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Comparative Effects of Brazil Nut (Bertholletia excelsa) and Levothyroxine on Selenium Status and Thyroid Peroxidase Activity in Male Albino Rats with Experimentally Induced Hypothyroidism

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ABSTRACT

This study investigated the therapeutic potential of Brazil nut (Bertholletia excelsa) supplementation, a rich natural source of selenium (Se), in a rat model of carbimazole (CBZ)-induced hypothyroidism, comparing its effects to standard levothyroxine therapy. Thirty-five adults male Wistar rats were used. Hypothyroidism was induced by administering CBZ (30 mg/kg/day, p.o.) for 22 days and confirmed via significant reductions in serum triiodothyronine (T_3) and thyroxine (T_4) and an elevation in thyroid-stimulating hormone (TSH). Subsequently, hypothyroid rats were divided into groups receiving either vehicle, Brazil nut powder (9.42 g/kg/day, p.o., providing ~290 µg Se/kg/day), or levothyroxine (20 µg/kg/day, p.o.) for 30 days, alongside healthy controls .Brazil nut supplementation significantly ameliorated the hypothyroid state, as evidenced by the restoration of serum T_3 and T_4 levels and the normalization of TSH in treated animals (HBN group). This effect was comparable to that achieved with levothyroxine. Importantly, CBZ-induced hypothyroidism led to a significant depletion of selenium levels in both serum and thyroid tissue. Brazil nut treatment effectively restored these selenium reserves. Immunohistochemical analysis revealed severe suppression of thyroid peroxidase (TPO) enzyme expression in hypothyroid rats, which was markedly improved by both Brazil nut and levothyroxine interventions .The findings demonstrate that Brazil nut supplementation effectively counteracts CBZ-induced hypothyroidism, normalizes thyroid hormone profiles, restores systemic and tissue selenium status, and enhances the immunohistochemical expression of the key thyroid enzyme TPO. These results suggest that Brazil nut, via its high bioavailable selenium content and associated antioxidant properties, represents a promising nutritional adjunct for managing hypothyroidism and mitigating associated oxidative stress and selenoprotein impairment.

1- Introduction

The endocrine system comprises a complex network of glands that control a majority of bodily functions within the body and metabolic routes by producing and releasing different hormones [1]. These hormones exert diverse physiological and structural effects by synthesizing proteins proteins and enzymes inside the cell, stimulate the cell division, influence the cell membrane permeability and either activate or inhibit the enzymes [2]. The thyroid gland is one of these glands, and it is important because it secretes hormones Triiodothyronine (T 3) and Thyroxine (T 4), which are vital in the regulation of several physiological processes and pathways such as metabolism and growth [3]. These hormones are also involved in cell differentiation and metabolism and they play a role in the metabolism of carbohydrates, fats, and proteins in most of the target tissues [4].

Some of the disorders that can involve the thyroid glands are hyperthyroidism and hypothyroidism [5]. Hypothyroidism is characterized by deficient secretion or reduced tissue activity of thyroid hormones (T 4 and T 3) [6]. It can be hereditary, acquired, or drug-induced. Congenital hypothyroidism (CHI) results from is developed due to genetic malformations or mutations within the development or production or functioning of the thyroid tissue [7]. Autoimmune diseases, radiotherapy, surgery of thyroidectomy [8], and iodine deficiency in the diet are some of the purchased causes [9]. Drugs are able to induce hypothyroidism either by interfering with thyroid hormone synthesis or secretion such as iodides, lithium, propylthiouracil, thioracil and methimazole [10,11].

Hypothyroidism requires a hormone characterization in order to rectify the physiological functions. The first type of hypothyroidism therapy implies that natural thyroxine is replaced with Synthetic L-thyroxine, that relies on the peripheral conversion into Triiodothyronine (FT3), the active hormone [12]. However, the adverse health effects may happen because of repeated usage, including the emergence of osteoporosis [13,14].

Phytotherapy products are also prescribed as preventive or curative to side effects of chemotherapy which is used in the treatment of various diseases including endocrine disorders [15]. They contain Brazilian nuts (Bertholletia excelsa) whose research has revealed that it provides a good source of bioactive compounds such as antioxidants, phenolic compounds, unsaturated fatty acid, amino acid, minerals (e.g., magnesium and selenium) and dietary fiber [16]. These substances are anti-inflammatory, antioxidant and immune-stimulating, and they have a protection and curative effect [17].

Phytotherapeutic agents are also investigated for their potential to mitigate disease processes, including endocrine disorders. We hypothesized that Brazil nut administration would ameliorate hypothyroid status by restoring serum and tissue selenium levels, thereby supporting the restoration of thyroid hormone profiles and protecting thyroid morphology and function, as assessed through TPO immunohistochemistry. The effects were systematically compared with those of standard levothyroxine therapy to explore the potential of Brazil nuts as a nutraceutical adjunct in thyroid management [18-21].

