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Comparative Evaluation Of The Potential Benefits Of Ashwagandha Root And Guggul Gums In Propyl Thiouracil -Induced Hypothyroidism In Female Rats

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ABSTRACT

Hypothyroidism is a common endocrine disorder marked by reduced production of thyroid hormones, leading to various metabolic imbalances. Propylthiouracil (PTU) is frequently employed to experimentally induce hypothyroidism in animal models for the assessment of potential treatments. The present study aimed to comparatively investigate the therapeutic effects of two traditional Ayurvedic herbs, Ashwagandha (Withania somnifera) root extract and Guggul (Commiphora mukul) gum resin, in PTU-induced hypothyroidism in female Wistar rats. The animals were divided into five groups: a normal control group, a hypothyroid control group (PTU-treated), and three treatment groups that received PTU along with either Ashwagandha or Guggul & Standard. Various parameters including lipid profile, serum levels of T3, T4, and TSH, as well as body weight, daily food intake, and blood glucose levels were monitored. The findings revealed that both Ashwagandha and Guggul effectively counteracted PTU-induced disruptions in thyroid hormone levels. However, Ashwagandha-treated rats exhibited more pronounced improvements in thyroid function compared to those treated with Guggul. These results suggest that both herbs possess significant thyroid-supportive properties, and their combined use could be explored as a complementary, natural strategy for managing hypothyroidism.

Keywords: Hypothyroidism, Ashwagandha, Guggul, Propylthiouracil (PTU), Thyroid hormones, T3, T4, TSH, Wistar rats, Herbal therapy.

INTRODUCTION

The thyroid gland, a key organ of the endocrine system, plays an indispensable role in regulating diverse biological processes through the synthesis and release of thyroid hormones. Located anteriorly in the neck and composed of two lobes connected by an isthmus, the gland is characterized by its bilobular structure and butterfly-like appearance. It produces the hormones triiodothyronine (T3) and thyroxine (T4), which are essential regulators of metabolism, growth, thermoregulation, and development [1]. The follicular cells within the gland are primarily responsible for the production of these hormones, synthesizing them from thyroglobulin a glycoprotein stored in colloid within the follicles [2]. Additionally, parafollicular cells (C-cells) secrete calcitonin, a hormone that contributes to the regulation of calcium and phosphate metabolism, further illustrating the gland's integral role in maintaining homeostasis [3].

The synthesis and secretion of thyroid hormones are tightly controlled by the hypothalamic-pituitary-thyroid axis. The hypothalamus secretes thyrotropin-releasing hormone (TRH), which stimulates the anterior pituitary gland to release thyroid-stimulating hormone (TSH). In turn, TSH acts on thyroid follicular cells to enhance iodine uptake, thyroglobulin synthesis, and enzymatic activity required for the production of T3 and T4. This endocrine feedback loop ensures that hormone levels are adjusted according to the body's physiological demands, stress responses, and nutritional status [4].

However, dysfunction of this system can lead to a range of thyroid disorders, with hypothyroidism being among the most prevalent. Hypothyroidism, characterized by insufficient production or secretion of thyroid hormones, slows metabolic activity and affects multiple organ systems. Common causes include autoimmune thyroiditis (such as Hashimoto's disease), iodine deficiency, genetic abnormalities, surgical removal of the gland, radiation exposure, and adverse effects of certain medications [5]. Clinical manifestations include fatigue, weight gain, cold intolerance, dry skin, cognitive impairment, and menstrual irregularities. If untreated, hypothyroidism may result in severe complications such as infertility, cardiovascular issues, neurological dysfunction, developmental delays in infants, and life-threatening myxedema coma [6].

The increasing prevalence of thyroid disorders, coupled with the limitations and side effects of conventional hormone replacement therapies, has spurred renewed interest in complementary and integrative medicine. Among the natural remedies extensively studied for thyroid health are **Ashwagandha** (*Withania somnifera*) and **Guggul gum** (*Commiphora wightii*), both of which have been used in Ayurvedic medicine for thousands of years [7].

