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## The effect of lemon juice on the concentration of glucose and some hormones in experimentally fattened male New Zealand rabbits

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### ABSTRACT

The current study was conducted to figure out the effect of experimental fattening of white New Zealand male rabbits and the use of lemon juice on the concentration of glucose and some hormones in the blood serum of these rabbits. 40 white male New Zealand rabbits were used, their ages ranged between 8-10 months, and weights between 1250-1400 g. They were divided into two groups of 20 rabbits/group and placed in separate cages. The first group was fed the standard provender, while the second group was fed a special fattening provender rich in fat for a period of 12 weeks. After the end of the period, all rabbits were weighed. Each group was divided into two groups with 10 rabbits/group: the control group, the lemon group, the fattening group and the fattening group with lemon. These groups were subjected to standard conditions of provender and water, and the lemon group and the fattening group with lemon were dosed with lemon juice 4 ml/kg for 8 weeks, where the dose was daily. The results showed that treatment with lemon juice led to a significant decrease at the probability level ( $p \geq 0.0001$ ) in the concentration levels of glucose, thyroid stimulating hormone (TSH), thyroxine, thyroxine and leptin in both the lemon group and the fattening group with lemon compared to the control group and the fattening group respectively. At the same time, there was a significant increase in the insulin hormone and adiponectin in both the lemon and fattening groups with lemon compared to the control and fattening groups, respectively.

**Keywords:** obesity, leptin, adiponectin, insulin, thyroxine, thyroxine, thyroid-stimulating hormone, lemon juice.

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### INTRODUCTION

Obesity is a complex multifactorial disease. Since 1980, the prevalence of overweight and obesity has doubled worldwide to nearly a third of the world's population. Obesity rates increased at all ages and both genders, regardless of socioeconomic status and ethnicity, despite the varying rates of obesity prevalence and its geographical distribution<sup>1</sup>. According to the World Health Organization, obesity is defined as the abnormal or excessive increase of body fat under the skin or around the organs<sup>2</sup> resulting from the consumption of unhealthy food, as the consumption of fast food plays a significant role<sup>3</sup>, and

obesity directly contributes to the development of many chronic diseases such as cardiovascular disease, type 2 diabetes mellitus, hypertension, breathing and sleep disorders<sup>5</sup>. Obesity is also associated with cerebrovascular diseases related to a decrease in the thickness of the cerebral cortex and dementia<sup>6</sup>. Obesity is a growing health problem in our society; its treatment is a challenge, and many drugs have been used to reduce weight and reduce the risks of associated diseases. However, many weight loss drugs have been withdrawn from the market due to their dangerous side effects, such as aminorex, which causes pulmonary hypertension, and fenfluramine, which causes valvulopathy, and other drugs.<sup>7</sup> Therefore, many natural products and plants have appeared that are used to treat obesity due to their effectiveness and few side effects, such as Lemon Verbena and Hibiscus Flower Extract<sup>8</sup>; hot peppers have been used as a weight reducer because they contain many compounds such as antioxidants, polyphenols, vitamin C and flavonols, these compounds work to eliminate free radicals caused by obesity that lead to inflammation and metabolic disorders<sup>9</sup>, the extract of *Eucalyptus tereticornis* leaves was also used, which is a type of plant used in traditional medicine to treat diabetes, and extracts of eucalyptus leaves have been shown to regulate immune metabolism processes associated with obesity and reduce insulin resistance<sup>10</sup> and other plants. Citrus is one of the world's most important fruit tree crops, and lemon is the family's third most important type of citrus, Rutaceace. Lemon is a health-promoting fruit that is rich in many carotenoids, flavonoids, limonoids, hesperidin, Naringin, flavone citric acid, Terpenes and vitamins such as Vitamin C, E and Thiamine (B<sub>1</sub>), Riboflavin, (B<sub>2</sub>), Niacin (B<sub>3</sub>) and minerals such as iron, zinc, potassium, manganese, selenium and copper, as well as fibers such as pectin<sup>11</sup>. These components gave lemon juice great importance in medicinal uses. Studies have found that lemon juice plays an important role in preventing the formation of kidney stones<sup>12</sup> Lemon juice can also be used as an antimicrobial for many types of bacteria, such as *Escherichia coli* and *Streptococcus pyogenes*, as it inhibits the growth of these types of bacteria<sup>13</sup> and eating a tablespoon of lemon with 20 g of garlic lowered cholesterol in addition to lowering blood pressure for people suffering from high cholesterol<sup>14</sup> The use of a mixture of lemon juice, onion and garlic to reduce cholesterol level showed a decrease in LDL-c level and total cholesterol level and an increase in HDL-c level<sup>15</sup>.