2. Materials and Methods

2.1. Brazil Nut Preparation and Dosage

Dried Brazil nuts (*Bertholletia excelsa*) were purchased from a local market in Al-Qadisiyah Governorate, Iraq. The nuts were shelled, and kernels were ground into a fine, homogeneous powder using a commercial food processor. The powder was sieved (mesh size: 500 µm) to ensure uniformity and stored in airtight, light-protected containers at room temperature (25 ± 2°C) until use. The dosage of Brazil nut powder was calculated based on its known high selenium (Se) content. A target dose of 290 µg Se/kg body weight/day was selected, corresponding to a nut powder dose of 9.42 g/kg body weight/day, as established in prior studies demonstrating its efficacy in restoring selenium status without toxicity [22,23]. A fresh aqueous suspension was prepared daily by homogenizing the weighed powder in distilled water for oral gavage.

2.2. Experimental Animals and Ethical Considerations

Thirty-five adult male albino rats (*Rattus norvegicus*, Wistar strain), aged 10-11 weeks and weighing 170-200 g, were procured from the animal breeding unit of the College of Veterinary Medicine, University of Kufa. Animals were group-housed (3-4 per cage) in polypropylene cages with sterile paddy husk bedding in a controlled environment: temperature (22 ± 2°C), humidity (55 ± 10%), and a 12-hour light/dark cycle. They were fed a standard commercial pelleted diet (selenium content: ~0.15-0.2 mg/kg) and water *ad libitum*. All animals underwent a two-week acclimatization period prior to the start of experiments. The study protocol was reviewed and approved by the Institutional Animal Ethics Committee of the University of Al-Qadisiyah, and all procedures adhered to the guidelines for the care and use of laboratory animals.

2.3. Experimental Design and Induction of Hypothyroidism

The study was conducted in two sequential phases.

Phase 1: Induction and Validation of Hypothyroidism.

Twenty-nine rats were randomly assigned to receive carbimazole (CBZ), a thyroid peroxidase inhibitor, to induce hypothyroidism. CBZ (Sigma-Aldrich) was dissolved in 1% carboxymethyl cellulose (CMC) and administered via oral gavage at a dose of 30 mg/kg body weight/day for 22 consecutive days [24]. A control group (n=5) received an equivalent volume of the 1% CMC vehicle. At the end of this phase, all animals were fasted overnight and anesthetized with an intraperitoneal injection of ketamine/xylazine (80/10 mg/kg). Blood was collected via cardiac puncture, and serum was separated by centrifugation (3000 × g, 15 min, 4°C). Serum levels of triiodothyronine (T_3), thyroxine (T_4), and thyroid-stimulating hormone (TSH) were quantified using commercially available enzyme-linked immunosorbent assay (ELISA) kits (Cloud-Clone Corp., USA). Successful induction was confirmed by a significant decrease in T_3/T_4 and a compensatory increase in TSH in the CBZ-treated group compared to the control ($p < 0.01$).

Phase 2: Therapeutic Intervention.

The hypothyroid animals from Phase 1 were allowed a 3-day washout period without CBZ to stabilize. They were then re-randomized, along with a group of healthy rats, into five experimental groups (n=8 per group) for a 30-day treatment period as follows:

- **Group I (Normal Control, NC):** Healthy rats receiving vehicle (1% CMC, 1 mL/kg/day, p.o.).
- **Group II (Brazil Nut Control, BNC):** Healthy rats receiving Brazil nut suspension (9.42 g/kg/day, p.o.).
- **Group III (Hypothyroid Control, HC):** Hypothyroid rats receiving vehicle (1% CMC, 1 mL/kg/day, p.o.).
- **Group IV (Hypothyroid + Brazil Nut, HBN):** Hypothyroid rats co-administered CBZ (30 mg/kg/day, p.o.) and, one hour later, Brazil nut suspension (9.42 g/kg/day, p.o.).

- **Group V (Hypothyroid + Levothyroxine, HL):** Hypothyroid rats treated with Levothyroxine sodium (Merck) at a dose of 20 µg/kg/day, dissolved in distilled water and administered orally [25].

Body weight and general health were monitored weekly.

2.4. Sample Collection and Analytical Procedures

At the end of the 30-day treatment period, all animals were fasted overnight, anesthetized, and euthanized by exsanguination.

2.4.1. Biochemical Analysis

Blood was collected, and serum was prepared as described. Serum T_3, T_4, and TSH levels were re-assayed using ELISA. Serum selenium concentration was determined using graphite furnace atomic absorption spectrometry (GFAAS, PerkinElmer PinAAcle 900T) following established wet-digestion protocols [26].

2.4.2. Tissue Sampling and Selenium Assay

The thyroid gland was carefully dissected, cleared of connective tissue, and weighed. One lobe was snap-frozen in liquid nitrogen and stored at -80°C for selenium analysis. Tissue selenium was measured by GFAAS after nitric acid/perchloric acid digestion [26]. Results were expressed as µg Se per gram of wet tissue.