Ashwagandha

Commonly referred to as Indian ginseng or Indian winter cherry, Ashwagandha is renowned for its adaptogenic properties that enhance the body's resilience to stress and disease. Rich in bioactive constituents such as withanolides, alkaloids, flavonoids, and steroidal lactones, it exhibits neuroprotective, anti-inflammatory, antioxidant, and immunomodulatory effects [8]. Modern research suggests that Ashwagandha may help regulate thyroid hormone levels by influencing TSH secretion and supporting the synthesis of T3 and T4. It is particularly beneficial in cases of subclinical hypothyroidism and has been shown to improve glucose metabolism, reduce oxidative stress, and enhance cognitive function. Withaferin A, one of its major components, is also noted for its potential anticancer and antioxidant properties, which may normalize thyroid function and prevent cellular damage [9].

Guggul Gum

Guggul, the resin obtained from *Commiphora wightii*, has a storied history in Indian medicine, where it has been used to treat metabolic and inflammatory disorders. The resin contains a diverse array of phytochemicals, including guggulsterones, diterpenoids, triterpenoids, and steroids, which contribute to its therapeutic potential. Guggul's hypolipidemic effects have been widely recognized, with clinical studies showing its ability to lower cholesterol levels and support cardiovascular health [10]. Additionally, guggul exhibits thyroid-stimulatory activity by enhancing iodine uptake and promoting enzyme function in thyroid hormone synthesis. It is also studied for its anti-inflammatory, anticancer, immunomodulatory, and antioxidant effects, offering broad-spectrum support for metabolic and immune health [11].

Rationale for Integration

The therapeutic potential of Ashwagandha and Guggul in thyroid disorders lies not only in their individual properties but also in their ability to address the multifactorial nature of thyroid dysfunction. Their roles in modulating immune responses, reducing oxidative stress, supporting metabolic pathways, and influencing hormonal synthesis make them promising adjuncts in the management of hypothyroidism and related conditions. Furthermore, their relatively lower side-effect profile compared to conventional pharmaceuticals supports their inclusion in integrative treatment protocols.

This research aims to synthesize current scientific findings on the physiological role of the thyroid gland, the pathogenesis and complications of hypothyroidism, and the pharmacological benefits of Ashwagandha and Guggul in promoting thyroid health. By bridging traditional knowledge with contemporary biomedical research, this work seeks to provide clinicians and researchers with a deeper understanding of how natural agents can complement conventional therapies and contribute to holistic management strategies for thyroid disorders.

MATERIALS AND METHODS

Chemicals

S.No	Chemical name	Company
1	PTU	YUCCA Enterprises
2	Ashwagandha	YUCCA Enterprises
3	Guggul gums	YUCCA Enterprises
4	Levothyroxine	YUCCA Enterprises

Animals

Female Wistar albino rats weighing about 150-250g procured from VAB BIOSCIENCES, Ghatkesar, Hyderabad. Rats were housed in stainless steel cages on husk bedding at a temperature of 25°C ± 3°C and humidity (40% ± 5%) with 12 h light/12 h dark cycle. The animals were maintained on a standard laboratory diet and offered a constant supply of clean drinking water [12]. All procedures involved in animal housing, handling, and experimentation adhered to a protocol approved by the Institutional Animal Ethics Committee of SNVPMV. [IAEC NO. SNVP/1/2025/PC/40].

Experimental design:

Rats were randomly divided into five groups of six animals in each group; food was withdrawn 12 hrs. Before PTU administration.

Table 4.1.3 Experimental Design

S.No	Groups	Treatment	Dose & R.O. A
1	Group 1	Saline	1ml & P. O
2	Group 2	PTU	10mg/kg & P. O
3	Group 3	PTU + Leothyroxine	10mg/kg + 0.2 mg/kg & P. O
4	Group 4	PTU + Ashwagandha	10mg/kg + 200 mg/kg & P. O
5	Group 5	PTU + Guggul gums powder	10mg/kg + 200 mg/kg & P. O

Collection of Blood:

Blood collection from rats via the retro-orbital route involves anesthetizing the rat and gently inserting a sterile capillary tube at the medial canthus behind the eyeball to access the retro-orbital sinus. Blood is drawn by capillary action, after which pressure is applied to stop bleeding. The rat is then monitored until full recovery.

