

Antithyroidal Activity of *Aegle marmelos* Corr.

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Abstract

The aqueous extract from the leaves of *Aegle marmelos* Corr. was investigated to evaluate its possible effects on the L-thyroxine (L-T₄) induced hyperthyroidism and propylthiouracil induced hypothyroidism. While an alteration in serum T₃ and T₄ concentration was observed in L-Thyroxine (0.5mg/kg) and Propylthiouracil (10 mg/kg) treated animals, simultaneous administration of the plant extract at a dose of 250 mg/kg/d (p.o.) for 15days in hyperthyroid mice reduced T₃ and T₄ concentrations by 78% and 54% respectively. But no effect was shown on the level of T₃ and T₄ in Propylthiouracil treated animals.

These findings reveal that *Aegle marmelos* inhibits thyroid activity.

Key words : *Aegle marmelos*, Propylthiouracil, Thyroxine. Hypothyroidism, Hyperthyroidism

Thyroid hormones play an important role in development, metabolism, thermoregulation, and growth⁴ both in humans¹⁰ and in veterinary medicine⁸. Alterations in the level of these hormones lead not only to altered basal metabolic rate but also to many health problems. Hyperthyroidism is the most common endocrine disease in women² and hypothyroidism may occur in individuals of all ages affecting several different organs and systems³.

The most commonly used antithyroid drugs are carbimazole and its active metabolite methimazole. These drugs are used at a very high dose and show a subjective improvement within 10-14 days. But unfortunately thyrotoxicosis recurs in at least 50%, usually within 2 years of stopping treatment. Despite good drug compliance T₄ and TSH levels fluctuate between those of thyrotoxicosis and hypothyroidism¹¹.

Aegle marmelos Corr. (AM) is a native

plant of India. It belongs to Rutaceae family and commonly known as wood apple. AM is extensively described in the Vedic literature for the treatment of various diseases. AM is traditionally used to treat jaundice, constipation, chronic diarrhoea, dysentery, stomachache, fever, asthma, inflammations, febrile delirium, acute bronchitis, snakebite, upper respiratory tract infections⁹.

Although herbal medicines are being used in increasing number, very few scientific reports are available on the antithyroidal potential of plants extract⁶. Therefore in the present investigation an attempt has been made to explore the efficacy of AM leaves extract on the concentration of serum thyroid hormone in Swiss albino mice.

Chemicals :

Thyroxine was purchased from Biodeal Laboratories Ltd, India and Propyl thiouracil was purchased from Macleods Pharmaceuticals Ltd, India, ELISA (LISA Plus- RS 232) kits for the estimation of thyroid hormones were purchased from DSI s.r.l Italy.

Plant material and preparation of extract:

AM plant was procured from Sanjeevani, Bhopal for the estimation of serum thyroid hormone. *Aegle marmelos* leaves were dried in shade and powdered. 100 gms of leaf powder was mixed with 1000 ml of distilled water and kept for 72 hrs. The supernatant was collected and evaporated to dryness. This was used as the crude leaf extract to study the antithyroid effect.

Animals :

Swiss albino female mice 25 - 30 gm body weight were procured and housed in separate cages under 12 hours light and 12 hours dark periods. Mice were maintained on standard food pellets, water *ad libitum* and room temperature. Standard ethical guidelines of Committee for the Purpose of Control and Supervision on Experiments on Animals (CPCSEA) were followed after the approval of Institutional Animal Ethical Committee for Handling and Maintenance for Experimental Animals.

Experimental design :

Twenty one female mice were divided into three groups. Group I was treated as control and received equivalent amount of distilled water. Group II and III were treated with a dose of Thyroxine (0.5 mg/kg b.w) and Propylthiouracil (10mg/kg b.w) initially for 30 days to render them Hyperthyroidic and Hypothyroidic respectively. Blood samples were taken on the 30th day for analysis. From the day 31 both the groups were treated with *Aegle marmelos* (250 mg/kg b.w) for 15 days. Again blood samples were taken for final analysis.

