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Evaluation of Anti-Thyroid Activity of Hydro Alcoholic Extract of *Coriander sativum* in Experimental Animals.

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ABSTRACT

The present study was performed in order to evaluate the anti-thyroid potential of Coriander sativum seeds in albino rats. The hyperthyroidism was induced to albino rats orally using propyl-thio-uracil (PTU) for 14 days. The hyperthyroidism rats were administered Hydroalcoholic extract of Coriander sativum seeds (250 mg/kg and 500mg/kg) for 21 days. The serum was analyzed for the thyroid hormone level. Results demonstrated that 250 mg/kg and 500 mg/kg of hydroalcoholic extract produces significant anti-thyroid activity by decreasing the T₃ and T₄ level and lowered the TSH level in rats. The histopathological study of the thyroid gland justifies the anti-thyroid activity of Coriander sativum seeds. The findings of this study propose that the extract may have property to regulate thyroid levels in animals.

Keywords: Coriander sativum, Propyl-thio-uracil, hypothyroidism, thyroid hormone

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INTRODUCTION

Thyroid is an important endocrine organ in human body. The thyroid gland is situated low down at the front of neck weighing about 25 g. The gland has two lobes; each pear shaped hugging anterior lateral aspects of cervical trachea from oblique line of thyroid cartilage to 5th or 6th tracheal ring. The right lobe is often larger than left and isthmus joins them anterior at the level of 2nd and 3rd tracheal rings. The normal size of each lobe of the thyroid gland has been described to be 5 cm long, its greatest and anterior-posterior extent being 3 cm and 2 cm respectively. The isthmus measures about 1.25 cm transversely as well as vertically and is usually placed anterior to the second and third tracheal cartilages [1]. Isthmus is plastered quite firmly to the anterior surface of trachea. A small portion of gland substance, pyramidal lobe often projects upwards from isthmus, generally to the left of midline. The gland has its own capsule and is also enclosed by an envelope of pre tracheal fascia which is thickened and attached to the cricoid cartilage and upper tracheal rings [2]. Thyroid hormones play a vital role in normal human physiology with effects on almost all tissues to influence growth and development, maintain normal cognition, cardiovascular function, bone health, metabolism and energy balance [3].

Two thyroid hormones, thyroxine (T₄) and tri-iodothyronine (T₃) are involved in the regulation of myriad of body functions including lipid and carbohydrate metabolism, oxygen consumption, nerve conduction and reproduction. Alterations in their normal levels lead to physiological/clinical abnormalities, such as hypothyroidism and hyperthyroidism.

Hypothyroidism is a state in which the thyroid organ does not make enough thyroid hormone. Iodine insufficiency is frequently referred to as the most well-known reason for hypothyroidism overall however it can be brought about by numerous different variables. It can come about because of the absence of a thyroid organ or from iodine-131 treatment, and can likewise be connected with expanded anxiety. Serious hypothyroidism in babies can bring about cretinism. 2011 studies concluded that about 8% of women over 50 and men over 65 in the UK suffer from an under-active thyroid and that as many as 100,000 of these people could benefit from treatment they are currently not receiving [4].

The world health organization has been encouraging countries to employ the traditional medicine, in unresolved diseases therefore, there is a rising propensity toward application of herbal medicine, in chronic diseases. *Coriandrum sativum* is a species belonging to the Apiaceae (Umbelliferae) family, whose habitat is the Middle Eastern and Mediterranean regions [5]. In the Indian traditional medicine, coriander is used in disorders of digestive, respiratory and urinary system, as it has diaphoretic, diuretic, carminative, and stimulant effects. In Iranian traditional medicine, coriander has been indicated for a number of medical problems such as dyspeptic complaints, loss of appetite, anti-thyroid, convulsion, and insomnia [6,7].

The plant has been widely studied for its chemical constituents. The fruit of coriander contains anethol, borneol, bornyl acetate camphor, camphene, carvone, cineole, cymene, coriandrin, dihydrocoriandrin, coriandrone A, coriandrone B, coriandrone C-E, phydroxybenzoic acid, limonene, linoleic acid, myrcene [8].

The current medical therapies for hypothyroidism are often deemed inadequate because of difficulties in regulating the level of thyroid hormones through use of drugs. Thus, it is worth developing new plant-derived agents that enhance thyroid hormone in hypothyroidism and entail fewer adverse effects. Hence the present study was carried out to evaluate the efficacy of *Coriandrum sativum* on the thyroid dysfunction.

MATERIALS & METHODS

Collection of plant material

The seeds of *Coriander sativum* were collected from the local market of Bhopal (MP) in winter season. The plant material were dried and made coarsely powder for further use.

