaves have strong antioxidative⁶⁻⁷, antimicrobial⁸, anti inflammatory⁹ activity and also lowers the blood glucose level¹⁰. It also showed reduction in serum cholesterol¹¹ and colon carcinogenesis¹². Citrus *medica* L, (citron) cultivated in warm moist region in India used in the treatment of disease like diabetes and alzheimer's¹³. Flavonoids present in it also have an anti inflammatory, antihistamine and diuretic activity and also causes dilation of the coronaries¹⁴. Apart from these it is also used in nausea, cough, vomiting, asthma, and anti scorbutic¹⁵⁻¹⁹.

Despite these uses, literature is negligible on the importance of leaves extract in the treatment of thyroid hormone imbalance disorder. Hence in this case an experiment has been made to study the hitherto unknown efficacy of leaves extract of Murraya *koenigii* and Citrus *medica*, if any, on the serum thyroid hormones level.

Material and Methods

Thyroxine was purchased from Biodeal Laboratories Ltd, India. Elisa kits from DSI s.r.l Italy for the evaluation of thyroid hormones level.

Plant material and preparation of extracts: Murraya *koenigii* and Citrus *medica* plants were collected from Sanjeevani, Bhopal. and were identified and authenticated by Department of Botany, Govt MLB College, Bhopal. Plants were dried in shade and grated. 100 gm of each powder was mixed with 1000 ml of d.w and kept for 72 hrs.

Animals: Swiss albino female mice 25-30 gm body weight were procured and housed in different cages under 12 hrs light and dark periods. They were fed with standard food pellets, water ad libitum. Standard ethical guidelines were followed and protocol was approved by Institutional Animal Ethics Committee.

Experimental design: Twenty eight female mice were divided into four groups. Animals of group I received distill water and served as control group. Animals of group II were treated with 0.5mg/kg thyroxine while animals of group III and IV were administered with equivalent amount of thyroxine along with 250 mg/kg of M.*koenigii* and C. *medica* for 15 days. Blood samples were taken for analysis.

Biochemical estimation: Total triiodothyronine (TT₃), total thyroxine (TT₄) and thyroid stimulating hormone (TSH) were estimated by Enzyme linked immunosorbent assay (ELISA) following the protocol provided in the kits, as done earlier in our laboratory²⁰. In brief, ELISA was performed using conjugates, standards, buffer, substrate, washing and stop solution. The

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reaction mixture was comprised of standard/sample and conjugate. The tubes were mixed and incubated at 25°C for 90 mins. Wells were washed with washing solution and substrate was added, again incubated for 20 mins. Finally, the reaction was ceased by adding stop solution. Absorbance was taken at 450nm.

Statistical analysis: Results were expressed as Mean \pm Standard Error of Mean (S.E.M) and were analyzed by one way Anova followed by Newman-Keuls multiple comparison test.

Table-I
Effect of M. koenigii and C. medica on serum level of T3 and
T in thuraying induced hyperthyroid female mice

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Groups	T ₃ (ng/ml)	T ₄ (n mol/L)
Control	0.79±0.26	93.00±1.73
L-T ₄	6.80 ± 1.13^{x}	169.00 ± 2.08^{y}
L-T ₄ +MK	1.13±0.08 ^a	156.75 ± 2.68^{b}
L-T ₄ +CM	1.83 ± 0.30^{b}	77.30±15.07 ^a

Data are mean \pm s.e.m. x: P<0.01, y: P<0.001, compared to respective control values. a: P<0.001, b:P< 0.01, compared to respective L-thyroxine treated groups.

Results and Discussion

Significant results were obtained after administration of L-T₄ to normal mice increased the serum level of T₃ and T₄ indicating the attainment of hyperthyroidic condition. Simultaneous administration of Murraya *koenigii* significantly decreases the serum concentration of T₃ and T₄ by 83% and 7.6% respectively. While serum concentration of T₃ and T₄ decreased by 73% and 54% respectively in Citrus *medica* treated mice.

The metabolically active hormone T_3 is synthesized by the thyroid gland in small quantity and formed in liver by monodeiodination of T_4 ²¹. While T_4 is secreted by the thyroid gland itself.

The result of the present study shows that administration of levothyroxine (L-T₄) increased the serum level of T₃ and T₄ as compared with control group. The increased level of thyroxine (T₄) may be due to the absorbption of L-T₄ by gut which is further converted to triiodothyronine (T₃) by iodothyronine deiodinases²². Similar hyperthyroidic results were also shown in rats induced by thyroxine which shows increased level of thyroid hormones²³⁻²⁴.

Murraya *koenigii* and Citrus *medica* were found to decrease both the thyroid hormones indicating thyroid inhibitory role. C. *medica* decrease both serum T_3 and T_4 suggesting that it might cause hindrance in T_4 synthesis at thyroid gland level and at the level of peripheral mono-deiodination of T_4^{25} . M.*koenigii* also lowers the level of T_4 with a significant reduction in T_3 . This result suggests that M. *koenigii* might have inhibited some of the modulating effects on T_4 on hepatic enzyme by the blockade extra thyroidal conversion of T_4 to T_3^{26} .

Conclusion

In summary it can be said that out of the two Citrus *medica* appears to be more effective than Murraya *koenigii* in reducing thyroid function and therefore may be considered for the regulation of hyperthyroidism. However more experiment is required to describe its exact mechanism and probable medicinal values.

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