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The effect of propylthiouracil on some physiological parameters of the thyroid gland and histological changes in bone, and the role of aqueous extract of thyme in immature male rats

Mahmood Saadi Mahmood, Noor Ibrahim Hassan

Department of Biology, College of Education for Pure Sciences, University of Tikrit, Tikrit, Iraq

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ABSTRACT

This study evaluated the physiological and histological effects of Propylthiouracil (PTU) and aqueous extract of *Thymus vulgaris* on thyroid function and bone growth in albino rats. Thirty males were assigned to six groups: control, thyme (400 mg/kg), PTU (50 mg/kg), PTU (100 mg/kg), thyme + PTU (50 mg/kg), and thyme + PTU (100 mg/kg). Treatments continued for 60 days. Serum analysis demonstrated that PTU induced hypothyroidism, reflected by a significant reduction in T3 (255.4 ± 12.3 pg/ml in control vs. 356.1 ± 15.2 pg/ml in PTU 50 mg; $p < 0.05$), calcium (10.23 ± 0.44 vs. 8.92 ± 0.38 mg/dl at PTU 50 mg; $p < 0.01$), vitamin D3 (9.1 ± 0.41 vs. 8.24 ± 0.36 ng/ml at PTU 100 mg), and CT (43.85 ± 1.9 vs. 37.57 ± 1.8 pg/ml at PTU 100 mg). Thyme extract improved endocrine parameters (T3: 294.9 ± 13.2 pg/ml; GH: 470.8 ± 20.5 pg/ml; Ca: 10.28 ± 0.46 mg/dl) and preserved bone microarchitecture. Combined therapy markedly enhanced recovery, with significant restoration of T3 (440.8 ± 18.7 pg/ml at thyme + PTU 50 mg; $p < 0.01$) and Ca (10.89 ± 0.49 mg/dl at thyme + PTU 100 mg; $p < 0.01$). Histological evaluation confirmed follicular degeneration and trabecular thinning in the PTU groups, while thyme co-administration mitigated these alterations. Aqueous thyme extract demonstrated significant protective effects against PTU-induced thyroid dysfunction and bone degeneration. These findings highlight thyme as a promising natural therapeutic adjunct for hypothyroidism-associated bone disorders.

Keywords: Thymus vulgaris, Propylthiouracil, thyroid gland, bone marrow, immature rats.

Name: Mahmood Saadi Mahmood **E-mail:** Mahmoud.saadi@st.tu.edu.iq

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تأثير البروبيل ثيوراسيل على بعض المعايير الفسيولوجية للغدة الدرقية والتغيرات النسيجية في العظام ودور المستخلص المائي للزعتر في ذكور الفئران غير الناضجة

محمود سعدي محمود، نور إبراهيم حسن

قسم علوم الحياة، كلية التربية للعلوم الصرفة، جامعة تكريت، تكريت، العراق

الملخص

هدفت هذه الدراسة إلى تقييم التأثيرات الفسيولوجية والنسجية لعقار البروبايل ثيوراسيل (PTU) والمستخلص المائي لنبات الزعتر (*Thymus vulgaris*) على وظيفة الغدة الدرقية ونمو العظام في الجرذان البيض. استُخدم 30 ذكرًا وُزعت إلى ست مجموعات: سيطرة، زعتر (400 ملغم/كغم)، PTU (50 ملغم/كغم)، PTU (100 ملغم/كغم)، زعتر (50 PTU + ملغم/كغم)، وزعتر (100 PTU + ملغم/كغم). استمرت المعالجات لمدة 60 يومًا. أظهرت التحاليل المصلية أن الـ PTU سبّب قصورًا درقيًا تمثل بانخفاض معنوي في T3 (255.4 ± 12.3 بيكوغرام/مل في السيطرة مقابل 356.1 ± 15.2 عند 50 PTU ملغم؛ $p < 0.05$ ، الكالسيوم (10.23 ± 0.44 مقابل 8.92 ± 0.38 ملغم/دل؛ $p < 0.01$ ، فيتامين D3 (9.1 ± 0.41 مقابل 8.24 ± 0.36 نانوغرام/مل عند 100 PTU ملغم)، وهرمون الكالسيتونين (43.85 ± 1.9 مقابل 37.57 ± 1.8 بيكوغرام/مل عند 100 PTU ملغم). في المقابل، حسّن الزعتر المؤشرات الهرمونية (T3: 294.9 ± 13.2 ؛ GH: 470.8 ± 20.5؛ Ca: 10.28 ± 0.46) وحافظ على سلامة البنية النسيجية للعظام. عزّز العلاج المشترك النتائج بشكل أوضح، خصوصًا (T3 440.8 ± 18.7 ؛ $p < 0.01$) والكالسيوم (10.89 ± 0.49؛ $p < 0.01$). وأكّدت الفحوص النسيجية وجود تنكس في جريبات الغدة الدرقية وترقق في العظم بالمجموعات المعالجة بـPTU، بينما خفف الزعتر هذه التغيرات. أظهر المستخلص المائي للزعتر تأثيرًا وقائيًا ملحوظًا ضد القصور الدرقي واضطرابات العظام المستحثة بـPTU، مما يجعله خيارًا واعدًا كعلاج طبيعي مساعد في حالات القصور الدرقي المصحوب باضطرابات النمو العظمي.

INTRODUCTION

Propylthiouracil (PTU) is a thionamide widely used to manage hyperthyroidism by inhibiting thyroid peroxidase and the peripheral conversion of T4 to T3. Despite its therapeutic efficacy, recent studies have highlighted severe adverse effects, including hepatotoxicity, vasculitis, and altered bone metabolism[1, 2]. These complications are of particular concern in long-term or high-dose therapy, especially in children and during pregnancy. Thyroid dysfunction itself is closely linked to impaired skeletal development, since thyroid hormones regulate osteoblast differentiation, endochondral ossification, and calcium–vitamin D3 homeostasis [3]. In parallel, medicinal plants have gained renewed interest as natural therapeutic agents. Thymus vulgaris is rich in bioactive compounds such as thymol, carvacrol, flavonoids, and polyphenols, which exhibit potent antioxidant, anti-inflammatory, and bone-protective effects[4]. Recent evidence suggests that thyme extract enhances calcium absorption, improves antioxidant defense in thyroid tissue, and mitigates drug-induced oxidative damage [5-7]. The aqueous extract of thyme also exhibits protective physiological effects without significant side effects, making it a potential option for reducing the toxic effects of drugs such as propylthiouracil. This study aims to evaluate whether the aqueous extract of *Thymus vulgaris* can reduce the physiological and histological alterations induced by Propylthiouracil

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(PTU) in newborn rats, with emphasis on its potential to restore hormonal balance and protect thyroid and bone tissues, as a safe, natural therapeutic alternative.