Authentication of plant material

Herbarium file of plant part was prepared and authenticated by Dr. Zia UHHasan (Professor, Department of Botany), Saifia College Bhopal and Madhya Pradesh, India. Voucher specimen no. is 432/bot/Saifia/17.

Preparation extract

Hydro alcoholic extract of Coriander sativum seeds was prepared using soxhlet apparatus for oral administration. The doses of 250mg/kg and 450mg/kg body weight of extract were prepared.

Experimental animals

Wistar Albino rats weighing about (120-160gm) of either sex were obtained from animal house of SBRL Bhopal. The animals were maintain under standard condition i.e, housed in polypropylene cages and maintained at a temperature 27 ± 2 °C, relative humidity $65\pm 10\%$ under 12 hours light and dark cycle. The animals were acclimatized for 10 days under laboratory condition before carrying out the experiments. The animal house approved by the committee for the purpose of control and supervision on Experimental Animals (CPCSEA)-registrationnumber (1413/PO/E/S/11/CPCSEA). The study was carried out after the approval by the Institutional animal ethical committee (IACE) and form B proposal number. (SBRL/IAEC/ July2017/01)

Phytochemical screening

Phytochemical examinations were carried out for the hydroalcoholicextracts as per the standard methods discussed by Khandelwal, 2005 [9,10].

Acute toxicity (LD₅₀) studies

An attempt was made to determine LD₅₀ of hydroalcoholic extracts of Coriander sativum seeds at a dose of 2000mg/kg/p.o, in male albino rats. The extracts were found devoid of mortality of the animals. Hence 5000mg/kg was considered as cut off value. Therefore,the screening doses (extracts 250mg/kg and 500mg/kg)selected for the evaluation of anti-thyroid activity as per OECD guidelines no.423 [11]

Evaluation of anti-thyroid activity

Animals were randomly divided into four groups. Group I received normal saline instead of drug; Group II received PTU (0.9mg/100gm/ml/p.oral) for 14 days; Group III received extract at dose of 250 mg/kg body weight for 21 days, Group IV received extract at dose of 500 mg/kg body weight for 21 days. Hypothyroidism was induced in animals by adding 10 mg/kg/day propylthiouracil to drinking water for 20 days. The Group III and Group IV were treated with 250 and 500 mg/kg, respectively for 21 days. The animals were anesthetized after three weeks of treatment. About 5 ml of blood was collected by cardiac puncture, and immediately transferred into tubes containing EDTA. The plasma was separated by centrifuging the blood samples at $1077 \times g$ for 30 min at 4 °C, and the hormone levels in the plasma were determined [12,13].

Histopathology study of thyroid gland

At the end of studies, all animals were sacrificed by cervical dislocation. Thoracic and neck cavity was cut open to isolate thyroid gland from each animal. Isolated glands were cleaned off extraneous tissue, kept in freshly prepared 10% formalin for histopathological analysis [14].

Statistical analysis

The results are expressed as mean \pm SD of six independent experiments. Statistical significance between the groups was evaluated by one-way analysis of variance (ANOVA) followed by Dunet's test. A $P < 0.05$ value was considered as statistically significant.

RESULTS

Preliminary phytochemical analysis

The phytochemical screening of hydroalcoholic extracts of Coriander Sativum seeds revealed the presence of alkaloids, glycosides, flavonoids, saponins and tannins (Table 1). The presence of flavonoids assists for evaluation of Anti-thyroid activity.

Table 1: Phytochemical screening of hydroalcoholic extract of Coriander sativum

| Identification Test | Test name | hydroalcoholic extract |
|---------------------|--------------------------------|------------------------|
| Alkaloids | Mayer's test | + |
| | Wagner's test | + |
| Glycosides | Killer-killani test | + |
| Tannins | Gelatin test | + |
| | Ferric chloride test | + |
| Flavonoids | NAOH | + |
| | H ₂ SO ₄ | + |
| | Alkaline reagent test | + |
| Saponins | Foam test | + |

(+) = Present, (-) = Absent

Acute toxicity studies

An attempt was made to determine LD₅₀ of hydroalcoholic extracts of Coriander sativum seeds at a dose of 2000mg/kg/p.o, in male albino rats. There was no gross evidence of any abnormality observed up to a period of 4-6 hrs or mortality up to a period of 24 hrs at the maximum tolerated dose level. The extracts were found devoid of mortality of the animals. Hence 5000mg/kg was considered as cut off value. Therefore, the screening doses (hydroalcoholic extracts 250mg/kg and 500mg/kg.) Selected for the evaluation of anti-thyroid activity as per OECD guidelines no.423