2.4.3. Immunohistochemical Analysis

The contralateral thyroid lobe was fixed in 10% neutral buffered formalin for 24 hours, processed, and embedded in paraffin. Sections (5 µm thick) were mounted on poly-L-lysine-coated slides. Immunohistochemical staining for Thyroid Peroxidase (TPO) was performed using a standard streptavidin-biotin-peroxidase complex method. Briefly, sections were deparaffinized, subjected to antigen retrieval (citrate buffer, pH 6.0), and incubated with a primary monoclonal anti-TPO antibody (e.g., Abcam, ab215647, 1:200 dilution). Detection was achieved using a labeled polymer HRP system (Dako Envision^{+}) with 3,3'-diaminobenzidine (DAB) as the chromogen. Sections were counterstained with Mayer's hematoxylin. Staining intensity and distribution in follicular epithelial cells were evaluated semi-quantitatively by a blinded observer using a light microscope (Olympus BX53) and image analysis software (ImageJ, NIH).

2.5. Statistical Analysis

All data are presented as mean ± standard deviation (SD). Statistical analysis was performed using GraphPad Prism software (Version 10.0). Normality of distribution was assessed using the Shapiro-Wilk test. For multiple comparisons, one-way analysis of variance (ANOVA) was employed, followed by Tukey's post-hoc test for pairwise comparisons. A p-value of less than 0.05 was considered statistically significant.

3-Results

3.1 .Serum Thyroid Hormone Profiles

The induction of hypothyroidism via carbimazole (CBZ) was confirmed by significant alterations in serum thyroid hormone levels (Table 1). Rats in the hypothyroid control group (HC) exhibited a marked reduction in both triiodothyronine (HBN) and thyroxine (HL) concentrations alongside a compensatory elevation in thyroid-stimulating hormone (TSH), compared to the euthyroid negative control group (C) ($p<0.05$ for all). Therapeutic intervention with Brazil nut suspension (Group HBN) effectively ameliorated this condition, resulting in significant increases in HBN and HL and a concomitant decrease in TSH relative to the untreated hypothyroid group (BNC) ($p<0.05$). Notably, TSH levels in the Brazil nut-treated hypothyroid group

(HBN) were restored to levels statistically indistinguishable from the euthyroid control (NC) ($p>0.05$). Similarly, standard levothyroxine therapy (Group HL) normalized the thyroid hormone profile, showing significantly elevated HBN/HL and suppressed TSH compared to group HC ($p<0.05$). No statistically significant difference was observed between the therapeutic efficacy of Brazil nuts (HBN) and levothyroxine (HL) on final hormone levels ($p > 0.05$). Administration of Brazil nuts alone to healthy rats (Group BNC) did not disrupt thyroid homeostasis, as hormone levels remained comparable to the normal control (C) ($p > 0.05$).

Table (1) illustrates the effect of Brazilian nut and thyroxine on thyroid hormones HBN, HL, and thyroid-stimulating hormone (TSH) levels in male albino rats with CBZ-induced hypothyroidism.

Parameter / Groups	T3 (µIU/mL)	T4 (µIU/mL)	TSH (µIU/mL)
NC	1.80 ± 0.04 [a]	40.06 ± 3.20 [a]	0.007 ± 0.001 [b]
BNC	1.82 ± 0.04 [a]	39.34 ± 0.72 [a]	0.011 ± 0.005 [b]
HC	1.19 ± 0.06 [c]	19.52 ± 0.71 [c]	0.102 ± 0.009 [a]
HBN	1.61 ± 0.12 [b]	29.79 ± 1.25 [b]	0.008 ± 0.004 [b]
HL	1.64 ± 0.06 [b]	31.12 ± 0.92 [b]	0.014 ± 0.009 [b]
LSD (P < 0.05)	0.096	2.21	0.0091

- Values represent means ± standard error.
- Similar letters in the same column indicate no significant difference at the 5% significance level.
- Different letters in the same column indicate significant differences at the 5% significance level.

3.2 .Selenium Status in Serum and Thyroid Tissue

Hypothyroidism induced by CBZ (Group HC) led to a significant depletion of selenium in both the serum and thyroid tissue compared to all other groups ($p<0.05$; Table 2). Brazil nut supplementation in healthy animals (NC) maintained selenium levels comparable to the normal control (NC) ($p>0.05$), while therapeutic administration to hypothyroid rats (Group HBN) partially but significantly restored selenium concentrations in both compartments relative to the hypothyroid control (HC) ($p<0.05$). Levothyroxine treatment (Group HL) also resulted in a significant recovery of selenium levels compared to group HC ($p<0.05$), although the restoration in thyroid tissue was less pronounced than that achieved with Brazil nut supplementation (HBN) ($p<0.05$). The highest selenium levels in thyroid tissue were observed in the Brazil nut-only group (BNC).

Table (2) shows the effect of Brazilian nut and thyroxine on selenium levels in serum and thyroid tissue in male albino rats with CBZ-induced hypothyroidism.

Parameter / Groups	Selenium (serum) (µmol/L)	Selenium (tissue) (µmol/L)
NC	3.752 ± 0.53 a	5.65 ± 0.50 a b
BNC	4.251 ± 0.41 a	6.04 ± 0.27 a
HC	2.352 ± 0.16 c	3.928 ± 0.24 d
HBN	2.992 ± 0.22 b	5.4 ± 0.29 b c
HL	3.184 ± 0.42 b	4.64 ± 0.67 c
LSD (P < 0.05)	0.580	0.496

"The same information mentioned below Table (1)."