MATERIALS AND METHODS

Preparation of aqueous extract of thyme: Fresh leaves of *Thymus vulgaris* were purchased from local markets in Sulaymaniyah Governorate, thoroughly washed with distilled water, shade-dried at room temperature (25 ± 2°C), ground into fine powder, and stored in opaque glass bottles. To prepare the extract, 50 g of powdered leaves were soaked in 250 ml of distilled water (1:5 w/v). The mixture was stirred on a magnetic stirrer at 40°C for 60 min, then incubated in a shaking water bath at 150 rpm for 24 h. The suspension was filtered through a Whatman No. 1 filter paper, and the filtrate was dried in a hot-air oven at 40°C for 24 h to obtain a solid residue. The dried extract was weighed, dissolved in distilled water at the required concentration, and stored in airtight opaque bottles at 4°C until use. [8].

Estimation of active ingredients in the aqueous extract of thyme: The phytochemical constituents of the aqueous thyme extract were determined using validated spectrophotometric and chromatographic methods. Alkaloids were quantified using the BCG reagent at 470 nm. [9], glycosides by the Baljet method at 495 nm [10], total phenols using Folin–Ciocalteu reagent at 765 nm [11], and flavonoids by the aluminum chloride colorimetric assay at 510 nm [12]. Saponins were quantified gravimetrically after ethanol and butanol extractions. [13], while tannins were assessed using ferric chloride–gelatin complex at 540 nm [14]. High-performance liquid chromatography (HPLC) was also performed for selected phenolic compounds using a C18 column, a mobile phase of methanol: distilled water: formic acid (70:25:5 v/v/v), and UV detection at 280 nm. [15]. Chromatographic profiling allowed clear separation of phenolic constituents, with major peaks corresponding to thymol, carvacrol, rosmarinic acid, and caffeic acid, which are considered the principal bioactive markers of thyme extract.

Preparation of study animal : Thirty (30) clinically healthy male albino rats (*Rattus norvegicus*), aged 4–6 weeks and weighing 90 ± 5 g, were obtained from the Experimental Animal Unit, College of Veterinary Medicine, Tikrit University. Animals were acclimatized for one week under controlled laboratory conditions (temperature 25 ± 2°C, relative humidity 50–60%, 12 h light/dark cycle) with free access to standard pellet diet and tap water. The study was conducted over 60 days, from December 29, 2024, to February 25, 2025.

Classification of study animals: Animals were randomly divided into six equal groups (n = 5 per group) as follows: Group 1 (Control): received distilled water orally. Group 2 (Thyme): treated orally with aqueous thyme extract (400 mg/kg, 1 ml/day). Group 3 (PTU-50): treated orally with Propylthiouracil at 5 mg/kg body weight/day (therapeutic dose, dissolved in 0.5 ml distilled water). Group 4 (PTU-100): treated orally with Propylthiouracil at 10 mg/kg body weight/day (double therapeutic dose, dissolved in 1 ml distilled water). Group 5 (Thyme + PTU-50): treated with thyme extract (400 mg/kg) and PTU (5 mg/kg) orally. Group 6 (Thyme + PTU-100): treated with thyme extract (400 mg/kg) and PTU (10 mg/kg) orally. Treatments were administered daily by oral gavage for 60 consecutive days, according to previously established protocols. [16, 17]. Body weight and feed consumption were recorded weekly.

All animal procedures were performed according to the guidelines of the National Institutes of Health for the Care and Use of Laboratory Animals and were approved by the Ethics Committee of the College of Education for Pure Sciences, Tikrit University (Approval No.: TU-CEPS-2024-12).

Collecting blood and tissue samples : At the end of the treatment period, drug and extract administration were stopped for 24 h before dissection. Animals were anesthetized with chloroform, and blood samples were collected via

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jugular vein into gel tubes. Samples were centrifuged at 3000 rpm for 15 min, and the serum was separated using micropipettes. It was then stored at -80 °C until analysis, which included measuring thyroid hormone levels (T3, T4), GH, calcitonin, and PTH, as well as calcium (Ca), vitamin D3, and insulin-like growth factor (IGF-1). Femurs were removed from all animals for histological examination and evaluation of tissue changes resulting from the various treatments.

Method of work for the determination of vital hormones in blood serum: Serum levels of several hormones of T3, T4, GH, IGF-1, PTH, calcitonin, and vitamin D3 were determined by Sandwich-ELISA using commercial kits (Elabscience, Wuhan, China; Cat. No: E-EL-R0031, E-EL-R0032, E-EL-R0028, E-EL-R0017, E-EL-R0041, E-EL-R0220, E-EL-0025) with sensitivities ranging from 0.1–2 ng/mL and assay precision of intra-assay CV < 8% and inter-assay CV < 10%., Histological preparation of the femur was carried out according to protocol of [18] which included fixation in 10% formalin, decalcification of the bone with 5% nitric acid, percolation and waxing of the samples, then cutting them into 5-micrometer-thick sections, staining with hematoxylin and eosin, and finally microscopic examination after fixation with DPX.

Statistical analysis: The results were analyzed using One-way ANOVA and Duncan's test to differentiate between means at a significance level ($p \leq 0.05$), and the correlation coefficient was calculated using Minitab Version 17 [19].

RESULTS AND DISCUSSION

Effect of coefficients on some hormonal and physiological indicators in blood serum: The results showed no significant differences ($P \leq 0.05$) in thyroxine (T4) concentration across all groups compared with the control group. Morally, there was a concentration of triiodothyronine (T3) in all groups compared to the control, and a significant superiority of the aqueous extract groups and the drug (PTU) compared to the PTU-treated groups at concentrations of 50 and 100. mg/kg, indicating the extract's stimulating effect on T3 levels.

Results of the study (Figure 3) showed a significant increase ($P \leq 0.05$ (in growth hormone (GH) of the aqueous extracts group, and Propylthiouracil at a concentration (50 mg/kg), as well as in extracted and PTU-treated groups (50 and 100 mg/kg), compared to the control. On the other hand, there were no significant differences between the PTU group (100 mg/kg) and the control, and no significant difference was observed between thyme and PTU (50 mg/kg) compared with PTU alone. The Thyme and PTU group (100 mg/kg) showed a significant increase in GH concentration compared to the PTU group (100 mg/kg), indicating a potential role of the plant extract in promoting GH production under conditions of Hormonal suppression. The data are summarized in Table 1 and illustrated in Figures 1, 2, and 3.