## **MATERIALS AND METHODS**

### **Animals under study**

In this study, 40 male white New Zealand rabbits were used; their ages ranged between (8-10) months, and their weights ranged between (1250-1400) g. Obtained from local markets, they were placed in metal cages specially made for this purpose after ensuring they were free from diseases. Their dimensions are (60 × 60 × 50) cm, and they were under appropriate conditions of temperature ranging between (25-28°C) and a period of illumination of 14 hours per day and good ventilation; they were subjected to an introductory period of one week to acclimatize to the place and the provender before starting the experiment. The standard provender was given to the rabbits using plastic pots in equal quantities and in a constant sequence to all treated rabbits. Water was provided to the rabbits using pots made of plastic and fixed in the cage to prevent water spillage from them.

### **The plant used in the study**

Lemon fruits study, which were obtained from local markets and after making sure of their classification based on<sup>16</sup>, the fruits were cleaned from the soil, were

squeezed using a manual juicer and the resulting juice was filtered using three layers of gauze and was squeezed on the same day the treated rabbits were dosed.

### **Experiment design**

The study was conducted in two phases:

The first phase (rabbit fattening phase): The rabbits were randomly divided into two groups of 20 rabbits/group. After the preliminary period ended, the initial weights of the rabbits were taken. The first group (the group without fattening) began to be fed with the standard provender only, a special provender for rabbits with a protein content of 16.5%. This percentage is approved by the National Research Council (NRC) (1994) [Al-Kattan and Al-Ishlash, 2012]. The second group (the fattening group) was fed a special provender rich in fat by mixing 10% fat (2/3 corn oil and 1/3 tallow) to the standard provender for 12 weeks<sup>17</sup>.

The second phase (rabbits treatment phase): After the fattening phase ended, the rabbits of each group were weighed and then divided into:

Control group (without fattening): This group was treated by giving a standard provender, and the average weight of rabbits for this group was 1282.3 g.

Lemon group: This group was treated by giving a standard provender with lemon juice at a volume of 4 ml/kg body weight, and the average weight of rabbits for this group was 1291.6 g.

Fattening group: This group was treated with a standard provender, and the average weight of rabbits for this group was 2250.3 g.

The fattening group with lemon: This group was treated by giving a standard provender with lemon juice at a volume of 4 ml/kg body weight, and the average weight of rabbits for this group was 2251.1 g.

Note: The rabbits of the control and fattening groups were dosed with physiological saline solution to equalize the stress of holding rabbits<sup>18</sup>.

### **Sample collection**

Blood samples were obtained from rabbits by drawing blood from the heart directly by heart stab using a 10 ml medical syringe after eight weeks of treatment (slaughter day). The blood was placed in tubes with dry, tight covers free of anticoagulant materials and left at room temperature for 20 minutes until the blood clotted. A centrifugal process was conducted at 3000 rpm for 15 minutes to get the blood serum and the blood serum by freezing at -20 °c until the blood sugar and hormonal tests were performed.

### **Estimation of glucose concentration in blood serum**

The concentration of glucose in the blood was estimated using the measuring tapes of the Reflotron device manufactured by the German company Roche, based on the enzymatic method mentioned in<sup>19</sup>; by placing 32 microliters of the sample on the test strip, the sample will flow into the reaction area, D-glucose will be oxidized to  $\delta$ -D-gluconolactone with oxygen and in the presence of glucose oxidase (GOD) and produce hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>), which will oxidize the reagent in the test strip and the presence of phosphate oxidase (POD) and thus a dye will be formed in proportion to the concentration of glucose in the sample.

These reactions occur at 37 °c, and the dye is directly proportional to the glucose concentration in the serum. It is measured at a wavelength of 642 nm, and the glucose concentration appears on the device screen after 125 seconds and in the unit mg/100 ml.