Evaluation of biochemical parameters

The study was conducted for 28 days, weekly once the animal's body weight, and daily food intake by the animal was measured. On 29th day blood was collected and centrifuged to separate serum for the following biochemical parameters .Blood Glucose level,serum lipid profile (Total cholesterol, HDL cholesterol, LDL cholesterol and triglycerides), Thyroid profile (T3, T4 & TSH) was analysed [13].

Measurement of body weight:

The body weight of each female Wistar rat was measured using a digital electronic balance with an accuracy of ±0.1 g. Measurements were taken prior to the commencement of dosing (baseline) and subsequently weekly or depending on the study design animals were measured. Body weight data was calculated to monitor the general health and physiological response of the animals during the study. Any significant changes in body weight were noted and evaluated in relation to treatment effects

Estimation of Blood Glucose levels:

Blood glucose levels in rats were measured using a Dr.Morepen digital glucometer, with blood samples obtained via retro orbital route using a sterile lancet. Measurements were conducted at baseline and at specific intervals following treatment to monitor changes over time. For fasting blood glucose estimation, rats were deprived of food for 10–12 hours while maintaining free access to water to prevent dehydration. Glucose concentrations were recorded in mg/dL, allowing for evaluation of the treatment's effect on glucose homeostasis.

Estimation of thyroid profile

T3 and T4 levels were determined in serum using the T3 and T4 enzyme-linked fluorescent immunoassay kits (VIDAS®) on the last day of the experiment. The analysis was performed at Yoda diagnostics, Miyapur, hyderbad.

Estimation of Lipid Profile

In female rats, hypothyroidism is commonly induced using antithyroid drugs like propylthiouracil (PTU), typically administered in drinking water. After treatment, blood is collected and serum lipid profiles including total cholesterol (TC), triglycerides (TG), LDL-C, HDL-C, and VLDL. The analysis was performed at Yoda diagnostics, Miyapur, hyderabad.

RESULTS

Table : 1 Effect of Ashwagandha and Guggul gums on Lipid profile

Groups	CHL mg/dl	HDL mg/dl	LDLmg/dl	TG mg/dl
Normal	78 ±1.414	53.33±1.76	13.16 ±1.249	79.66 ±4.6
Positive	89.8 ± 6.296#	38.33 ±1.66#	26 ± 2.366##	109.33 ±4.27##
Standard	70.6 ±7.501	52.66±4.12*	13± 2.280**	79.5 ±2.17*
Ashwangandha	62.8 ±2.267*	44.66 ± 5.78*	24.66 ± 2.140	43.33 ± 4.04**
Guggul gums	79.5 ± 5.046	51.16 ± 3.78*	22.16± 1.939	42.166 ± 1.16**

