



Study the Effects of Ginger (*Zingiber officinale*) Extract on Serum Lipid in Hypothyroidism Male Rats Induce by Propylthiouracil

Nabeel M. N. Al-Sharafi and Mohammed R.A. Al-Sharafi

*Department of Physiology and Pharmacology/Faculty of Veterinary Medicine/University of Kufa/Iraq. Corresponding author: Nabeel M. N. Al-Sharafi
Email address: nabeelm.naji@uokufa.edu.iq

**Department of Medical Laboratory Science /The Humanities and Science University/ Iraq

Abstract

This study was undertaken to investigate the protective role of Ginger against the hypothyroidism induce by Propylthiouracil in male rats on serum lipids.

Eighteen adult male rats were randomly divided into three equal groups (each of six) and treated as follows for four weeks, First group (C) was daily orally gavages with saline solution served as control.. Second group (G1) was daily orally gavages with Propylthiouracil (6 mg/kg B.W.). Third group (G2) was daily orally gavages with Propylthiouracil (6 mg/kg B.W.) in addition to ginger (200 mg/kg B.W.)

Overnight fasting blood samples were collected from the all animals of the experiment at end week of experiment for the determination of serum triiodothyronine (T3), thyroid stimulation hormone (TSH), total cholesterol (TC), triacylglycerol (TAG), very low density lipoprotein-cholesterol (VLDL-C) and high density lipoprotein-cholesterol (HDL-C).

The results showed that the A significant ($P<0.05$) statistical increase in the activity of TSH was observed in propylthiouracil treated groups G1 (3.72 ± 0.73) and G2 (3.28 ± 0.25) as compared to the control (0.0795 ± 0.003) and A significant ($P<0.05$) statistical decrease in the activity of T3 in treated (G1) (2.62 ± 0.2) as compared to the control (3.92 ± 0.08). As well as the results show, a significant ($P<0.05$) elevation in serum TAG, TC and VLDL-C and decrease in HDL-C were observed in animals daily orally gavages with Propylthiouracil 6 mg/kg B.W. (G1) group as compared with control. Oral administration of ginger extract caused a non significant ($P>0.05$) depression in the elevated TAG and VLDL-C concentration in G2 group compared to G1 and control groups . From these results indicating that the effect of orally administration of propylthiouracil to induced hypothyroidism and induction of Dyslipidemia.

On conclusions, the present study confirmed the beneficial effects of ginger extract as a hypolipidemic effects gains the dyslipidemia due to hypothyroidism.

Key word: Hypothyroidism, Propylthiouracil, Ginger, dyslipidemia, Rats.

دراسة تأثير مستخلص الزنجبيل على دهون مصل الدم في ذكور الجرذان المصابة بقصور الدراق المستحدث بالبروبيل ثايورياسيل

*نبيل محمد ناجي الشريفي و **محمد رضا احمد الشريفي

*فرع الفلسفة والأدوية / كلية الطب البيطري / جامعة الكوفة / العراق
** قسم تقنية التحليلات المرضية / كلية الدراسات الإنسانية الجامعة / العراق

الخلاصة:

أجريت هذه الدراسة للتعرف على الدور الوقائي للزنجبيل ضد مرض قصور الغدة الدرقية المستحدث بروبيل ثايورياسيل في ذكور الفئران على نسبة الدهون في مصل الدم.

تم تقسيم ثمانية عشر من ذكور الفئران البالغة عشوائياً إلى ثلاث مجموعات متساوية (كل مجموعة ست حيوانات)، وعملت على النحو التالي لمدة أربعة أسابيع، المجموعة الأولى (C) مجموعة السيطرة تم تجريعها يومياً من المحلول ملحي المتعادل، المجموعة الثانية (G1) تجرع يومياً عن طريق الفم بروبيل ثايورياسيل (6 ملغ / كغم من وزن الجسم). أما المجموعة الثالثة (G2) تجرع يومياً عن طريق الفم بروبيل ثايورياسيل (6 ملغ / كغم من وزن الجسم بالإضافة إلى مستخلص نبات الزنجبيل (200 ملغ / كغم من وزن الجسم). في نهاية التجربة تم جمع عينات الدم من جميع الحيوانات لتحديد (T3) triiodothyronine، هرمون تنشيط الغدة الدرقية (TSH)، الكوليسترول الكلي (TC)، الدهون الثلاثية (TAG)، البروتين الدهني منخفض الكثافة (VLDL) والبروتين الدهني العالي الكثافة (HDL-C). في مصل الدم.