### **Hormonal tests**

The hormones of insulin, leptin, adiponectin, thyroid-stimulating hormone (TSH), T<sub>3</sub> thyronine and T<sub>4</sub> thyroxine were determined in the blood serum of New Zealand male rabbits using the ready-made Accubind ELISA Microwells assay kit, supplied by the American company Monobind Inc., and using the Semi-Automated ELISA shaker-reader device manufactured by the German company Rayto. This test was based on the principle of Direct Sandwich at wavelength 450 nm, and the final results were obtained through the values of the standard curve fixed in the device used <sup>20</sup>.

### **Statistical analysis**

Statistical analysis was carried out using a completely randomized design (CRD), one-way analysis of variance, and the differences between groups were determined using Duncan's Multiple Range tests for all measurements covered by the study, and the level of statistical discrimination was ( $P \leq 0.01$ ), using <sup>21</sup>.

## **RESULTS**

### **The concentration of glucose in the blood serum**

Table 1 shows a significant decrease in glucose concentration in the blood serum of white New Zealand male rabbits at the probability level ( $P \leq 0.0001$ ) for the lemon group compared to the rest of the treatments. The mean was  $3.21 \pm 82.77$  mg/100 ml compared to the control group, whose mean was  $\pm 107.19$  3.26. While the fattening group showed a significant increase in glucose concentration with a mean of  $5.21 \pm 153.52$  mg/100 ml compared to the rest of the treatments. While the fattening group with lemon showed a significant decrease in glucose concentration compared to the fattening group if its mean was  $4.33 \pm 102.72$  mg/100 ml.

### **Insulin hormone in blood serum**

It is clear from Table 1 that there was no significant difference in the concentration of insulin hormone in the blood serum of white New Zealand male rabbits at the probability level ( $P \leq 0.0001$ ) for the lemon group and its mean was  $0.16 \pm 6.17$  pg/ml compared to the control group whose mean was  $0.06 \pm 6.23$  pg/ml, while the fattening group showed a significant increase in the insulin hormone concentration in the blood serum of white New Zealand male rabbits and its mean was  $0.35 \pm 7.25$  pg/ml, while there was a significant decrease in the insulin hormone concentration in the blood serum of white New Zealand male rabbits of the fattening group with lemon, the mean was  $0.03 \pm 6.66$  pg/ml compared to the fattening group.

It was mentioned that feeding mice polyphenols extracted from lemon peels rich in flavonoids with a high-fat diet led to a decrease in the level of the hormone insulin, and this was attributed to the ability of flavonoids to reduce tissue resistance to insulin, thus reducing the level of glucose in the blood and thus reducing the secretion of the insulin hormone. The reason for this is that lemon juice contains Naringin, which leads to lowering the level of the insulin hormone, as well as reducing insulin resistance, and this was indicated by <sup>28</sup>, who observed a significant decrease in the concentration of the hormone insulin and insulin resistance in female mice with polycystic ovary syndrome after being treated with naringin and morin extracts.

As for a reason for the significant increase in the concentration of the insulin hormone in the fattening group compared to the rest of the treatments, it may be attributed to the increase in insulin resistance, as the fatty tissue works to release free fatty acid, reactive oxygen species and proinflammatory cytokines, which leads to the occurrence of systemic inflammation that prevents insulin response and increases the level of glucose and thus increases the secretion of insulin<sup>29</sup>. The reason may be due to an increase in hepatic glucose building and its release into the blood, and this leads to an increase in the secretion of the hormone insulin and a rise in its level in the blood<sup>30</sup>. Alternatively, due to increased leptin resistance and leptin secretion in cases of obesity, which increases the secretion of the insulin hormone<sup>31</sup>.

### **The concentration of leptin in the blood serum**

It is evident from Table 1 that there was a significant decrease in the concentration of leptin hormone in the blood serum of white New Zealand male rabbits at a probability level ( $P \leq 0.0001$ ) for the lemon group and with a mean of  $0.06 \pm 4.39$  pg/ml compared to the control group, whose mean was  $0.06 \pm 4.58$  pg/ml, while the fattening group with lemon showed a significant decrease in the concentration of leptin hormone with a mean of  $900.06 \pm 4$  pg/ml compared to the fattening group whose mean was  $0.14 \pm 5.85$  pg/ml.