Anti-thyroid activity of extract

From the results, it was observed that groups except normal control group showed elevated T₃, T₄ value and diminished TSH value. The animal treated with hydroalcoholic extract showed elevated T₃, T₄ level and diminished TSH reversed to that of normal in a dose dependent manner and the high dose of hydroalcoholic extract of Coriander sativum shows higher anti-thyroid activity (Table 3)

Table 3: Thyroid function test values of hydroalcoholic extract of Coriander sativum

| Groups | Treatment | T ₃ (ng/dl) | T ₄ (ng/dl) | TSH(μIU/mL) |
|-----------|---|--------------------------|-------------------------|------------------------|
| Group I | Normal control | 23.65±0.11 | 2.53±0.62 | 0.21±0.25 |
| Group II | Positive control [Hyperthyroid induced animals (PTU 0.9 mg/100gm/ml) for 14 days] | 144.53±0.35 ^a | 19.18±0.67 ^a | 8.68±0.45 ^a |
| Group III | Hyperthyroid + hydroalcoholic extract C. sativum (250 mg/kg) for 21 days | 132.81±0.258* | 9.45± 0.21* | 4.87±0.43 |
| Group IV | Hyperthyroid + hydroalcoholic extract C. sativum (500 mg/kg) for 21 days | 69.75±0.66* | 3.5±0.89* | 1.24±0.19** |

Values are expressed as mean ± SD (Number of animals, n=6); significantly different at ^aP<0.05 when compared with normal control group, *P<0.05 when compared with positive control group

Histopathology

The histopathological studies were under taken to study of tissue section of the thyroid gland of different experimental groups of rats. The figure shows histopathological results (Fig 1).

Thyroid gland of normal rats showed numerous follicles some of which contain colloid. A colloid varies from thick to thin with occasional scalloping. The follicular cells have round nuclei surrounded by a clear cytoplasm. Thyroid gland of rats induced with propylthiouracil showed follicles lined by follicular epithelial cells. Thyroid follicle shows 65-75% of luminal colloids. In about 15% of follicles, the lumen was completely filled with colloid. There was no papillary infolding of the epithelium. Section of thyroid gland of hypothyroid rats treated with Coriander sativumplant extracts showed follicle lined by follicular epithelial cells which appeared normal. Many of follicular colloids showed scalloping. There is no papillary infolding of the epithelial cells (Fig 1).