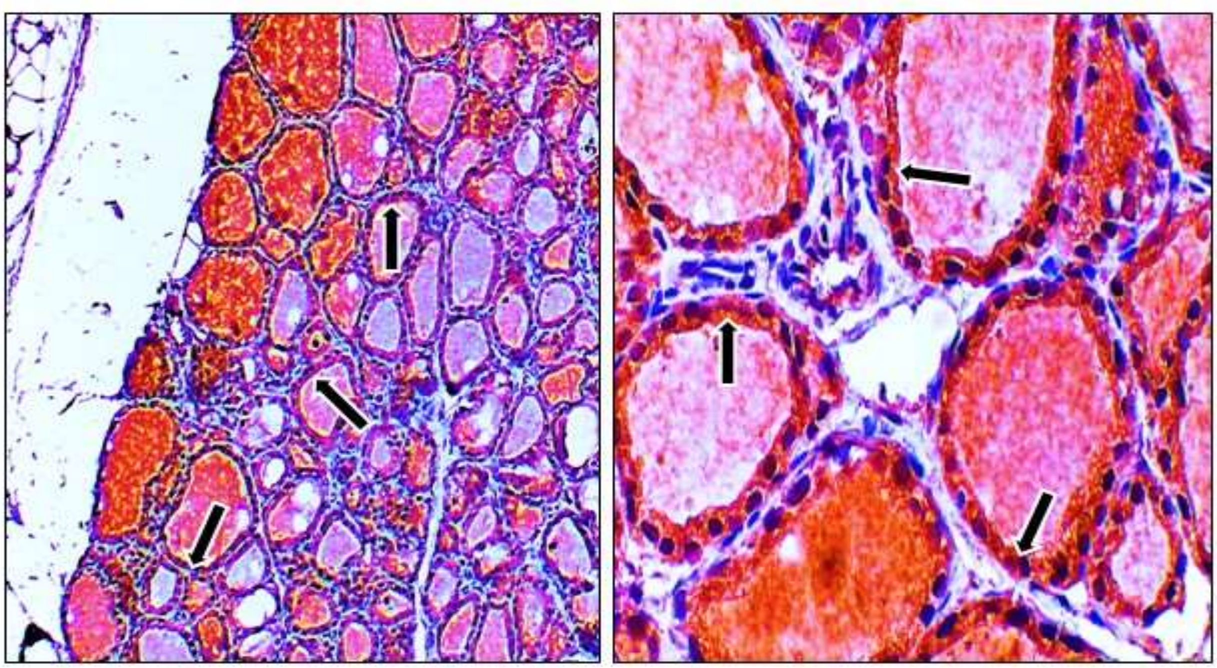
3.3. Thyroid Peroxidase (TPO) Immunohistochemical Expression

Immunohistochemical analysis of thyroid peroxidase (TPO) expression revealed profound changes across experimental groups (Table 3, Figure 1). Strong cytoplasmic immunoreactivity for TPO was observed in the follicular epithelial cells of both the normal control (NC) and Brazil nut-only (BNC) groups, indicating high basal enzyme expression. In contrast, thyroid tissues from the CBZ-induced hypothyroid group (HC) exhibited dramatically weak TPO immunostaining, confirming the direct inhibitory action of carbimazole on this critical enzyme. Therapeutic intervention with Brazil nuts (Group HBN) substantially reversed this suppression, resulting in strong TPO immunoreactivity that was significantly greater than in the hypothyroid control (HC) and levothyroxine-treated (HL) groups ($p<0.05$). Levothyroxine treatment (HL) itself led to a significant, though intermediate, recovery of TPO expression compared to the hypothyroid group (HC) ($p<0.05$).