(Manuha et al., 2019) Also, it was recommended for people with obesity to consume lemon juice because it contains vitamin C, and it showed a percentage of 32.16 mg per 100 ml of lemon juice and its ability to reduce fat mass as well as the level of concentration of the leptin hormone in obese people.

### **Adiponectin in the blood serum**

Table 1 shows a significant increase in the concentration of the hormone adiponectin in the blood serum of white New Zealand male rabbits in the lemon group. Its mean was  $0.34 \pm 8.33$  mg/L compared to the control group, where its mean was  $0.09 \pm 6.78$  mg/L. At the same time, there was a significant decrease in the concentration of adiponectin hormone in the blood serum of New Zealand male rabbits in the fattening group. Its mean was about  $0.11 \pm 4.45$  mg/L compared to the rest of the treatments. It was also noticed that there was an improvement in the concentration of adiponectin hormone in the fattening group with lemon, and its mean was  $6.74 \pm 0.25$  mg/L; it reached the level of the control group with no significant difference between them.

The results of the current study showed a significant increase in the concentration of the adiponectin hormone in the blood serum of white New Zealand male rabbits in the lemon group and the fattening with lemon group, and this is consistent with what<sup>35</sup> stated in the blood serum of overweight women in the Lemon detox program with a low-calorie diet consisting of a mixture of a drink containing lemon juice to a low concentration of the hormone adiponectin, due to the fact that lemon juice contains flavonoids such as Quercetin, which act as anti-inflammatory by inhibiting TNF- $\alpha$ <sup>36</sup>, or that flavonoids increase the effectiveness of the insulin hormone, which affects the gene expression of adiponectin and increases its secretion<sup>37</sup> or as a result of containing a group of B vitamins that increase the secretion of the hormone adiponectin and this is what<sup>38</sup> indicated, as Vitamin B<sub>3</sub> stimulates the production of adiponectin hormone, by stimulating receptors in fat cells and activating immune cells such as white blood cells, mononuclear cells and neutrophils and stimulating these receptors leads to a rapid increase in the production of the adiponectin hormone and thus reduces fatty tissue, Vitamin B<sub>3</sub> also has an inhibitory effect on TNF- $\alpha$  and interleukin-6 (IL-6), which inhibit adiponectin expression in fat cells<sup>39</sup>.<sup>40</sup> also mentioned that magnesium increases the concentration of the adiponectin hormone when it is taken through foods containing magnesium.

Standard Groups	blood glucose mg/100 ml	Leptin pg/ml	Insulin pg/ml	Adiponectin
control group (Standard provender with plain water)	3.26±107.19 B	0.06±4.58 DE	0.06±6.23 DE	0.09±6.78 C
fattening group (Special provender for fattening with plain water)	5.21±153.52 A	0.14±5.85 A	0.11±7.25 A	0.11±4.45 E
lemon group (lemon juice 4ml/kg body weight)	3.21±82.77 F	0.06±4.39 F	0.16±6.17 E	0.34±8.33 B
A fattening group with lemon (lemon juice 4 ml/kg body weight)	4.33±102.72 C	0.06±4.90 C	0.03±6.66 C	±6.74 0.25 C

**Table 1. Effect of lemon juice and boiled cumin seed extract on the concentration of leptin, insulin and adiponectin in the serum of white male New Zealand rabbits.**

Values are expressed as mean ( $\pm$ ), standard deviation, and number of rabbits/group = 10

Diverse numbers with different letters vertically indicate the presence of a significant difference at the level of probability ( $P \leq 0.0001$ ).