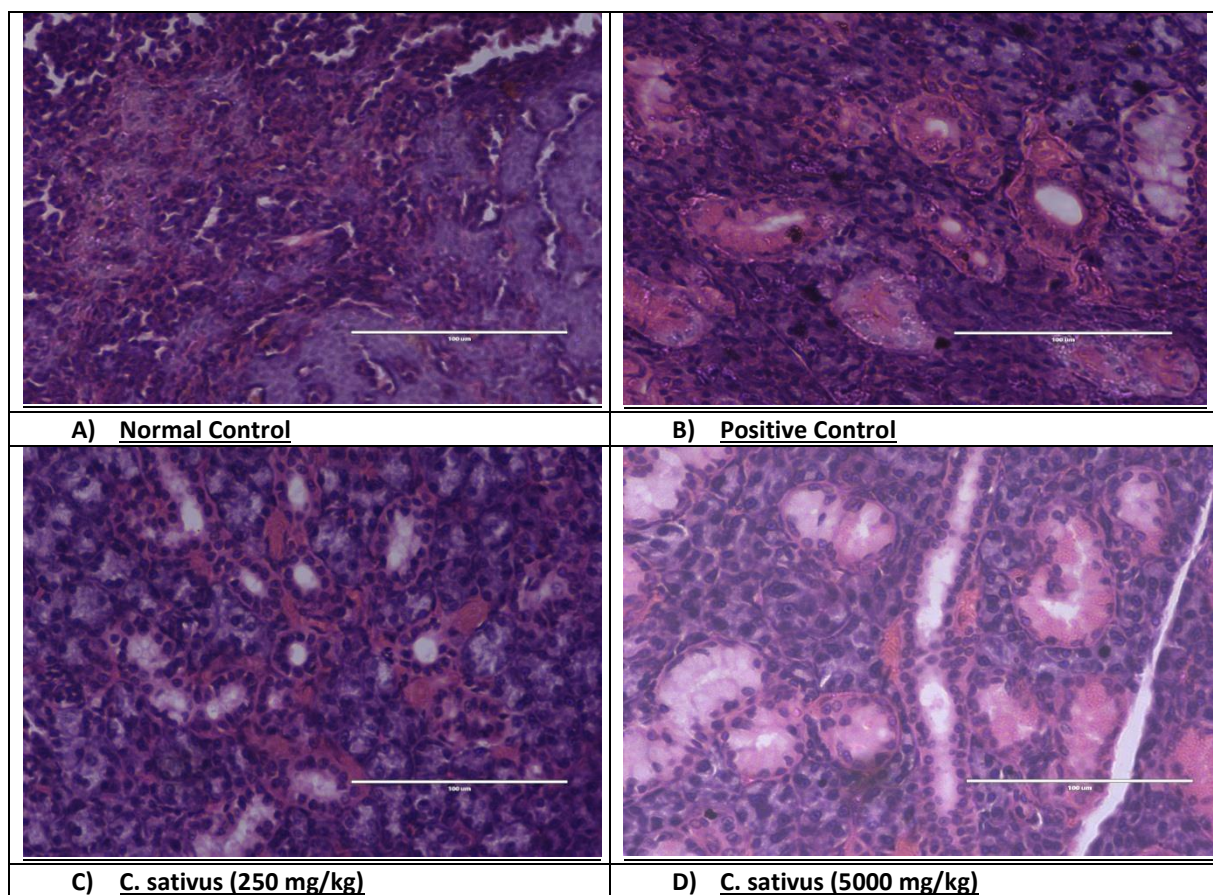


Fig 1: Histopathology of thyroid glands in different groups

DISCUSSIONS

Herbs have always been the principle from the medicine in India, although very less reports are available on the adverse effect of thyroid medication. Some of the side effect of the anti-thyroid medications includes a potentially fatal reduction in the level of white blood cells, agranulocytosis, granulocytopenia, aplastic anaemia, fulminant liver failure, rashes and peripheral neuritis. In the present study one the locally available plant Coriandersativumwas selected. Hypothyroidism was induced by propyl-thio-uracil. T₃, T₄ and TSH levels were evaluated for determining the Anti-thyroid activity of the plant. Histopathological examination was conducted in order to determine the effectiveness of tested extracts.

The preliminary phytochemical analysis of the hydroalcoholic extract of Coriander sativumseeds designated the presences of alkaloids, glycosides, flavonoids, saponins and tannins and the most prominent

one was found to be flavonoids. Flavonoids inhibit many enzymes including thyroid peroxidase, 5 α -deiodinase, the key enzymes of thyroid hormone synthesis etc [15].

It has been reported that inhibition of Thyroid Peroxidase by dietary flavonoids found that almost all of the flavonoids except flavanone and flavone inhibited tyrosine iodination by thyroid peroxidase, but with markedly different potencies. Consumption of flavonoids by experimental animals reduces both iodide ion uptake and iodide ion incorporation into thyroid hormones. In vitro, several flavonoids reduce iodide ion uptake as well as inhibited TPO dependent iodination [12,16]. These data are consistent with the anti-thyroid effects of flavonoids observed in humans and experimental animals.

Further the findings of toxicity study of extract exhibited extracts failed to produce toxic effects at the dose of 5000 mg/kg body weight. It is safe to use, and dose selected for present study was 250 mg/kg and 500 mg/kg.

The data recorded on thyroid hormone profile in control and Coriander sativum fed rats are presented. The results showed increase in thyroid activity. The TSH level correlated well inversely with T3 and T4 levels. The group which received maximum test dose (500 mg/kg bw) showed maximum percentage increase in hormone concentration of T3 and T4 whereas a maximum percentage decrease in TSH levels was observed when compared to the lower dose levels, which clearly proves that the response was dose effective and Coriander sativum seeds extracts can be used in hypothyroidism condition to normalize hormone levels. Thyroid hormones play important role on growth and development of the body and regulate metabolism. So, with an increase in thyroid activity, marked changes in thyroid hormone production, metabolism and action occur. This may result in an increased prevalence of sub-clinical thyroid disease that is associated with thyroid dysfunction. Many factors can influence the concentration of these hormones and therefore disturb the general body metabolism. This may be due to the high amount of flavonoids present in the leaves of Coriander sativum.

Histopathology studies of thyroid organ of the hyper thyroid instigated and treated rats were considered and were contrasted with control rats. The hyperthyroidism was observed in positive control animals due to increase of colloid in follicular epithelial cells and luminal colloids. The extracted treated animals demonstrated normal follicle lined by follicular epithelial cells. The findings indicate the hydroalcoholic extract of Coriander sativum seeds stimulant to thyroid functions.

CONCLUSION

The outcomes of present study exhibited that hydroalcoholic extract of Coriander sativum seeds can possibly overcome hyperthyroidism in albino rats. Although further investigations are required to reveal the exact mechanism of action(s) of thyroid hormone regulation by Coriander sativum seeds extract. However, the authors emphasize that further studies are required to observe the dose dependent effect of seeds extract which might be effective and safe in improving hypothyroidism levels.

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