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EFFECTS OF AQUEOUS FRUIT EXTRACT OF HARITAKI (*TERMINALIA CHEBULA*) ON REGULATION OF HYPOTHYROIDISM

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ABSTRACT: The thyroid, an important part of the human endocrine system, is involved in the regulation of oxygen use, basal metabolic rate, cellular metabolism, and growth. As it acts as a regulator for the body, abnormalities of the thyroid should be reckoned with, and measures to prevent such occurrences should be followed. Hypothyroidism can be described as the inability of the thyroid gland to produce sufficient thyroid hormone to fulfill the metabolic demands of the body. Usage of medicinal plants and their active compounds for the treatment of diseases has, in recent years, showing a lot of promise in chemotherapy. Also, the lack of major side effects, as observed with the usage of such therapy led to an increase in the people's tendency to use these compounds. In the present study, the effect of aqueous extracts of *Terminalia chebula* fruit on Thyroid parameters in rats during seven-day oral administration of a low dose of 250 mg/kg and a high dose of 500 mg/kg was investigated. The parameters evaluated the ameliorative effect of aqueous fruit extract in the regulation of thyroidism in rat model. The result showed a significant increase in T3 and T4 at the dose of 250 mg/kg and 500 mg/kg body weight when compared to the control. However, TSH showed a significant decrease in the case of both low dose and high dose as compared to the control. The results of this study suggest that the extract may have beneficial effect on stimulants to thyroid functions.

INTRODUCTION: The thyroid, an important part of the human endocrine system, is involved in the regulation of oxygen use, basal metabolic rate, cellular metabolism, and growth [1]. It secretes the hormones thyroxine (T4) and triiodothyronine (T3), which play essential roles in growth and development and determine the basal metabolic rate. The thyroid hormones are secreted into the blood and act at the cellular level through the activation of genes involved in protein synthesis, maturation of the nervous system, and increase the rate of cell respiration in tissues, thus elevating the basal metabolic rate (BMR) [2].

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Consequently, any variations in these hormone levels lead to disturbed BMR and present with certain signs and symptoms leading to thyroid disease. A decrease in the thyroid hormone levels is known as hypothyroidism, which may occur due to multiple reasons including a deficiency in iodine consumption, glandular lesions, autoimmune attacks, and impaired pituitary activity [3, 4].

If left untreated, hypothyroidism has been observed to lead to a wide range of abnormalities, including fatigue sensation, weight gain, dryness of skin, depression and behavioral fluctuations, loss of hair, face swelling, and increased cholesterol [5]. Thyroid disease is one of the most common endocrine disorders worldwide whose incidence increases with increasing age [6]. According to recent data from various studies, 42 million people suffer from thyroid diseases in India alone. About 1 to 2% of the adult population is known to suffer from

thyroid disorders [7]. Thyroid disorders more commonly occur in females as compared to males, with the common prevalence ratio of thyroid diseases being 4:1. The prevalence of hypothyroidism is around 0.3% to 0.4%, which increases with age, and females tend to be more affected [8]. The need for treatment of these disorders has risen in recent years due to its increasing prevalence, with hormone replacement being the primary therapy of choice. However, alternative medicinal approaches are gaining popularity in view of their efficacy with minimal side effects. Medicinal plants have been used throughout human history for the treatment of diseases. Plant-based medicines tend to produce lesser side effects. Medicinal compounds can also be extracted from herbs and spices used as food seasoning [9].

In recent years there has been a tremendous upsurge of interest in medicinal plants, especially those used in Ayurveda, Siddha, Unani, Modern Arnchi, Homeopathy, and Naturopathy. Drugs obtained from plants are believed to be much safer and exhibit a remarkable efficacy in the treatment of various ailments. Human and environmental interactions are prominently affected by folk medicinal traditions [10]. *Terminalia chebula* is one of the oldest known medicinal plant species belonging to the family *Combretaceae* [11]. It is called as 'haritaki' since it is said to carry away all diseases or it is sacred to God Siva (Hari). The fruit of this plant is reported to possess the phytoconstituents responsible for antibacterial, antidiabetic, antioxidant, antidiarrhoeal, anti-carcinogenic, antiarthritic, hepatoprotective, anti-inflammatory and antiviral activities [12-20] like gallic acid, ellagic acid and corilagin [21]. The present communication was designed to explore the impact of fruit extract of *T. chebula* on the Thyroid profile of mammalian animal model male albino rats.

MATERIALS AND METHODS:

Collection of Plant Material: The fresh fruits of *Terminalia chebula* were collected from Ranchi, Jharkhand (India) dried in the shade six to seven days and then crushed into coarse powdery substance by using an electric grinder. The coarse powdery substance was dried again and was then sieved to get fine powder using the fine plastic sieve and stored in an airtight bottle in the laboratory until required [22-24].