### 3.5. Serum thyroid-stimulating hormone (TSH) concentration

Table 2 shows a significant increase in the concentration of TSH hormone in the blood serum of white New Zealand male rabbits at the level of probability ( $P \leq 0.0001$ ) for the lemon group with a mean of  $0.04 \pm 0.89$  compared to the control group, where its mean was  $(0.03 \pm 0.73 \text{ ng/ml})$ . It showed a significant decrease in the TSH concentration in the blood serum of white New Zealand male rabbits for the fattening group. Its mean was  $0.05 \pm 0.49 \text{ ng/ml}$  compared with the rest of the treatments. In contrast, the fattening group with lemon showed  $0.04 \pm 0.70 \text{ ng/ml}$  improvement in the level of TSH in the blood serum of white New Zealand male rabbits. It reached the level of TSH hormone in the blood serum of white New Zealand male rabbits of the control group with no significant difference between them.

### The concentration of thyroxine in the blood serum

Table 2 shows a significant increase in the concentration of  $T_3$  hormone in the blood serum of white New Zealand male rabbits at the level of probability ( $P \leq 0.0001$ ) for the lemon group and with a mean of  $0.10 \pm 1.72 \text{ ng/ml}$  compared to the control group, whose mean was  $0.03 \pm 1.30 \text{ ng/ml}$ . In contrast, the fattening group showed a significant decrease in the concentration of  $T_3$  hormone in the blood serum of white New Zealand male rabbits, with a mean of  $0.05 \pm 0.76 \text{ ng/ml}$  compared to the rest of the treatments. As for the fattening group with lemon, it improved the level of  $T_3$  hormone in the blood serum of white New Zealand male rabbits, and its mean was  $0.05 \pm 1.21 \text{ ng/ml}$  with no significant difference between them.

### Thyroxine concentration in the blood serum (T<sub>4</sub>)

Table 2 shows a significant increase in the concentration of T<sub>4</sub> hormone in the blood serum of white New Zealand male rabbits at the probability level ( $P \leq 0.0001$ ) for the lemon group, and the mean of the lemon group was  $0.30 \pm 13.08$  ng/ml. In contrast, the fattening group showed a significant decrease in the concentration of T<sub>4</sub> hormone in the blood serum of white New Zealand male rabbits, with a mean of  $0.10 \pm 8.72$  ng/ml compared with the rest of the treatments. As for the fattening group with lemon, there was an increase in the level of T<sub>4</sub> hormone to reach the level of the control group with no significant difference between them. Their mean was  $0.08 \pm 9.33$  ng/ml, respectively, while the mean for the control group was  $0.06 \pm 9.53$  ng/ml.

The results of the current study showed a significant increase in the concentration of TSH, T<sub>3</sub> and T<sub>4</sub> in the serum of New Zealand male rabbits treated with lemon juice compared to the control group and the fattening group. This may be due to the fact that lemon juice contains flavonoids, including rutin, which improve the gene expression of TSH and increase its secretion from the pituitary gland. It also affects the sodium-iodide symporter by which the thyroid gland takes up iodide to make its hormones. It also stimulates the enzyme thyroperoxidase, the key hormone for the formation of thyroid hormones; rutin has an anti-proliferative effect on thyroid cancer cells<sup>43</sup>. Also (Jallod and Al-Kattan 2016) indicated a significant increase in the total capacity of antioxidants in the blood serum of experimentally fattened male rabbits because lemon juice contains flavonoids, which is one of the multiple phenols and is considered one of the most powerful antioxidants that remove free radicals by reducing Oxidative stress and the production of GSH, thus reducing free radicals, and the resulting increase in thyroid secretion<sup>44</sup>.

Standard Groups	TSH ng/ml	T <sub>3</sub> ng/ml	T <sub>4</sub> ng/ml
control group (Standard provender with plain water)	$0.03 \pm 0.73$ C	$0.03 \pm 1.30$ D	$0.06 \pm 9.53$ C
fattening group (Special provender for fat- tening with plain water)	$0.05 \pm 0.49$ D	$0.05 \pm 0.76$ G	$0.10 \pm 8.72$ F
lemon group (lemon juice 4ml/kg body weight)	$0.04 \pm 0.89$ A	$0.10 \pm 1.72$ B	$0.30 \pm 13.08$ B
The fattening group with lemon (lemon juice 4ml/kg body weight)	$0.04 \pm 0.70$ C	$0.05 \pm 1.21$ E	$0.08 \pm 9.33$ D

**Table 2.** Effect of lemon juice and boiled cumin seed extract on the concentration of thyroid stimulating hormone and thyroid hormones in the sera of white male New Zealand rabbits.