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Table 1: Effect of Propylthiouracil (PTU) and aqueous thyme extract at the levels of (T3, T4, GH) in male white rats

Parameters / Groups	GH (pg/ml) St Dev ±mean	T3 (pg/ml) St Dev ±mean	T4 (ng/ml) St Dev ±mean
Control	447.1±34.0 c	255.4±44.2 e	21.2±3.1 a
TM	470.8±53.0 b	294.9±40.6 d	21.1±4.5 a
PTU(50mg)	579.9±26.7 a	356.1±33.3 c	19.2±5 a
PTU(100mg)	442.5±41.9 c	345.5±58.7 c	21.7±3.2 a
TM+PTU(50MG)	570.7±26.6 a	440.8±56.1 a	21.5±2.5 a
TM+PTU(100MG)	573.1±31.6 a	389.3±55.3 b	20.6±4.5 a

The numbers represent the mean ± standard error. The different letters indicate significant differences (P≤ 0.05) between the groups. (TM = thyme, Propylthiouracil = PTU, number of animals in each group: 5 animals.

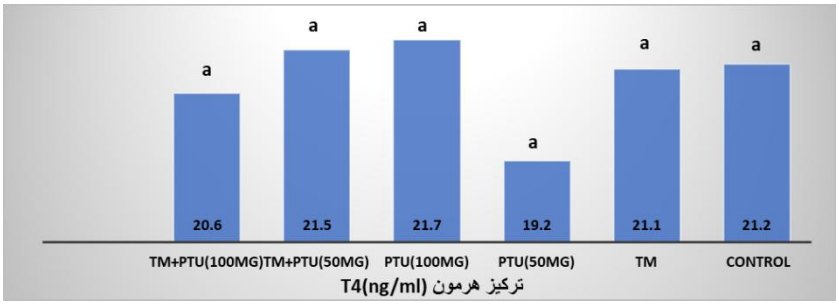

Fig. 1: Effect of Propylthiouracil and thyme aqueous extract on the concentration of T4 hormone in blood serum. (TM = thyme, Propylthiouracil = PTU, number of animals in each group: 5 animals.)

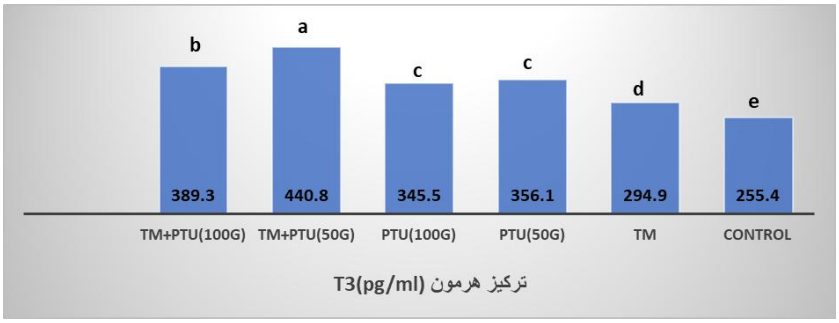

Fig. 2: Effect of Propylthiouracil and thyme aqueous extract on the concentration of T3 hormone in blood serum

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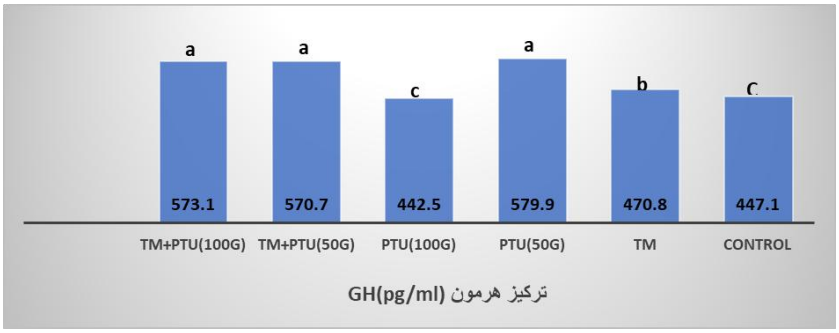

Fig. 3: Effect of Propylthiouracil and thyme aqueous extract on the concentration of GH hormone in blood serum

In the Calcitonin hormone (CT) group, treatment with 50 mg of the drug; in the thyme group, treatment with the extract; and in the PTU group (50, 100 mg) significantly increased (P≤ 0.05) CT concentration compared to the control. On the other hand, CT concentration in the PTU group decreased to 100 mg. CT concentration was significantly higher in the group treated with PTU 100mg and thyme compared with the PTU group alone (Figure 4). However, no significant differences were recorded between the PTU groups, the drug, and the extract at both concentrations (50 and 100 mg/kg), as shown in Figure 5. A significant decrease (P≤ 0.05) in vitamin D3 concentration was observed in the thyme and drug (100 mg) groups compared with the control. Another treatment showed no significant difference compared to the control. A significant superiority was also observed in the group treated with thyme and PTU (100 mg) compared to PTU (100 mg) alone (Figure 6).

The concentration of calcium (Ca) increased significantly in the thyme and PTU (100 mg) group compared to the control. The concentration of Ca decreased in the PTU (50 and 100 mg) groups compared to the control group. No significant differences were observed between the thyme-only and thyme with PTU (50 mg) groups and the control. The Ca levels increased in the thyme and PTU (50 and 100 mg) groups compared to those treated with PTU only at the same concentrations, as shown in Figure 7. The PTU (50 mg) and thyme with PTU (50 mg) groups showed a significant increase (P≤ 0.05) in IGF-1 concentration compared to the control, while no significant differences were observed in the other groups. Also, no significant differences were observed between thyme and PTU compared to PTU alone at both concentrations (Figure 8), and the data are summarized in Table 2.