Extract Preparation: 50 g of the sieved powder was subjected to extraction in a Soxhlet apparatus at room temperature using ~350 mL distilled water. The extract obtained was filtered, concentrated in the rotary flash evaporator, and maintained at 45 ºC the percentage yield of each extract was calculated [25, 26].

Animals: Male Albino rats (175-200 g) were used in the study. They were maintained under standard laboratory conditions at an ambient temperature of 25 ± 2°C and 50 ± 15% relative humidity with a 12-h light/12-h dark cycle. Animals were fed with a commercial pellet diet and water *ad libitum*.

Acute Toxicity Studies: Acute toxicity studies were determined by using a fixed-dose method according to OECD guidelines. Healthy adult mice, weighing 175-200 g were used.

Twenty albino rats of either sex were used to determine the LD_{50} of the aqueous extract of fruit of *Terminalia chebula*. The animals were randomly divided into two groups of 10 rats, each and administered and observed for 90 days as follows:

Group 1: received 1 ml of distilled water orally.

Group 2: received 250 mg/kg body weight of extract orally.

Group 3: received 500 mg/kg of body weight of extract orally. Mortality was not observed up to 500 mg/kg of body weight in case of aqueous fruit extract of *Terminalia chebula*.

Sample Collection: At the end of each experimental period, the rats were reweighed, starved for 24 h and sacrificed under chloroform anesthesia. 5 mL of blood was collected from each animal by cardiac puncture using a sterile needle and syringe. Part of the blood sample was put into test tubes and allowed to clot for 30 min before centrifuging at 800 g (Wisperfuge, 1384, Samson, Holland) for 5 min. The supernatant was used for lipid analysis. The remaining blood sample was put in an EDTA bottle for hematological determinations.

Analytical Procedure:

Estimation of Thyroid Hormones: Estimation of serum T_3, T_4, and TSH was done by chemiluminescence immunoassay method [27].

Statistical Analysis: All results were expressed as mean ± standard error of the mean (S. E. M). Data was analyzed using one-way ANOVA followed by Dennett's- test, $p<0.05$ was considered as statistically significant.

RESULTS AND DISCUSSION: The effects of oral administration of aqueous extract of *Terminalia chebula* fruit on thyroid indices present in **Table 1** and **Fig. 1-4**. T3- The total triiodothyronine, T4-The total thyroxine count showed a significant increase and TSH. The thyroid stimulating hormone showed a significant decrease in the case of both low dose and high dose (group 2 and group 3 respectively) as compared to the control group 1.

TABLE 1: EFFECT OF *TERMINALIA CHEBULA* EXTRACT ON THYROID PROFILE OF RATS

Parameters	Group 1	Group 2	Group 3
T3 (ng/dl)	31.83 ± 1.213	133.1 ± 2.40[a,d]	114.1±1.70[a,d]
T4 (µg/dl)	2.766 ± 0.110	11.53 ± 0.15[b,b]	11.42 ± 0.11[b,e]
TSH (µIU/ml)	114.6 ± 2.494	4.443 ± 0.12[c,b]	4.725 ± 0.11[c,b]

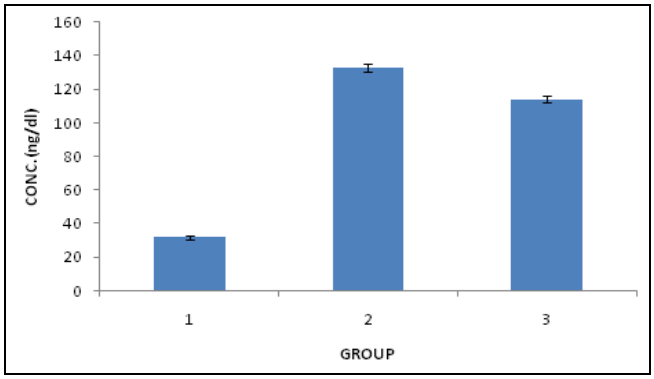

FIG. 1: EFFECT OF FRUIT EXTRACT OF *TERMINALIA CHEBULA* ON T3.