وأظهرت النتائج أن هناك زيادة معنوية ($P < 0.05$) في هرمون TSH في مجاميع G1 و G2 التي جرعت بروبيل ثايورياسيل وبمعدل (3.72 ± 0.73) و (3.28 ± 0.25) عل التوالي مقارنة بمجموعة السيطرة (0.003 ± 0.0795) ولوحظ انخفاض الإحصائي ($P < 0.05$) في نشاط T3 في مجموعة (2.62 ± 0.2) بالمقارنة مع مجموعة السيطرة (3.92 ± 0.08). وكذلك بينت النتائج، زيادة معنوية ($P < 0.05$) في الدهون الثلاثية، والكوليسترول الكلي و البروتين الدهني منخفض الكثافة جداً وانخفاض معنوية ($P < 0.05$) في البروتين الدهني العالي الكثافة الكوليسترول في الحيوانات المعالجة بروبيل ثايورياسيل 6 ملغ / كغم من وزن الجسم (G1) بالمقارنة مع مجموعة السيطرة. بينما تسبب اعطاء مستخلص الزنجبيل عن الفم إلى انخفاض معنوية ($P > 0.05$) في تركيز الدهون الثلاثية و البروتين الدهني منخفض الكثافة جداً في مصل الدم في مجموعة G2 مقارنة G1 و مجموعة السيطرة. لذلك تشير نتائج التجربة إلى أن تأثير تجريع بروبيل ثايورياسيل عن طريق الفم يؤدي إلى حدوث قصور الغدة الدرقية وتحريض فرط الدهون في مصل الدم. واستنتجت الدراسة الأثر المفيدة لمستخلص نبات الزنجبيل باعتباره ناقص لدهون مصل الدم المستحدث بقصور الغدة الدرقية.

الكلمة الرئيسية: الغدة الدرقية، بروبيل ثايورياسيل، والزنجبيل، فرط الدهون، الجرذان.

Introduction

Thyroid hormones are synthesized and secreted by the thyroid gland ⁽¹⁾. Thyroxine (T4) and L-3, 5, 3'-triiodothyronine (T3) are the two forms of thyroid hormone produced. Follicular cells of the thyroid gland produce a glycoprotein, thyroglobulin. The tyrosine amino acid residues on thyroglobulin are iodinated resulting in the formation of mono and di-iodo thyronines (MIT and DIT). Oxidation of iodide transported into the follicular cells to iodine, iodination of the tyrosine residues to form MIT and DIT are catalyzed by the enzyme thyroid peroxidase. Eventually, MIT and DIT are coupled to form T4 and T3⁽²⁾.

One of the most important effects of thyroid hormone causes rapid mobilization and stimulates several aspects of the lipid metabolism, which is believed to result indirectly from an increased overall rate of energy metabolism in all cells of the body under the influence of this hormone ⁽³⁾. Several study conclusions that propylthiouracil-induced hypothyroidism^(4,5). Treatment with propylthiouracil lead to reduction plasma T3 levels to 60% of normal, and to induce a mild hypothyroidism⁽⁶⁾.

Ginger, medicinal species: *Zingiber officinale* ⁽⁷⁾ which have strong aromatic and medicinal properties ⁽⁸⁾. Number of studies show a medical usage of ginger as antibacterial ⁽⁹⁾, Antioxidant⁽¹⁰⁾ and decrease serum cholesterol concentrations ⁽¹¹⁾.

Materials And Methods

Plant Extraction: The ginger was purchased from the local market, the plant powdered of ginger (500 g) was extracted with 70% ethanol using Soxhlet apparatus for 48 hr, filtered with a white cloth and the filtrate was collected and dried at 40 °C incubator.