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Table 2: Effect of Propylthiouracil (PTU) and aqueous thyme extract at the levels of (CT, PTH, D3, Ca, IGF-1) in male white rats

Parameters / Groups	PTH (pg/ml) St Dev ±mean	CT (pg/ml) St Dev ±mean	IGF-1 (pg/ml) St Dev ±mean	Ca (mg/dl) St Dev ±mean	VD3 (ng/ml) St Dev ±mean
Control	23.18±5.84 d	43.85±8.87 c	317.7±47.2 b	10.23±0.45 b	9.10±0.79 ab
TM	27.05±8.05 c	47.97±8.22 bc	325.6±46.2 b	10.28±0.88 b	7.33±2.15 c
PTU(50mg)	37.96±3.87 a	52.48±8.51 a	362.7±52.7 a	8.92±0.38 d	9.84±0.44 a
PTU(100mg)	5.16±32.32 b	37.57±4.71 d	331.3±36.5 b	9.82±0.46 c	8.24±1.51 b
TM+PTU(50MG)	35.84±7.94 ab	54.19±3.76 a	350.4±49.8 a	10.40±0.44 b	9.16±0.36 ab
TM+PTU(100MG)	32.07±1.60 b	50.28±5.48 ab	332.8±37.9 b	10.89±0.55 a	9.36±0.82 a

The numbers represent the mean ± standard error. The different letters indicate significant differences (P≤ 0.05) between the groups.

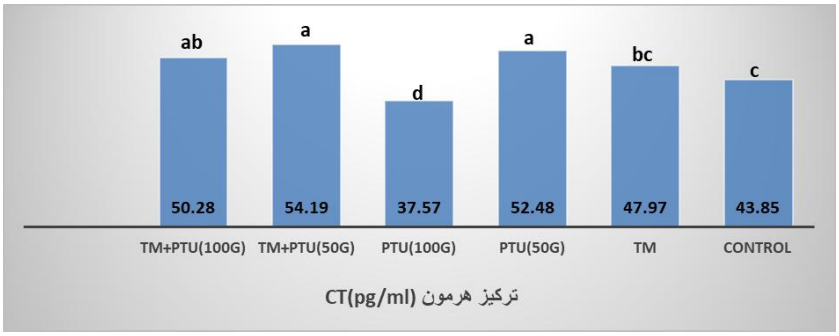

Fig. 4: **Effect of Propylthiouracil and thyme aqueous extract on the concentration of CT hormone in blood serum**

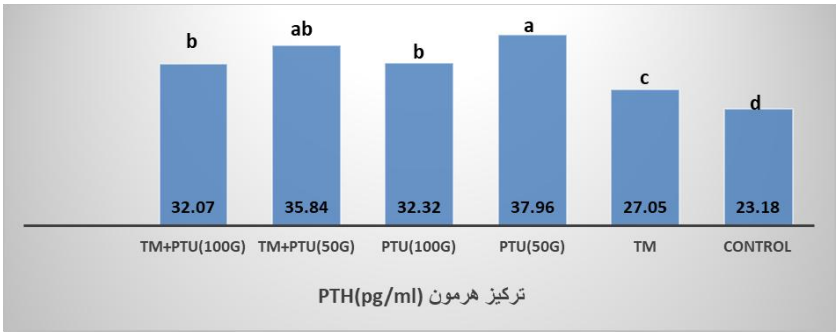

Fig. 5: **Effect of Propylthiouracil and thyme aqueous extract on the concentration of PTH hormone in blood serum**

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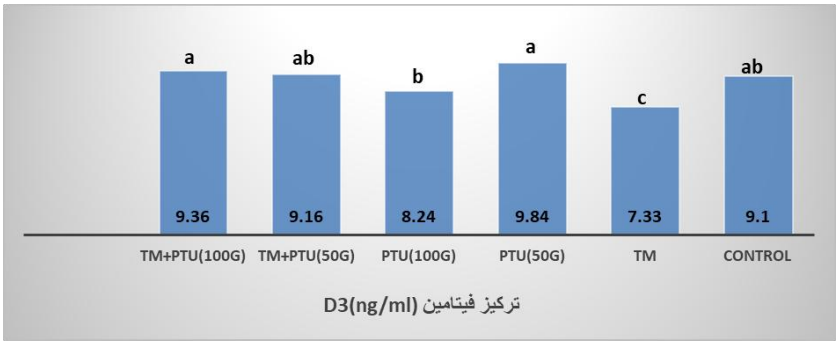

Fig. 6: **Effect of Propylthiouracil and thyme aqueous extract on the concentration of D3 in blood serum**

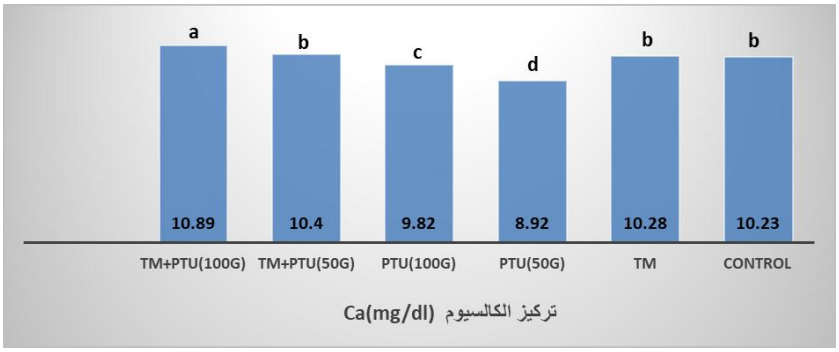

Fig. 7: **Effect of Propylthiouracil and thyme aqueous extract on the concentration of Ca in blood serum**

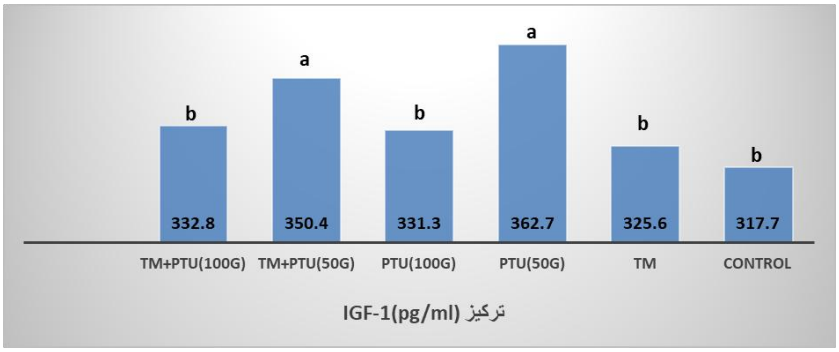

Fig. 8: **Effect of Propylthiouracil and thyme aqueous extract on the concentration of IGF-1 in blood serum**

Thyroid hormones play an essential role in regulating metabolism and growth, mainly through enhancing the action of growth factors such as insulin-like growth factor (IGF-I) [20]. Evidence suggests that thyme extract may improve metabolism and reduce weight gain, reflecting its potential role in supporting thyroid function. [21]. The lack of significant changes in T4 and T3 levels in some groups treated with thyme or propylthiouracil (PTU) may be explained by the young age of the animals and the cold experimental conditions. In line with these findings, earlier studies have demonstrated that flavonoids and other active compounds in thyme enhance iodine absorption and upregulate transporters involved in thyroid hormone synthesis, thereby alleviating PTU-induced hypothyroidism. [22]. This mechanism provides a plausible explanation for the observed increase in T3 concentrations in groups treated with the thyme and PTU combination.