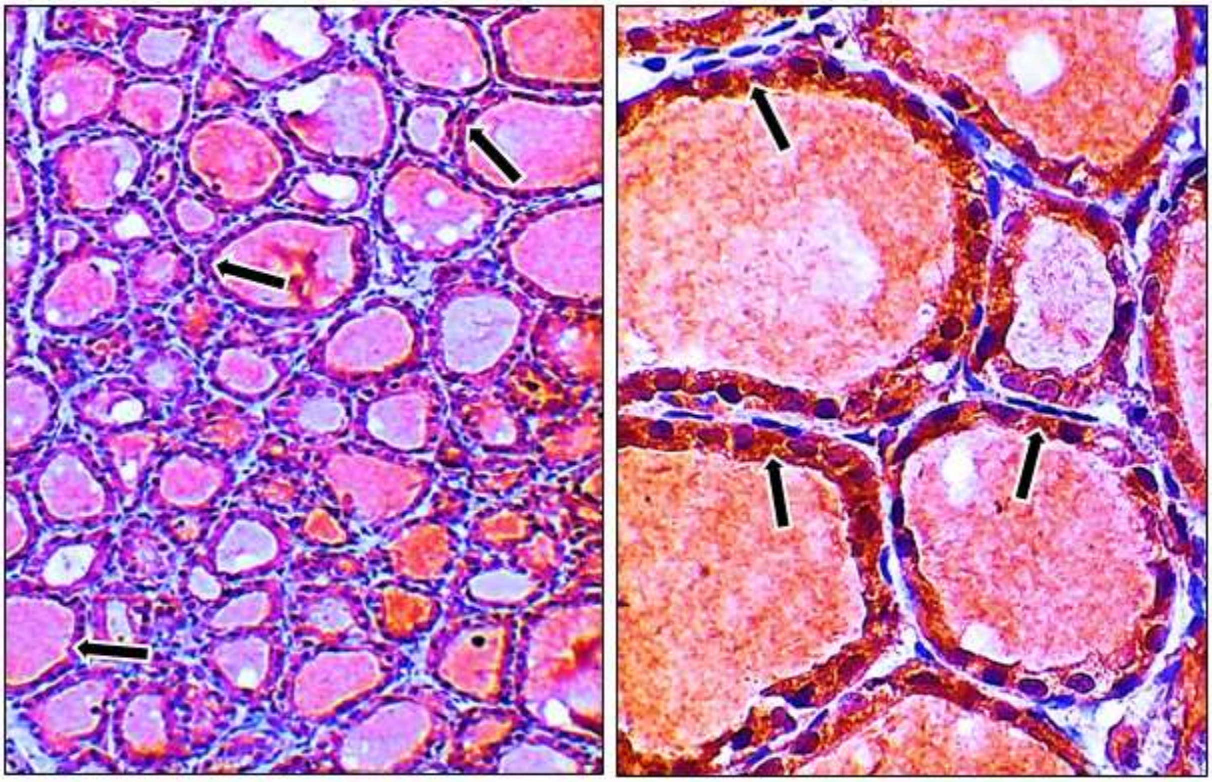
Table (3): Effect of Brazilian Nut and Thyroxine on TPO Enzyme Expression Levels in Thyroid Tissue of Male Rats with CBZ-Induced Hypothyroidism

Parameter / Groups	TPO Expression Score (%)
NC	11.24 ± 0.23 a
BNC	11.40 ± 0.54 a
HC	2.64 ± 0.58 d
HBN	9.08 ± 0.70 b
HL	7.62 ± 0.75 c
LSD	0.784

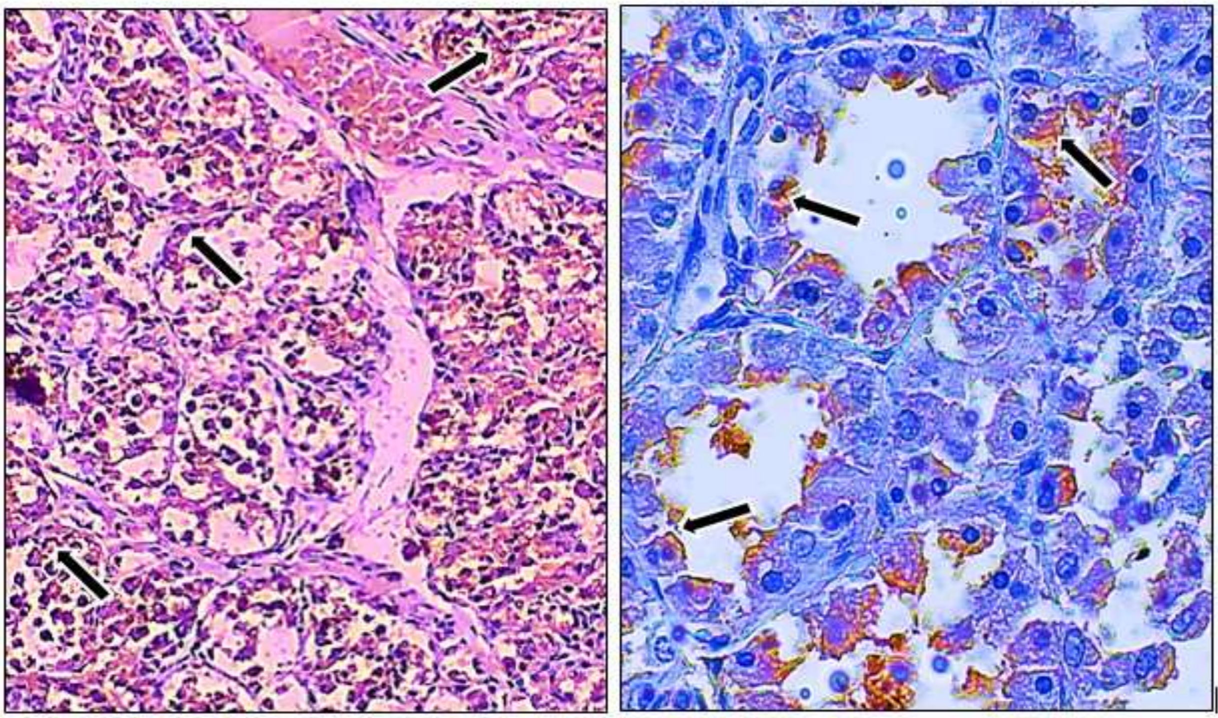
"The same information mentioned below Table (1)."