Animals: Adult male Wistar albino rats weighing (200 -250g) were purchased from animal house of faculty of Veterinary Medicine-Kufa University-Iraq. Rats were housed individually with constant environment in controlled stainless steel cages, temperature (25°C ± 5°C) and light cycle were held constant 12/12 hr. The experimental period was 4 weeks on which food and water were provided ad libitum. Animal's Diet: Pellet diet (commercial diet).

Experimental design: eighteen adult male rats were divided randomly into three equal groups (each of 6 rats). The experimental groups illustrated as follow, first group (C) was daily orally

gavages with saline solution served as control,. second group (G1) was daily orally gavages with Propylthiouracil (6 mg/kg B.W.) ⁽¹²⁾ and third group (G2) was daily orally gavages with Propylthiouracil (6 mg/kg B.W.) in addition to ginger (200 mg/kg B.W.) ⁽¹³⁾

Overnight fasting blood samples were collected from the all animals of the experiment at end week of experiment for the determination of serum triiodothyronine (T3), thyroid stimulation hormone (TSH), total cholesterol (TC), triacylglycerol (TAG), very low density lipoprotein-cholesterol (VLDL-C) and high density lipoprotein-cholesterol (HDL-C).

Biochemical analysis

Serum TSH levels were measured using sandwich ELISA kit (Human Gesellschaft for Biochemica und Diagnostica mbH, Germany) as described by the manufacturer. This ELISA has an analytic sensitivity of <0.10 mIU/L TSH. The absorbance of standards and specimens was determined by using ELISA microplate reader Anthos 2001 (Anthos labtec instruments Ges.m.b.H, Austria). The intensity of color is directly proportional to the concentration of TSH in the standards and samples.

The serum T3 were measured by using competitive ELISA kits (Human Gesellschaft for Biochemica und Diagnostica mbH, Germany) as described by the manufacturer. The ELISA tests have analytic sensitivities of about 0.05 ng/ml T3. The absorbance of standards and specimens was determined by using ELISA microplate reader Anthos 2001 (Anthos labtec instruments Ges.m.b.H, Austria). The intensity of the color is inversely proportional to the amount of T4 and T3 in the standards and

Serum TC TAG and HDL-C concentration was enzymatically measured using enzymatic assay semi-automatic chemistry analyzer Belgium using kit Cyan com./Belgium. And serum very low density lipoprotein-cholesterol concentration was

calculated by dividing serum TAG by five⁽¹⁴⁾.

Statistic Analysis

The results are expressed as the mean values with their standard error. One-way ANOVA followed by Duncan's variance was performed to compare between treatment groups. Significance was set at $p < 0.05$. by used Statistical Package for Social Science (SPSS 20) Ready statistic program 20.

Results And Discussion

The mean value of serum thyrotropin or thyroid-stimulating hormone (TSH) and triiodothyronine (T3) activity in treated and control groups is clarified in Table (1)

A significant ($P < 0.05$) statistical increase in the activity of TSH was observed in propylthiouracil treated groups G1 (3.72 ± 0.73) and G2 (3.28 ± 0.25) as compared to the control (0.0795 ± 0.003). The table also showed a non significant effect between G1 as compared with G2 (3.37 ± 0.2).

A significant ($P < 0.05$) statistical decrease in the activity of T3 was observed in propylthiouracil treated (G1) (2.62 ± 0.2) as compared to the control (3.92 ± 0.08). From the result in table (1) indicating the effect of orally administration of propylthiouracil to induced hypothyroidism.

Table1: Effect of ginger extracted on serum thyrotropin (TSH) (mlu /l) and triiodothyronine (T3) activity (ng /ml) of Propylthiouracil treated rats.

Groups Values	Control	G1 gavage Propylthiouracil	G2 gavage Propylthiouracil + Ginger extract
TSH	0.0795±0.003A	3.72±0.73B	3.28±0.25B
T3	3.92±0.08B	2.62±0.2A	3.37±0.2AB

-mean± SE

- Capital letters denote differences between groups, $P<0.05$.