The results also revealed a significant increase in growth hormone (GH) in thyme-treated groups and in the PTU (50 mg) group, either alone or combined with thyme, compared to the control. This finding highlights the physiological effects of thyme on GH secretion. A similar effect was reported by [23], who

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found that thyme powder supplementation improved growth performance in quails, reinforcing its stimulatory role on growth-related hormones. Moreover, the role of GH in bone formation through osteoblast stimulation and new bone deposition [24] suggests that thyme's effect could be mediated not only via endocrine modulation but also by its antioxidant-rich composition that protects tissues and supports skeletal growth.

A significant increase in calcitonin (CT) concentrations was recorded in most thyme-treated groups compared to the control. This aligns with evidence that thymol and other thyme-derived monoterpenes inhibit osteoclast activity and promote calcium absorption. [25]. Enhanced intestinal calcium absorption induced by thyme [26] likely explains the rise in CT secretion, since elevated calcium stimulates C-cell activity in the thyroid gland. CT is a key hormone for bone stabilization, as it reduces blood calcium levels by inhibiting osteoclasts and increasing bone calcium deposition. [27]. Conversely, the 100 mg PTU group showed reduced CT levels, consistent with earlier reports describing impaired C-cell activity and reduced CT secretion under PTU-induced hypothyroidism. [28]. The data therefore suggest that thyme's active components may counteract PTU's negative effects on C-cells, indirectly sustaining calcium balance and bone health.

PTH concentrations were significantly elevated in all treated groups compared to the control, indicating compensatory regulation of calcium homeostasis. This agrees with reports that hypocalcemia induces secondary hyperparathyroidism. [29]. The stimulatory effect of thyme on PTH secretion observed in this study is supported by evidence that herbal extracts like thyme enhance intestinal calcium absorption and contribute to calcium balance. [30]. Increased PTH plays a dual role: first, it stimulates bone resorption, which subsequently triggers osteoblast activation and new bone formation. [31]. PTU-treated groups also exhibited increased PTH levels, consistent with earlier findings of thioamide-induced alterations in calcium metabolism. [32]. The absence of additive effects in the thyme + PTU groups suggests that calcium balance had reached a physiological plateau, limiting further PTH stimulation.

A reduction in vitamin D3 concentrations was observed in thyme and high-dose PTU (100 mg) groups. This aligns with reports linking low vitamin D3 levels to immune and thyroid dysfunction. [33]. Its reduction could negatively impact skeletal growth. Nevertheless, thyme extract improved calcium status in some groups, consistent with evidence highlighting its mineral content and role in bone protection. [34]. These effects may offset PTU-induced disruptions, as calcium deficiency is known to accelerate oxidative damage, bone resorption, and compromised bone biomechanical strength. [35]. The current findings underscore the protective potential of thyme, which, by enhancing calcium absorption and bone mineral density, could serve as a natural adjunct in the prevention of osteoporosis.

Significant increases in IGF-1 were detected in the PTU (50 mg) and thyme + PTU groups compared to controls. IGF-1, a liver-derived mediator of GH effects, is indispensable for growth and tissue repair [36]. may explain PTU's stimulatory effect, as supported by studies reporting elevated IGF-1 in antithyroid-treated animals [37]. Moreover, T3 stimulation of IGF-1 receptor expression in chondrocytes [38] emphasizes the cross-talk between thyroid and growth pathways. The anabolic role of IGF-1 in bone stem cell proliferation and fracture healing [39] Further confirms its contribution to bone health. The absence of significant IGF-1 changes in thyme-only or high PTU dose groups suggests that either hormonal disruption overrode GH/IGF-1 signaling or thyme's effect alone was insufficient. These complex interactions reaffirm the integrated regulation of growth by thyroid, pituitary, and IGF-1 axes.

This mechanism not only protects thyroid tissue but also preserves bone-forming cells from oxidative damage. Thyroid hormones are vital for skeletal maturation and mineralization [40], and PTU-induced hypothyroidism has been linked to

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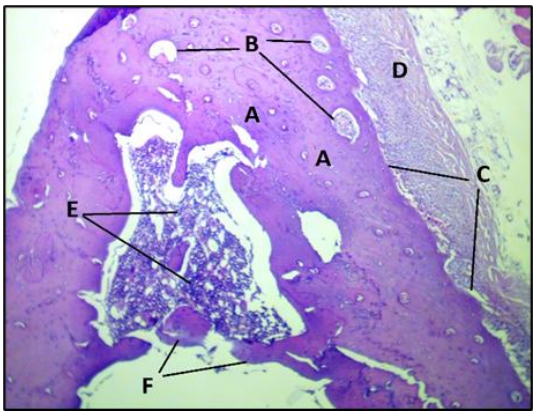
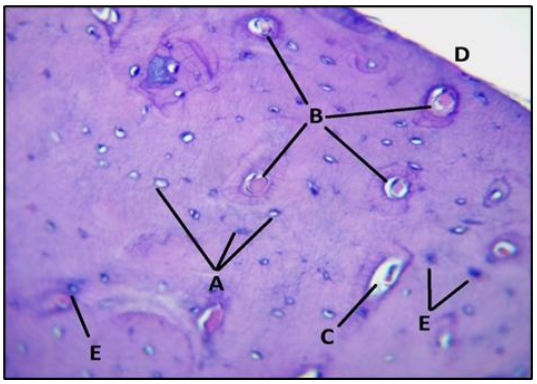
osteoblast inhibition, increased osteoclast activity, and reduced expression of osteogenic markers like RUNX2 and osteocalcin [41]. By counteracting these effects, thyme extract appears to maintain thyroid secretory function and support bone formation through its antioxidant and mineral-rich profile. Consistent with previous studies, thyme's phenolic constituents (thymol, carvacrol) reinforced antioxidant defenses and suppressed oxidative stress [42]. Thus, maintaining thyroid integrity and bone health through natural antioxidants, such as thyme, represents a promising approach to mitigating PTU-induced hypothyroidism and skeletal deterioration.