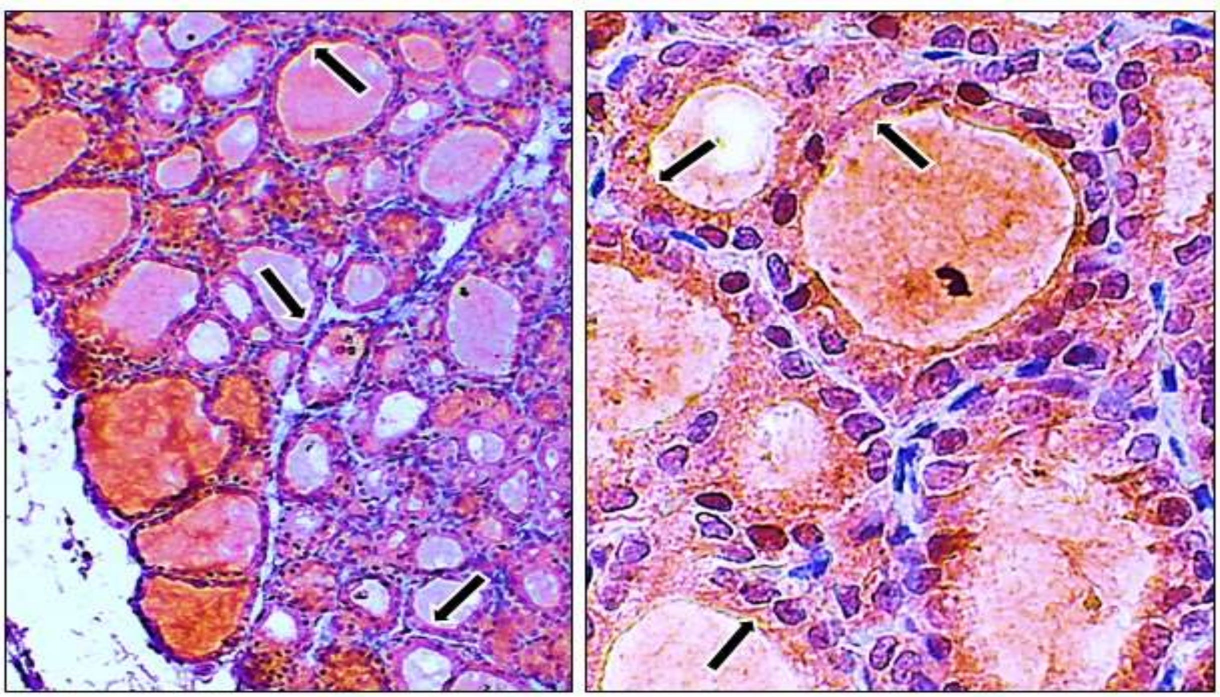
The above figure shows a histological section of thyroid tissue from the negative control group (NC), illustrating: A & B/ strong immunoreactivity of the primary antibody against TPO in thyroid cells (black arrow), indicating abundant TPO production in the cytoplasm of thyroid cells. A: 100X and B: 400X. Hematoxylin and DAB.



The above figure shows a histological section of thyroid tissue from the Brazilian nut suspension-treated group (BNC), illustrating: A & B/ strong immunoreactivity of the primary TPO antibody in thyroid cells (black arrow), reflected by intense tissue staining, indicating abundant TPO production in cytoplasm of thyroid cells. A: 100X and B: 400X. Hematoxylin and DAB.