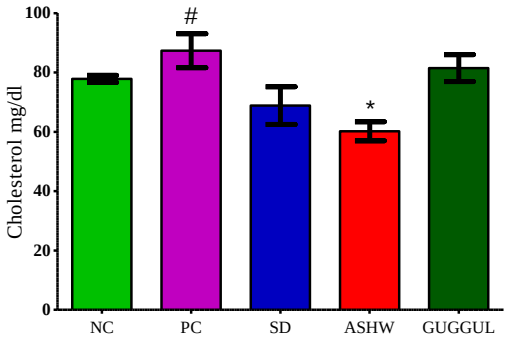


Figure 1: Effect of Ashwagandha and Guggul gums on Cholestrol mg/dl

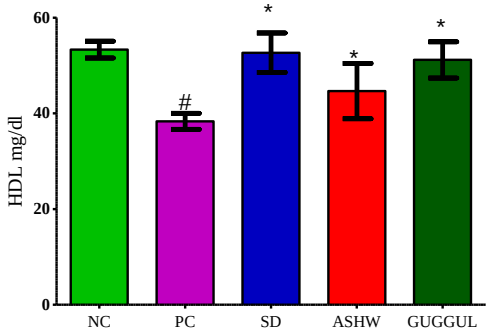
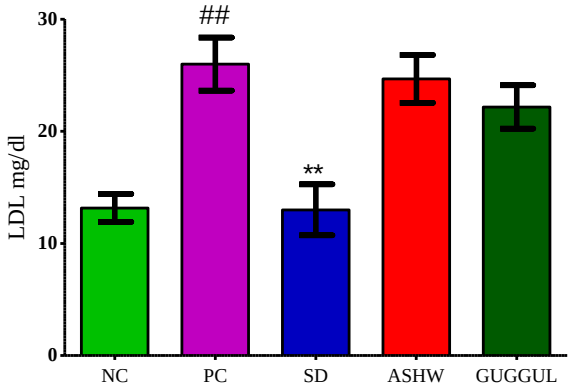
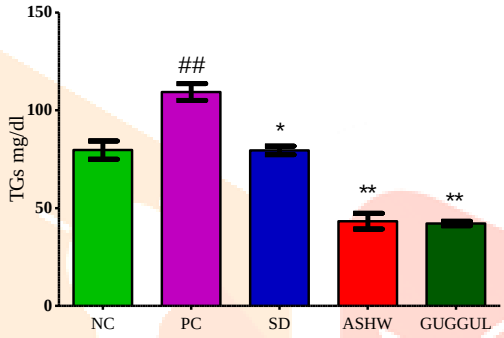


Figure 2: Effect of Ashwagandha and Guggul gums on HDL mg/dl



Effect of Ashwagandha and Guggul gums on LDL mg/dl



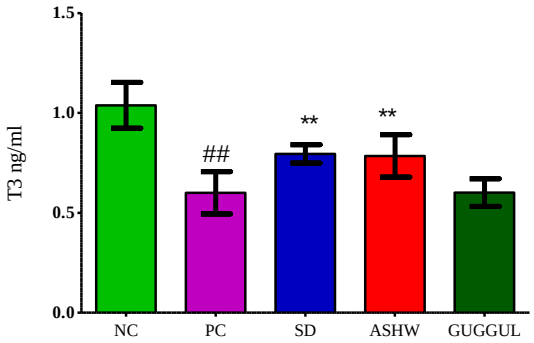
Effect of Ashwagandha and Guggul gums on TGs mg/dl

Each value represents mean ±SD. Data was analyzed by using ANOVA followed by Dunnett's multiple comparison test. Positive control was compared with other groups *** represents p<0.0001, ** indicates p<0.001, * indicates p<0.01, d indicates p<0.05.

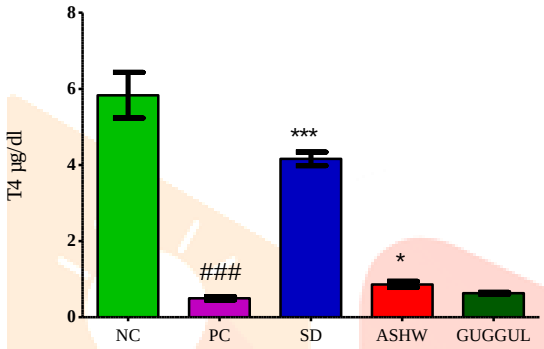
Effect of Ashwagandha and Guggul gums on thyroid profile:

Table 5.2 Effect of Ashwagandha and Guggul gums on thyroid profile

Groups	T3	T4
Normal	1.03±0.11	5.83± 0.60
Positive	0.6 ±0.10##	0.49 ± 0.04###
Standard	0.7 ± 0.04**	4.16± 0.17***
Ashwangandha	0.78 ±0.10**	0.61± 0.02*
Guggul gums	0.60 ± 0.06	0.6 ± 0.02



Effect of Ashwagandha and Guggul gums on T3 ng/dl



Effect of Ashwagandha and Guggul gums on T4 ug/dl

Each value represents mean ±SD. Data was analyzed by using ANOVA followed by Dunnett's multiple comparison test. Positive control was compared with other groups *** represents $p<0.0001$, ** indicates $p<0.001$, * indicates $p<0.01$, d indicates $p<0.05$.