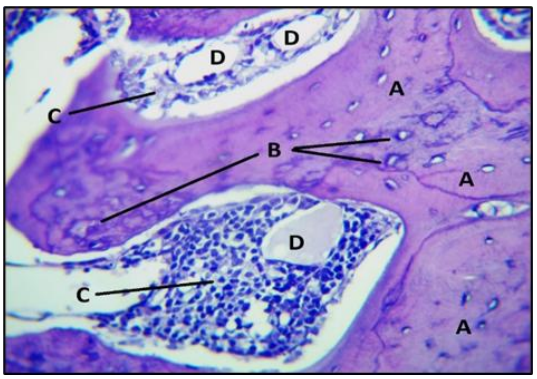
Histological findings of bone: The control group showed normal bone structure, characterized by regular osteocytes within fovea, Haversian canals, and a bone marrow rich in white blood cells and megakaryocytes (Image 1). The thyme group showed near-normal organization, with Haversian and Volkmann canals, remnants of cartilage tissue, and healthy blood vessels (Image 2). In the PTU (50 mg) group, osteocyte degeneration, ground-substance cavitation, and cellular infiltration with partial bone destruction were observed (Image 3). The higher dose (100 mg) showed widespread atrophy, osteoclasts, and degenerated cartilage foci (Image 4). Treatment with thyme and PTU (50 mg) showed a relative improvement, with osteoblasts regularized and some minor changes preserved (Image 5). Meanwhile, the thyme (100 mg PTU) group demonstrated a clear protective role with regular osteocytes and the presence of megakaryocytes, despite the persistence of some changes (Image 6).



IMG 1: Section of bone tissue showing osteocytes (A), Haversian canals (B), periosteum (C), colloidal fiber bundles (D), bone marrow tissue (E), and osteophytes (F) (H&E X 400).



IMG 2: Section of compact bone tissue, osteocytes within fossae (A), Haversian canals with blood vessels (B), Volkmann's canal (C), periosteum (D), cartilage remnants (E)(H&E X 400).



IMG 3: A section showing bone tissue containing osteocytes inside the follicles (A), degeneration of some bone cells (B), bone marrow containing lymphatic tissue (C), and fat cells (D) (H&E X 400).

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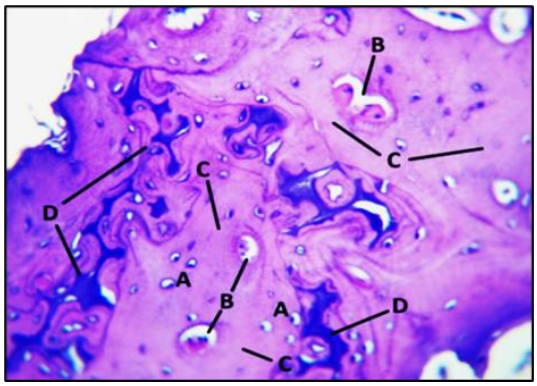
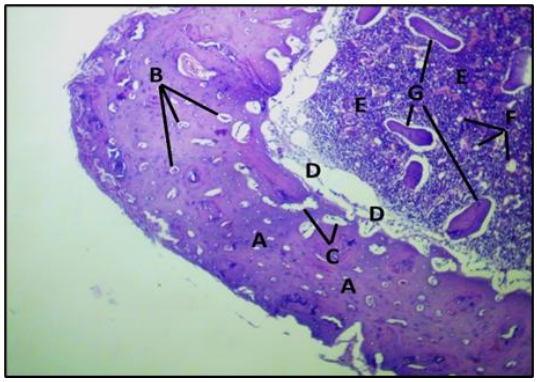
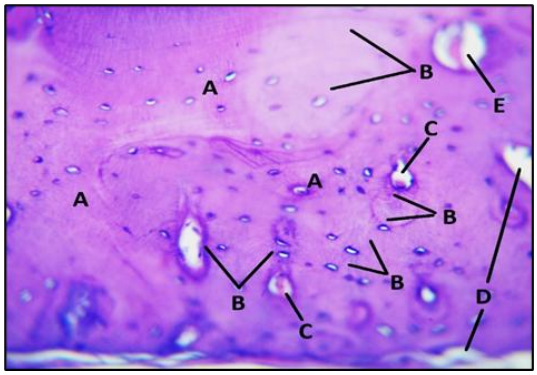


IMG 4: Section in the cortex of solid bone, showing osteocytes in fossae (A), Haversian canals (B), osteoblasts (C), and dark-stained degenerative cartilage tissue (D) (H&E X 400).



IMG 5: Section of the bone cortex tissue containing osteocytes (A), Haversian canals (B), Volkmann's canals (C), the inner bone periosteum (D), bone marrow containing hemolymph tissue (E), fat cells (F), and bone septa (G) (H & E X 400).



IMG 6: Section of solid bone tissue showing osteocytes in fossae (A), bone plates (B), Haversian canals (C), Volkmann's canal (D), and bone tissue pockets (E) (H&E X 400).

Histological examination of bones from animals treated with thyme showed a significant improvement in bone tissue structure, with osteocytes appearing regular within the fovea, clear Haversian and Volkmann canals, and normal vascular proliferation without obvious pathological findings in the bone marrow. These results indicate that thyme supports bone growth and maintains bone structural integrity. This is attributed to its content of phenolic compounds, flavonoids, and minerals such as calcium and phosphorus, which play important roles in bone formation and in limiting bone resorption. [43]. In contrast, animals treated with PTU at both therapeutic and double doses showed histopathological changes, including osteocyte degeneration, pockets within the ground substance, and lymphocyte infiltration. This indicates a disruption in bone regeneration and osteoclast activity. This is consistent with previous studies indicating that pharmacologically induced hypoparathyroidism affects bone health by inhibiting calcium absorption and reducing osteoblast activity. [44]. Since thyroid hormones influence many physiological processes, such as growth and development, they increase the basal growth rate. Increased trace elements, essential nutrients with regulatory and antioxidant functions, promote growth. This is consistent with a study. [45]. In groups treated with the drug and the extract, a clear reparative response was observed, characterized by regular osteocyte formation and a relatively normal appearance of bone tissue; this reflects thyme's protective role against drug-induced osteotoxicity. This is attributed to the effectiveness of antioxidant compounds such as thymol and carvacrol, which contribute to inhibiting oxidative stress, reducing bone resorption, and stimulating osteocyte regeneration [46]. These results suggest that using thyme as a natural supplement can reduce the negative effects of drugs on bone by supporting the balance between osteoclasts and osteoblasts and enhancing immune function in bone marrow, which has also been documented in studies such as [47] which demonstrated the safety of thyme during chronic use and its ability to support bone growth and improve hematopoiesis.