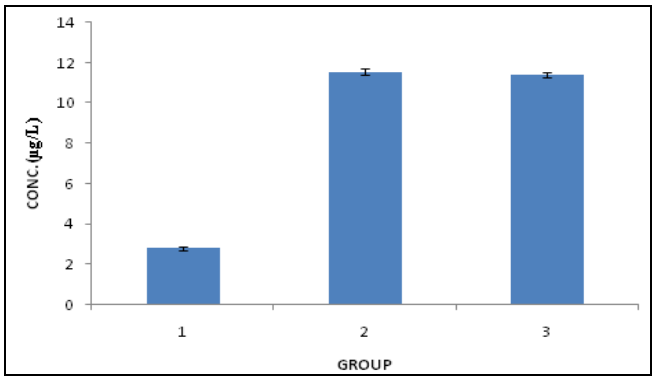

FIG. 2: EFFECT OF FRUIT EXTRACT OF *TERMINALIA CHEBULA* ON T4

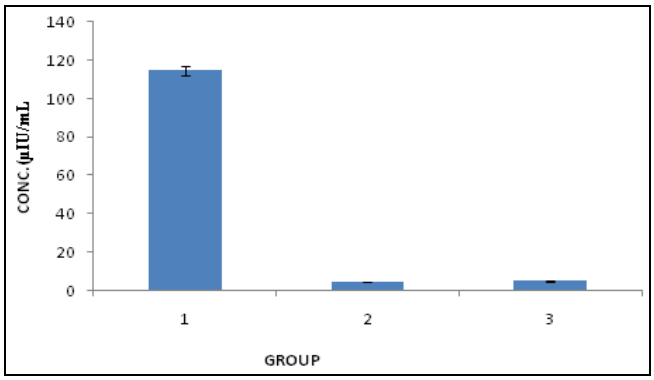

FIG. 3: EFFECT OF FRUIT EXTRACT OF *TERMINALIA CHEBULA* ON TSH

The hormonal activities of the thyroid gland are majorly regulated by the pituitary glycoprotein hormone, thyroid-stimulating hormone (TSH) [28]. Regulation of the levels of TSH is brought about by the hypothalamus as well as by other regulatory mechanisms, resulting in a feedback loop such that on TSH increase, thyroid hormones decrease and vice versa. External factors that modify thyroid hormones include thiocyanate from tobacco, smoke, perchlorate, and drugs, which contain different amounts of iodine and hence, can influence the structure and function of thyroid hormones [29]. The amount of the thyroid hormones T3 (triiodothyronine) and T4 (thyroxine) in the blood plasma are considered a substantive evaluation of thyroid function. The present study was conducted to evaluate the beneficial effect of *T. chebula* extract in the management of hypothyroidism. In this study, it is seen that *T. chebula* extract increases the level of T3 and T4. The TSH level correlated inversely with T3 and T4 levels, which clearly prove *T. chebula* extracts can be used in hypothyroidism. The results observed with various other plant extracts such as Caraway [30] Everyouth Dreamshape [31] and *Ficus carica* leaf extracts [32] was similar to our results. Other studies

have shown that *C. pictus* [33], *Urtica dioica* [34,] and *Crataeva nurvala* [35] extracts can successfully treat experimental hypothyroidism. Similarly, Ashwagandha extracts have shown promise in normalizing thyroid indices in subclinical cases [36].

A recent study has also shown that a combination of ethanolic extract of *Bauhinia variegates* and *Commiphora mukul* gum resin was also capable of reducing methimazole -induced hypothyroidism [37]. Elevated TSH level directly reflects impaired thyroid hormone production [38].

TSH co-relates better with T4 than T3 because while T4 is mainly produced by the pituitary gland, T3 in the blood comprises only 7% secreted T3, and the rest is converted from T4 peripherally. This, in turn, depends on numerous factors including bioavailability of the converting enzyme, namely deiodonase, drugs, diseases in which inactive T3 is formed [39]. The present findings clearly indicate that *T. chebula* extracts are responsible for anti hypothyroidism activity.

CONCLUSION: Using medicinal plants and natural products to treat thyroid dysfunction is invariable necessary to avoid side effects of hormonal therapy. The present study concludes that the fruit extracts of *T. chebula* elevate serum concentration of T3 and T4 in rats at the doses of 250 mg/kg and 500 mg/kg, respectively.

However, we emphasize that further studies are required to identify the precise mechanism of action and isolation of active principle (s) responsible for such activities, which might be effective and safe in ameliorating hypothyroidism.

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CONFLICTS OF INTEREST: The authors declare that there is no conflict of interest regarding the publication of this paper.

Authors' Contribution: Kumari Babli and Tarkeshwar Kumar contributed equally. Both Kumari Babli and Tarkeshwar Kumar carried out the experiment and conceived the original idea. Manoj Kumar verified the analytical methods. M. P. Sinha helped supervise the entire project.

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Ethical Approval: Plant sample of *Terminalia chebula* was identified with the help of the Department of Botany, Ranchi University, Ranchi, Jharkhand. The experiments were performed after prior approval of the study protocol by the institutional animal ethics committee (IAEC no. AEC/RU/28Z), Ranchi University, Ranchi, Jharkhand, India.

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