Body weight:

Table 5.3 Effect of Ashwagandha and Guggul gums on Body weight

Groups	Body Weight
Normal	189.25± 3.250
Positive	177.5± 6.357
Standard	177± 3.109
Ashwangandha	160.25± 4.768
Guggul gums	168.5± 6.357

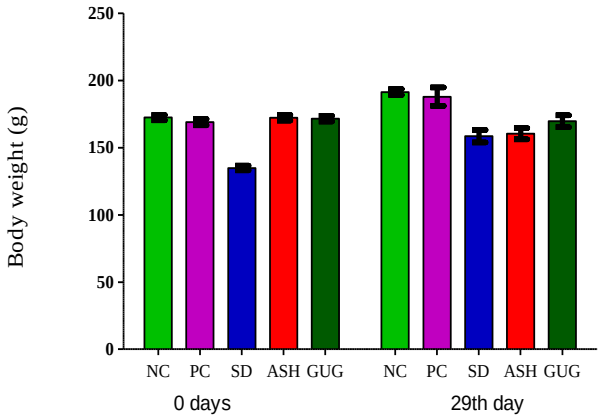


Fig 5.3 Effect of Ashwagandha and Guggul gums on Body weight

Blood Glucose Levels:

Effect of Ashwagandha and Guggul gums on Blood Glucose Levels

Groups	Blood Glucose Level
Normal	101.4± 2.600
Positive	120.8±3.040##
Standard	103.2±1.463**
Ashwangandha	88.2± 2.871**
Guggul gums	115.6±3.586

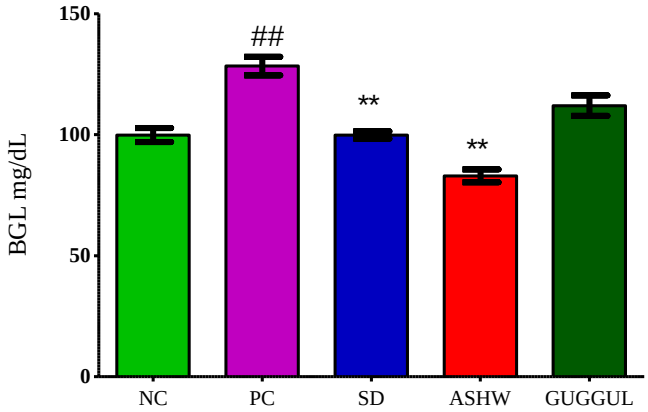


Fig 5.4 Effect of Ashwagandha and Guggul gums on Blood Glucose Levels

Each value represents mean ±SD. Data was analyzed by using ANOVA followed by Dunnett's multiple comparison test. Positive control was compared with other groups *** represents $p<0.0001$, ** indicates $p<0.001$, * indicates $p<0.01$, d indicates $p<0.05$.

DISCUSSION

This study aimed to compare the therapeutic potential of Ashwagandha (*Withania somnifera*) and Guggul (*Commiphora mukul*) in an experimental model of hypothyroidism and metabolic disturbances. The findings demonstrate that both herbs possess significant beneficial effects, with Ashwagandha showing greater efficacy across multiple parameters.

Lipid Profile

The positive group exhibited marked dyslipidemia, characterized by elevated total cholesterol, triglycerides, and LDL, along with reduced HDL. These alterations confirm the successful induction of metabolic disturbances. Ashwagandha treatment significantly improved the lipid profile by reducing CHL, LDL ($p<0.01$), and TG ($p<0.001$), while enhancing HDL ($p<0.01$), consistent with its reported hypolipidemic and antioxidant effects [14,15]. Guggul also showed improvements, especially in TG and HDL levels, ($p<0.01$), which align with previous findings regarding its bile acid-enhancing and lipolytic properties [16]. The superior lipid-lowering effect of Ashwagandha suggests a broader systemic impact, possibly through enhanced hepatic lipid metabolism and oxidative stress reduction.