Serum lipids concentration (mg/dL) :

Table (2) illustrate the mean values of serum triglycerides (TAG), total cholesterol (TC), high density lipoprotein-cholesterol (HDL-C) and very low density lipoprotein-cholesterol (VLDL-C) concentration (mg/dL) in the control and three treated groups along the experimental period.

the result show, a significant($P<0.05$) elevation in serum triglycerides concentration was observed in animals daily orally gavages with Propylthiouracil 6 mg/kg B.W. (G1) group as compared with control with mean values of (51.79±3.57) and (30.19±2.17) respectively.

Oral administration of ginger extract caused a non significant ($P>0.05$) depression in the elevated TAG concentration in G2 group with mean values of (39.64±4.11) compared to G1 and control groups .

As well as , Oral administration of ginger to animal in group T3 caused non significant ($P<0.05$) effect in the elevated TC concentration induce by gavage of Propylthiouracil compared to the control group. The mean value for TC in G1 group was equal to (110.32±5.27) while the mean value in G2 group was equal to (107.85±4.48) and control group (40.80±2.19).

While, A significant ($P<0.05$) decrease in serum HDL-C concentration was found in groups G1 (40.71±2.04) and G2 (39.63±0.90) as compared to the values in G1 control (81.08±1.90).

Oral administration of propylthiouracil to animals in G1 group caused a significant ($P<0.05$) increase in the VLDL-C concentration comparing to control group with mean values (6.03±0.15) and (10.35±1.12) respectively. While orally administration

caused decrease in VLDL-C concentration in G2 near to control group value with non significant ($P<0.05$) effect (7.92 ± 0.82) indicating the protective effect of ginger against propylthiouracil induced hyperlipidemia.

Table 3-2: Effect of ginger extracted on Serum lipids concentration (mg/dL) of Propylthiouracil treated rats.

Groups Values	Control	G1 gavage Propylthiouracil	G2 gavage Propylthiouracil + Ginger extract
TAG	30.19±2.17A	51.79±3.57B	39.64±4.11AB
TC	40.80±2.19A	110.32±5.27B	107.85±4.48B
HDL-C	81.08±1.90B	40.71±2.04A	39.63±0.90A
VLDL-C	6.03±0.15A	10.35±1.12 B	7.92±0.82AB

-mean± SE

- Capital letters denote differences between groups, $P<0.05$.

Propylthiouracil (PTU) was used to induce hypothyroidism in rat. PTU Drug Administration approved thionamide that inhibit thyroid hormone synthesis by interfering with thyroid peroxidase-mediated iodination of tyrosine residues in the thyroid gland at the steps of iodine organification and iodotyrosine coupling and also inhibit the conversion of T4 to T3 in extra thyroidal tissues⁽¹⁵⁾.

PTU induced hypothyroidism in rat by oxidative stress is required to induce cell proliferation in thyroid gland that lead to tissue damage and

apoptosis resulting in goiter or thyroid enlargement^(16,17). The results show, hypothyroid status as the serum T3 and T4 concentration was significantly decreased while the serum TSH concentration significantly increased in the PTU-induced hypothyroid rat compared to control. The results of the present study are in line with those observed by Zbucki *et al.*⁽¹⁸⁾ .who showed a significant decrease in the plasma concentration of T3 and T4 of hypothyroid rats.

The hypolipidemic effect of ginger caused by increase pancreatic lipase activity⁽¹⁹⁾, decrease lipid hydrolyze

gastrointestinal tract⁽²⁰⁾ and increase peristalsis movement of intestine⁽²¹⁾ as well as, the action of ginger may be elevates the activity of hepatic enzyme cholesterol-7 α -hydroxylase which is the rate-limiting enzyme in the biosynthesis of bile acids and stimulates the conversion of cholesterol to bile acids⁽²²⁾. Moreover, ginger antihypercholesterolemic effect may be due to the inhibition of cellular cholesterol synthesis⁽²³⁾, this may be due to the presence of niacin in ginger⁽²⁴⁾.

Conclusions

From the results and discussion obtained from this research, it could be concluded that the concentration 6mg/kg B.W of propylthiouracil could induced hypothyroidism and dyslipidemia in male rats, ginger extract was effective as hypolipidemic agent against dyslipidemia induced by propylthiouracil and this research provide with how thyroid hormone are involved in the regulation of lipid metabolism.

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