CONCLUSIONS

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This study demonstrated that Propylthiouracil (PTU), particularly at high doses, induced hypothyroidism and adverse effects on thyroid and bone tissues. Aqueous thyme extract showed protective effects by improving hormonal balance, calcium status, and bone structure. Combined treatment reduced PTU effects, indicating thyme as a potential natural adjunct therapy.

REFERENCES

1. Mason KA, Schoelwer MJ, Rogol AD. Androgens During Infancy, Childhood, and Adolescence: Physiology and Use in Clinical Practice. Endocrine Reviews. 2020;41(3). https://doi.org/10.1210/endrev/bnaa003
2. Liu C-C, Zhang Y, Makris A, Rasmussen HH, Hennessy A. S-glutathionylation of the Na+-K+ Pump: A Novel Redox Mechanism in Preeclampsia. The Journal of Clinical Endocrinology & Metabolism. 2020;106(4):e1091-e100. https://doi.org/10.1210/clinem/dgaa918
3. Mohamed F, Seedat F, Raal FJ. Novel therapies for familial hypercholesterolemia. Current Opinion in Endocrinology, Diabetes and Obesity. 2021;28(2):188-95. https://doi.org/10.1097/MED.0000000000000590
4. Sapkota M, Li L, Kim SW, Soh Y. Thymol inhibits RANKL-induced osteoclastogenesis in RAW264.7 and BMM cells and LPS-induced bone loss in mice. Food Chem Toxicol. 2018;120:418-29. https://doi.org/10.1016/j.fct.2018.07.032
5. Waheed M, Hussain MB, Saeed F, Afzaal M, Ahmed A, Irfan R, et al. Phytochemical Profiling and Therapeutic Potential of Thyme (Thymus spp.): A Medicinal Herb. Food Sci Nutr. 2024;12(12):9893-912. https://doi.org/10.1002/fsn3.4563
6. Mehson F, Rasmi A, Khaleel S. Histological study of thyroid gland in case of experimentally induced hypothyroidism by carbimazole in domestic female rabbits (Lepus cuniculus domastica). 2017.
7. Li X, Zhang T, Zhang H, Liu S, Tian L. Effects of levothyroxine therapy on bone and mineral metabolism in hypothyroidism: a systematic review and meta-analysis. BMC Endocr Disord. 2025;25(1):11. https://doi.org/10.1186/s12902-024-01819-7
8. Ozma MA, Khodadadi E, Pakdel F, Kamounah FS, Yousefi M, Yousefi B, et al. Baicalin is a natural antimicrobial and anti-biofilm agent. Journal of Herbal Medicine. 2021;27:100432. https://doi.org/10.1016/j.hermed.2021.100432
9. Thakur J, Dwivedi MD, Singh N, Uniyal PL, Goel S, Pandey AK. Applicability of Start Codon Targeted (SCoT) and Inter Simple Sequence Repeat (ISSR) markers in assessing genetic diversity in Crepidium acuminatum (D. Don) Szlach. Journal of Applied Research on Medicinal and Aromatic Plants. 2021;23:100310. https://doi.org/10.1016/j.jarmap.2021.100310
10. Kasimedu S, Shaik M, Mirzazadeh Y. Modern and Traditional Approaches in Alkaloid Extraction and Phytochemical Screening: Techniques, Integration Strategies, and Future Perspectives. Asian Journal of Green Chemistry. 2025;9:937-60. https://doi.org/10.48309/AJGC.2025.521737.1740
11. Sadgrove NJ, Padilla-González GF, Phumthum M. Fundamental Chemistry of Essential Oils and Volatile Organic Compounds, Methods of Analysis and Authentication. Plants. 2022;11(6):789. https://doi.org/10.3390/plants11060789
12. Shraim AM, Ahmed TA, Rahman MM, Hijji YM. Determination of total flavonoid content by aluminum chloride assay: A critical evaluation. LWT. 2021;150:111932. https://doi.org/10.1016/j.lwt.2021.111932
13. Said Ashour A, Mahfud A, Abed El Aziz M. A review on saponins from medicinal plants: chemistry, isolation, and determination. Journal of Nanomedicine Research. 2019;8:6-12. https://doi.org/10.15406/jnmr.2019.07.00199
14. Huang H, Lv Y, Sun X, Fu S, Lou X, Liu Z. Rapid determination of tannin in Danshen and Guanxinning injections using UV spectrophotometry for quality control. Journal of Innovative Optical Health Sciences. 2018;11. https://doi.org/10.1142/S1793545818500347

15. Kumari M, Kumar J. Chicken feather waste degradation by Alternaria tenuissima and its application on plant growth. Journal of Applied and Natural Science. 2020;12(3):411. https://doi.org/10.31018/jans.v12i3.2345

16. H.F O, A.A E-M, E.M E-S. Role of Thyme Extract against Some Biochemical Alterations Induced by Propylthiouracil in Male Rats. Journal of Food and Nutrition Research. 2025;7(11):794-800. https://doi.org/10.12691/jfnr-7-11-6

17. Hatim SA. Physiological and histological effects of propylthiouracil in laboratory rats [Master's thesis]. Baghdad, Iraq: University of Baghdad; 2019.

18. Bancroft JD, Gamble M. Theory and practice of histological techniques. 8 ed. London, UK: Elsevier; 2019.

19. Minitab LLC. Minitab statistical software, version 20: User guide. State College, PA: Minitab Press; 2021.

20. Asaad AM, Kakey IS. Investigating the Relationship Between Insulin-Like Growth Factor-I and Thyroid Hormones in Thyroid Disorder Patients. ARO-THE SCIENTIFIC JOURNAL OF KOYA UNIVERSITY. 2025;13(2):18-25. https://doi.org/10.14500/aro.12181

21. Abdulkarimi R, Daneshyar M, Aghazadeh AM. Thyme (Thymus vulgaris) extract consumption darkens the liver, lowers blood cholesterol, and proportionally increases liver and abdominal fat weights in broiler chickens. Italian Journal of Animal Science. 2011;10. https://doi.org/10.4081/ijas.2011.e20

22. Shalaby AA, Bahr HI. Thyroid-regulating and hepatobiliary protective actions of Thymus vulgaris L. in a rat model. Indian Journal of Applied Research. 2016;6(1):17-22.