Biochemical estimation :

Total triiodothyronine (TT₃), total thyroxine (TT₄) and thyroid stimulating hormone (TSH) were measured with Enzyme linked immunosorbent assay (ELISA) kits. In brief, ELISA was performed using conjugate, standards, buffer, substrate, washing and stop solution. The reaction mixture 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 terminated by adding stop solution. Absorbance was taken at 450nm.

Statistical analysis :

All results were expressed as Mean \pm Standard Error of Mean (S.E.M.). Data was

analyzed using one-way ANOVA followed by Tukeys test.

Following the administration of L-Thyroxine at a dose of 0.5 mg/kg/day for 30 days increased the serum concentration of both the thyroid hormones T₃ and T₄ with a decrease in TSH levels. However, simultaneous administration of *Aegle marmelos* plant extract at a dose of 250 mg/kg restored the level of thyroid hormones towards normalcy. (Table 1).

Table-1. Effect of *Aegle marmelos* Corr. on T₃ (mg/ml), T₄ (n mol/L) and TSH (μ IU/ml) in Thyroxine induced Hyperthyroid female mice

	T ₃	T ₄	TSH
Control	0.79 \pm 0.26	93 \pm 1.73	1.67 \pm 0.32
Hyper	6.8 \pm 1.23 ^a	169 \pm 2.08 ^b	0.35 \pm 0.07 ^a
AM	1.47 \pm 0.07 ^x	77 \pm 4.04 ^y	1.46 \pm 0.28 ^x

Data expressed in Mean \pm SEM (n = 7) a: P < 0.05, b: P < 0.001 compared to respective control values.

x: P < 0.05, y: P < 0.001 compared to L-thyroxine treated group

Similarly the administration of Propylthiouracil at a dose of 10 mg/kg/day for 30 days decreased the serum concentration of both the thyroid hormones T₃ and T₄ and increased

TSH level but no effect was observed on the level of thyroid hormone after the administration of *Aegle marmelos* for 15 days. (Table 2).

Table-2. Effect of *Aegle marmelos* on T₃ (ng/ml), T₄ (n mol/L) and TSH (μ IU/ml) in PTU induce Hypothyroid female mice

	T ₃	T ₄	TSH
Control	0.79 \pm 0.26	93 \pm 1.73	1.67 \pm 0.32
Hypo	0.49 \pm 0.01 ^a	52.33 \pm 1.45 ^b	4.8 \pm 0.36 ^b
AM	0.61 \pm 0.06 ^x	47.75 \pm 0.47 ^x	5.0 \pm 0.01 ^x

Data expressed in Mean \pm SEM (n = 7) a: P > 0.05, b: P < 0.001 compared to respective control values.

x: P > 0.05 compared to PTU treated group

Results of the experiment clearly revealed that *Aegle marmelos* has antithyroidal property as it inhibited serum T_4 and T_3 concentration. Secreting Thyroid Stimulating Hormone (TSH) controls releasing thyroid hormones. The amount of TSH secreting is also adjusted by level of thyroid hormones in blood. By reduction in these hormones TSH secreting will be increased⁵. In this study it appears that *Aegle marmelos* inhibits T_4 synthesis both at the glandular level (the only source for T_4 generation) and at the level of peripheral conversion of T_4 to T_3 , the major source of the latter hormone⁷. In fact, many plant extracts are known to interfere with thyroid hormone homeostasis at various levels, including binding of thyroid stimulating hormone receptor, thyroid iodide transport, thyroid hormone secretion from the gland, and extrathyroidal 5-monodeiodination of T_4 *in vivo*¹. The thyroid inhibitory role of *Aegle marmelos* might also have been mediated either through one of the aforementioned mechanisms or through an inhibition of thyroid peroxidase, the key enzyme in thyroid hormone biosynthesis.

In conclusion, our finding indicates that *Aegle marmelos* inhibits hyperthyroidism as it decreased the T_3 and T_4 concentration. However, further investigation is required to delineate its precise mechanism in the

amelioration of Hyperthyroidism.

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