Thyroid Profile

The hypothyroid model was validated by decreased levels of T3 and T4. Ashwagandha effectively restored both hormones, suggesting stimulation of thyroid hormone synthesis via antioxidant-mediated mechanisms, as previously described [17]. Guggul, while significantly improving T4 levels, showed limited efficacy in enhancing T3, possibly due to insufficient stimulation of peripheral conversion or shorter treatment duration [18]. Standart drug is showing more significant increase in T4 ($p<0.0001$)These results reinforce Ashwagandha's role as a potent thyroid modulator and highlight the need for further exploration of Guggul's dose-dependent effects($p<0.001$).

Body Weight

A reduction in body weight across treatment groups reflects disease-associated metabolic dysfunction. Ashwagandha-treated animals showed greater weight loss, which may be attributed to its adaptogenic and thermogenic properties that enhance metabolism and fat utilization [19]. Guggul also promoted weight reduction, though to a lesser extent, likely through stimulation of lipolysis mediated by guggulsterones.

While weight loss is therapeutically beneficial in obesity, in hypothyroid models it likely indicates metabolic modulation rather than adverse wasting.

Blood Glucose Levels

Elevated glucose in the disease model suggests stress- or disease-induced hyperglycemia. Ashwagandha's ability to reduce glucose levels even below baseline confirms its hypoglycemic activity ($p<0.001$), possibly by enhancing insulin sensitivity and glucose uptake [20]. Guggul's modest glucose-lowering effect indicates limited antidiabetic potential in this model, requiring further investigation regarding dosage and duration. The standard treatment normalized glucose levels, validating the experimental model ($p<0.001$).

Overall Implications

The comparative analysis highlights that while both Ashwagandha and Guggul improve metabolic and thyroid-related dysfunctions, Ashwagandha demonstrates superior efficacy in restoring hormonal balance and managing lipid and glucose abnormalities. These findings support its potential as a natural adjunct in hypothyroidism management. Guggul's partial response suggests that optimized dosing or combination therapy may enhance its effectiveness.

Future Directions

Given the synergistic potential of both herbs, future studies should explore their combined administration to achieve more comprehensive therapeutic effects. Additionally, investigations into long-term outcomes, molecular mechanisms, and clinical translation will further clarify their role in endocrine and metabolic health.

CONCLUSION

The present study confirms that Ashwagandha (Withania somnifera) is more potent than Guggul gum (Commiphora mukul) in modulating metabolic and endocrine disturbances in a disease-induced model. Ashwagandha exhibited greater efficacy in improving lipid profile, enhancing thyroid hormone levels, reducing hyperglycemia, and normalizing body weight, likely due to its antioxidant, anti-inflammatory, and adaptogenic constituents such as withanolides. In contrast, Guggul gum showed moderate benefits in thyroid function and glucose regulation but effectively improved HDL levels and lipid metabolism through guggulsterones influencing nuclear receptors. These results support the traditional use of both herbs in managing hypothyroidism, dyslipidemia, diabetes, and metabolic disorders, while emphasizing Ashwagandha's superior therapeutic potential. Further molecular studies, long-term safety evaluations, and clinical trials are needed to validate these findings and explore combinatorial therapies. Overall,

Ashwagandha and Guggul gum offer promising natural interventions, with Ashwagandha providing a stronger effect in restoring metabolic and endocrine homeostasis.

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AUTHORS CONTRIBUTIONS

Designing the study, Planning the research, carrying out the project, and writing the manuscript: P. Rajyaakshmi Devi & M. Sreekanth, Statistical analysis: Bhargavi, Lohitha, Zeenath: Biochemical evaluation & Manuscript drafting: Mote Srinath,. All authors have read and agreed to the published version of the manuscript.

CONFLICT OF INTERESTS

There are no conflicts of interest to disclose in this research.

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