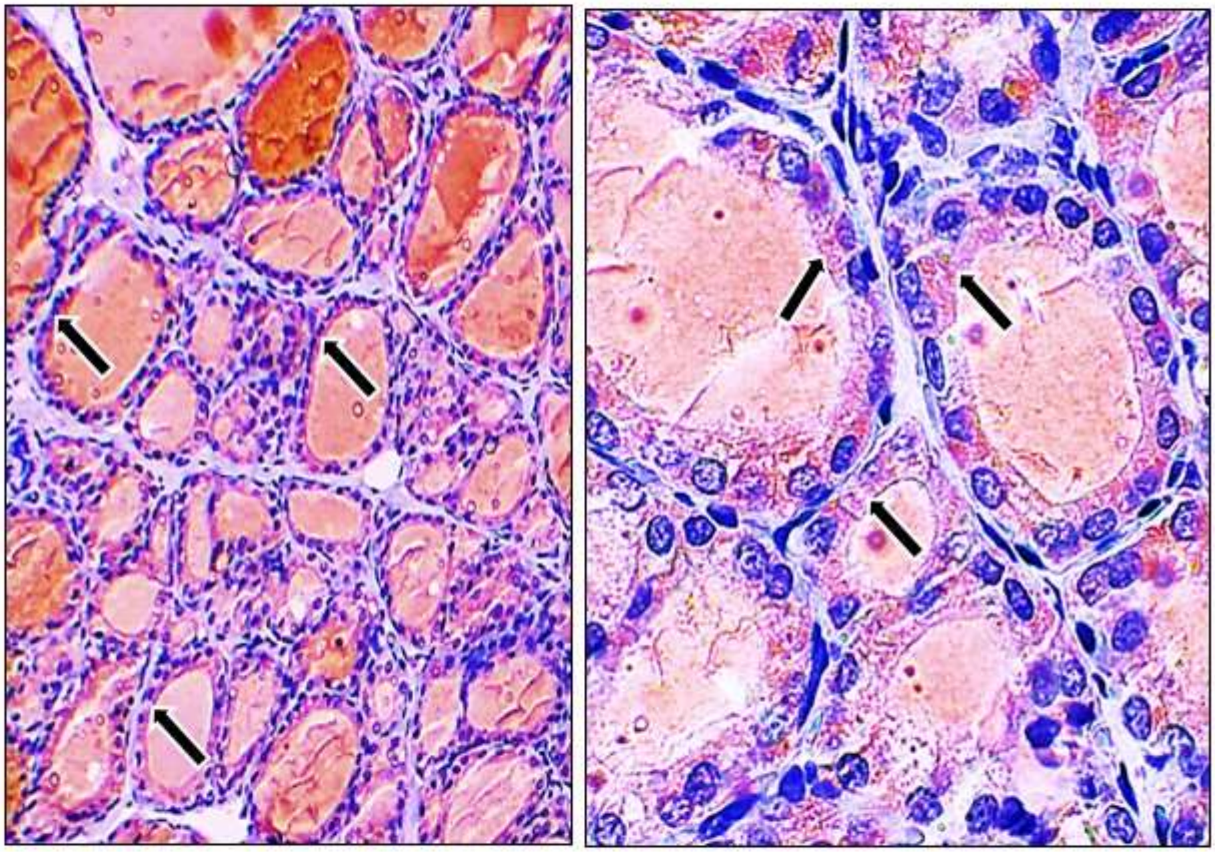


The above figure shows a histological section of thyroid tissue from the CBZ-only treated group (HC), illustrating: A & B/ weak immunoreactivity of the primary TPO antibody in thyroid cells (black arrow), indicating decreased TPO levels in the cytoplasm of thyroid cells, resulting in reduced tissue staining compared to other groups. A: 100X and B: 400X. Hematoxylin and DAB.



The above figure shows a histological section of thyroid tissue from the group treated with Brazilian nut suspension and CBZ (HBN), illustrating: A & B/ strong immunoreactivity of the primary TPO antibody in the cytoplasm of thyroid cells (black

arrow), indicating increased TPO production, as demonstrated by intense tissue staining. A: 100X and B: 400X. Hematoxylin and DAB.



The above figure presents a histology section of the thyroid tissue of the group that was treated with levothyroxine (HL): A and B/ mild immunoreactivity of the primary TPO antibody in the cytoplasm of thyroid cells (black arrow). A: 100X and B: 400X. Hematoxylin and DAB.

4-Discussion

This study provides compelling evidence for the therapeutic efficacy of Brazil nut supplementation in a rodent model of carbimazole (CBZ)-induced hypothyroidism. Our findings demonstrate that Brazil nut administration not only restores thyroid hormone homeostasis but also mitigates the associated selenium depletion and supports the structural and functional integrity of the thyroid gland, as evidenced by the recovery of thyroid peroxidase (TPO) expression.

4-1Restoration of Thyroid Hormone Homeostasis

The successful induction of hypothyroidism was confirmed by the characteristic hormonal profile in the CBZ-treated group (T2): significantly depressed serum T_3 and T_4 levels accompanied by a compensatory surge in TSH. This is a direct consequence of CBZ's known mechanism as a thyroid peroxidase (TPO) inhibitor, which blocks the iodination of thyroglobulin, a critical step in thyroid hormone synthesis [27, 28]. The resulting low thyroid hormone levels disrupt the negative feedback on the pituitary, leading to sustained TSH hypersecretion in a futile attempt to stimulate the inhibited gland [29].

The central finding of this study is the significant amelioration of this hypothyroid state by Brazil nut supplementation (Group T3). The restoration of T_3 and T_4 levels and the normalization of TSH observed in this group can be attributed primarily to the high bioavailable selenium content of Brazil nuts. Selenium is an essential cofactor for key selenoenzymes involved in thyroid physiology. First, as a component of glutathione peroxidases (GPx), selenium plays a crucial antioxidant role by scavenging hydrogen peroxide (H_2O_2) generated during hormone synthesis, thereby protecting thyrocytes from oxidative damage that can impair function [30, 31]. Second, selenium is integral to the deiodinase enzymes (DIO), particularly type 1 and type 2, which catalyze the peripheral conversion of T_4 to the biologically active T_3 [32]. By enhancing deiodinase activity, Brazil nut supplementation likely facilitated the conversion of residual T_4, contributing to the observed rise in serum T_3 and the subsequent normalization of the hypothalamic-pituitary-thyroid axis feedback, as indicated by the reduction in TSH. The efficacy of Brazil nuts was comparable to standard levothyroxine therapy (Group T4), which works through direct hormone replacement and subsequent suppression of TSH via negative feedback [33, 34]. Furthermore, the maintenance of euthyroid status in healthy rats supplemented with Brazil nuts alone (Group T1) underscores its safety and potential role in supporting optimal thyroid function, possibly through bolstering antioxidant defenses and ensuring efficient T_4-to-T_3 conversion [38,35].