23. Haji RM, Ahmed NA, Ahmed SA. Effect of COVID-19 on the Severity of Signs and Symptoms of Autoimmune Diseases. Kurdistan Journal of Applied Research. 2022;7(1):37-44. https://doi.org/10.24017/Science.2022.1.4

24. Nelson textbook of pediatrics. 21 ed. Philadelphia, PA: Elsevier; 2020.

25. Broulík P. [Calcitonin and its role in the regulation of calcium-phosphate metabolism]. Cas Lek Cesk. 2010;149(6):285-7.

26. Xie J. Calcitonin and Bone Physiology: In Vitro, In Vivo, and Clinical Insights. International Journal of Endocrinology. 2020;2020:3236828. https://doi.org/10.3390/jcm5110096

27. Lamora A, Talbot J, Mullard M, Brounais-Le Royer B, Redini F, Verrecchia F. TGF-β Signaling in Bone Remodeling and Osteosarcoma Progression. Journal of Clinical Medicine. 2016;5(11):96.

28. Saber DF, Marbut MM, Zbaar SA. The Influence of the Parathyroid Gland On Beta-Thalassaemia Patients in Kirkuk City. Tikrit Journal of Pure Science. 2019;24(2):10-3. https://doi.org/10.25130/J.V24I2.793

29. Swanson V, Hart J, Byrne-Davis L, Merritt R, Maltinsky W. Enhancing Behavior Change Skills in Health Extension Workers in Ethiopia: Evaluation of an Intervention to Improve Maternal and Infant Nutrition. Nutrients. 2021;13(6):1995. https://doi.org/10.3390/nu13061995

30. Silva BC, Costa AG, Cusano NE, Kousteni S, Bilezikian JP. Catabolic and anabolic actions of parathyroid hormone on the skeleton. J Endocrinol Invest. 2011;34(10):801-10. https://doi.org/10.3275/7925

31. Mewani V, Dhillon S, Cai X, Wang X. Transient Primary Hyperparathyroidism: A Case Report. AACE Clinical Case Reports. 2016;2(3):e182-e5.

32. Mohamed KA, Abbas SK. Vitamin D Deficiency in Iraqi Women with Hashimoto Thyroiditis. Tikrit Journal of Pure Science. 2025;30:2. https://tjpsj.org/index.php/tjps/article/view/1758

33. Elbahnasawy AS, Valeeva ER, El-Sayed EM, Rakhimov, II. The Impact of Thyme and Rosemary on the Prevention of Osteoporosis in Rats. J Nutr Metab. 2019;2019:1431384. https://doi.org/10.1155/2019/1431384

34. Al-Khalifa R, Hassan M. The Impact of Thyme and Rosemary on the Prevention of Osteoporosis in

Rats. Journal of Applied Pharmaceutical Science. 2019;9(4):54-60.

35. Huang F, Luo L, Wu Y, Xia D, Xu F, Gao J, et al. Trilobatin promotes angiogenesis after cerebral ischemia–reperfusion injury via SIRT7/VEGFA signaling pathway in rats. Phytotherapy Research. 2022;36(7):2940-51. https://doi.org/10.1002/ptr.7487

36. Pollack R, Koch N, Mazeh H, Cahn A, Katz L, Appelbaum L. Consistency of Thyroid Imaging Reporting and Data System Reporting in Community-Based Imaging Centers Versus a Large Tertiary Hospital. Endocrine Practice. 2022;28(8):754-9. https://doi.org/10.1016/j.eprac.2022.04.007

37. Chen J, Ge J, Zha M, Miao J-J, Sun Z-L, Yu J-Y. Effects of uric acid-lowering treatment on glycemia: a systematic review and meta-analysis. Frontiers in Endocrinology. 2020;11:577. https://doi.org/10.3389/fendo.2020.00577

38. Clemmons DR. Modifying IGF1 activity: an approach to treat endocrine disorders, atherosclerosis and cancer. Nat Rev Drug Discov. 2007;6(10):821-33. https://doi.org/10.1038/nrd2359

39. Smith TJ, Schneider JE. Insulin-Like Growth Factor Pathway and the Thyroid. Frontiers in Endocrinology. 2021;12:653627.

40. Locatelli V, Bianchi VE. Effect of GH/IGF-1 on Bone Metabolism and Osteoporosis. International Journal of Endocrinology. 2014;2014:235060.

41. Bassett JH, Williams GR. Role of Thyroid Hormones in Skeletal Development and Bone Maintenance. Endocr Rev. 2016;37(2):135-87. https://doi.org/10.1210/er.2015-1106

42. Kong X-J, Liu J, Liu K, Koh M, Sherman H, Liu S, et al. Probiotic and Oxytocin Combination Therapy in Patients with Autism Spectrum Disorder: A Randomized, Double-Blinded, Placebo-Controlled Pilot Trial. Nutrients. 2021;13(5):1552. https://doi.org/10.3390/nu13051552

43. Ahmed SE, Maher FT, Naji NA. Effect of Thyroid Hormones and Trace Elements (Zn, Mg) on Obesity. Tikrit Journal of Pure Science. 2018;21(6):78-84.

44. Elkomy MM, Abdallah HM, El-Sheikh MMM, El-Bayomi K, Hassan H. Anti-osteoporotic effect of medical herbs and calcium carbonate. Journal of Traditional Chinese Medicine. 2015.

45. Zeyadi M, Khalifa F. The protective role of almond and thyme in carbonated beverage-induced osteoporosis in male albino rats. International Journal of Health Sciences. 2022;6(S5):880-90.

46. Carlberg C. Vitamin D and Pigmented Skin. Nutrients. 2022;14(2):325. https://doi.org/10.3390/nu14020325

47. Kapoor B, Kaur G, Gupta M, Gupta R. Sub-chronic safety evaluation of aqueous extract of Alangium salvifolium (L.f.) Wangerin lives in rats. J Adv Pharm Technol Res. 2017;8(3):108-13. https://doi.org/10.4103/japtr.japtr_69_17