4-2Reversal of Selenium Depletion

A notable pathophysiological consequence of CBZ-induced hypothyroidism observed in our model was a significant depletion of selenium in both serum and thyroid tissue (Group T2). This depletion aligns with the established link between hypothyroidism and increased oxidative stress, which escalates the demand for selenium as a constituent of antioxidant selenoenzymes like GPx [39, 40]. Additionally, hypothyroidism can impair gastrointestinal motility and absorptive function, potentially reducing the bioavailability of dietary trace elements, including selenium [41]. CBZ itself may also contribute to this malabsorptive state [42].

Brazil nut supplementation effectively counteracted this deficit. The significant rise in serum and tissue selenium levels in the HBN group (T3) directly results from the nuts' exceptionally high selenium content and its high bioavailability [43]. This restoration of selenium pools is critical, as it provides the necessary substrate for the synthesis of functional selenoenzymes. The concurrent improvement in thyroid hormone levels suggests a causal relationship: restored selenoprotein activity (e.g., GPx, DIO) supports hormonal synthesis and metabolism. Interestingly, levothyroxine treatment (T4) also improved selenium status relative to the hypothyroid control, likely secondary to the overall improvement in metabolic and gastrointestinal function upon hormonal normalization [45, 46]. The superior restoration of thyroid tissue selenium in the Brazil nut group compared to the levothyroxine group highlights the direct nutritive impact of the supplementation beyond mere hormonal correction.

4-3 Recovery of Thyroid Peroxidase (TPO) Expression

The immunohistochemical analysis of TPO provides a structural correlate to the functional hormonal data. The profound suppression of TPO expression in the hypothyroid group (T2) visually confirms the direct enzymatic inhibition by CBZ [50]. The accumulation of H_2O_2 due to uncoupled metabolism in a stressed, TSH-stimulated gland likely exacerbates oxidative damage, further compromising cellular health and enzyme integrity [51-53].

The most striking finding in this regard was the robust recovery of TPO immunoreactivity in the thyroid follicles of Brazil nut-treated hypothyroid rats (Group T3). This recovery significantly surpassed that seen with levothyroxine monotherapy (Group T4). We propose that this effect is mediated through a multi-faceted mechanism driven by selenium. By supplying ample selenium, Brazil nuts support the synthesis and activity of GPx, effectively mitigating H_2O_2-mediated oxidative stress and creating a cellular environment conducive to the recovery and sustained expression of TPO [54]. Furthermore, other bioactive compounds in Brazil nuts, such as polyphenols and flavonoids, may exert additional anti-inflammatory and antioxidant effects that support thyrocyte health and protein synthesis [36, 37]. In contrast, while levothyroxine treatment reduces TSH-driven gland stimulation and associated oxidative stress, leading to a partial recovery of TPO [55-57], it does not provide the direct nutritional substrate (selenium) required for optimal selenoenzyme-mediated protection and recovery.

4-4Conclusion and Implications

In conclusion, this study demonstrates that Brazil nut supplementation is an effective intervention in a model of drug-induced hypothyroidism. Its efficacy is mediated through a triad of actions: (1) restoring systemic and intrathyroidal selenium status, (2) ameliorating oxidative stress and supporting the recovery of the essential hormone-synthesizing enzyme TPO, and (3) normalizing thyroid hormone profiles via support of deiodinase activity and overall glandular function. These effects were either comparable to or, in the case of TPO expression, superior to standard levothyroxine therapy. These findings position Brazil nuts as a promising nutritional adjunct, not merely a source of selenium, but as a functional food that can address the oxidative and enzymatic pathologies associated with hypothyroidism. Future clinical studies are warranted to translate these findings into practical dietary recommendations for individuals with thyroid disorders.

5- Conclusion

The findings of this study demonstrate that dietary supplementation with Brazil nut powder exerts a significant restorative effect on the hypothyroid state induced by carbimazole in an experimental rodent model. This therapeutic action is mechanistically linked to the potent selenium-repleting capacity of Brazil nuts, which effectively replenished systemic and thyroidal selenium pools. The restoration of adequate selenium status is crucial, as this trace element serves as an essential cofactor for the iodothyronine deiodinases responsible for the peripheral conversion of T_4 to the active T_3 hormone, and for the antioxidant glutathione peroxidase enzymes that protect thyroid tissue from hydrogen peroxide-mediated oxidative damage generated during hormone synthesis. Importantly, while standard levothyroxine monotherapy successfully normalized circulating thyroid hormone and TSH levels through direct hormone replacement, it did not address the underlying selenium deficiency precipitated by the antithyroid drug. In contrast, Brazil nut supplementation not only supported the normalization of the pituitary-thyroid axis but also enhanced the intrathyroidal expression and activity of Thyroid Peroxidase (TPO), the key enzyme catalyzing thyroid hormone biosynthesis. This suggests a dual mode of action: direct provision of selenium for selenoprotein synthesis and a potential protective effect on follicular cell integrity, thereby improving the gland's functional capacity. In conclusion, this research provides compelling preclinical evidence that Brazil nut consumption, as a natural and food-based source of bioavailable selenium, offers a complementary nutritional strategy for managing hypothyroidism, particularly in cases associated with or exacerbated by selenium deficiency. It highlights the importance of evaluating and correcting micronutrient status alongside conventional hormone replacement therapy. Future clinical trials are warranted to translate these findings into dietary recommendations for subpopulations with concurrent hypothyroidism and marginal selenium intake.

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