Values are expressed as mean ( $\pm$ ), standard deviation, and number of rabbits/group = 10.

Diverse numbers with different letters vertically indicate the presence of a significant difference at the level of probability ( $P \leq 0.0001$ ).

## DISCUSSION

The significant decrease in glucose concentration in all groups treated with lemon juice does not depend on increasing the concentration of the insulin hormone, but through its effect on reducing insulin resistance and a change in glucose metabolism, and this could be related to modifying the action of the insulin hormone and this is consistent with what was stated by <sup>22</sup>, they indicated that mice dosed with lemon juice extract reduced glucose concentration as a result of reducing insulin resistance or outside the effect of the pancreas by inhibiting glucose absorption from the intestine or carbohydrate metabolism or absorption because it contains soluble fiber such as pectin, which works to inhibit glucose absorption in the intestine and inhibiting the activity of the enzyme  $\alpha$ -amylase, which is one of the most important enzymes that works to convert carbohydrates into simple sugars and thus reduce the concentration of glucose in the blood <sup>23, 24</sup> or lemon juice reduces glucose concentration because it contains compounds such as Hesperidin and Naringin, which are considered flavonoids and improve the regulation of fatty acid and cholesterol metabolism and their effect on the enzymes responsible for the Gluconeogenesis process <sup>25</sup> or it contains magnesium and phosphorous, which studies have shown its ability to reduce glucose concentration if its deficiency is one of the causes of obesity and type 2 diabetes <sup>26</sup>. As for a reason for the significant increase in the concentration of glucose level in the blood serum of New Zealand male rabbits in the fattening group, it may be due to the increase in glucose building from non-carbohydrate sources (gluconeogenesis) <sup>55</sup> or the increase in the accumulation of white fat as a result of obesity leads to an increase in the secretion of cytokines, as can be adipocytes stimulate the production of types of free radicals, which in turn increases the unregulated production of adipokines and increases the inflammatory state, which leads to an increase in insulin resistance <sup>53, 54</sup>. The current study showed a significant decrease in the concentration of the insulin hormone in the fattening group with lemon compared to the obese group. This may be because lemon juice contains multiple phenols, which have an important role in reducing the concentration of the hormone insulin in the blood, which was indicated by <sup>27</sup>. The reason for the significant decrease in the concentration of leptin hormone in the blood serum of male New Zealand rabbits in the lemon and fattening with lemon groups can be explained by the fact that lemon juice contains multiple phenols that reduce leptin resistance and reduce fat mass and this is what <sup>27</sup> included, feeding mice with polyphenols extracted from lemon peels with a high-fat diet reduced the concentration of leptin hormone compared to the group that was fed on a high-fat diet only, this was attributed to the ability of multiple phenols to reduce the level of deposited fats, by decreasing leptin resistance and decreasing the level of leptin mRNA. As well as what was indicated by <sup>32</sup> in a study they conducted for obese people, the study showed a significant decrease in the concentration of leptin hormone in the blood serum of people treated with multiple phenols extracted from the plant *Lemon verbena*. The current study also showed a significant increase in the concentration of leptin hormone in the serum of New Zealand male rabbits in the fattening group. This result is consistent with what <sup>33</sup> in their study, as people who eat unhealthy foods rich in fat increase the incidence of obesity as well as an increase in the concentration of the leptin hormone compared to people who eat healthy food and drink fruit juices



regularly, and the reason for this is that the hormone leptin is secreted from the white fat tissue accumulated in obese people, as well as increasing the resistance of the leptin hormone, which leads to a decrease in satiety, as the concentration of the leptin hormone is strongly related to the mass of fat<sup>34</sup>. As for a reason for a significant decrease in the concentration of the adiponectin hormone in the blood serum of white New Zealand male rabbits in the fattening group compared to the rest of the treatments, the reason for this may be due to the correlation of its ratio with the level of glucose and insulin in the blood<sup>41</sup>. Or through its effect on increasing the secretion of TNF- $\alpha$  and IL-6, which are secreted from adipose tissue, increase inflammation in adipose tissue and increase tissue resistance to insulin, thus increasing the release of fatty acids that inhibit the synthesis of the hormone adiponectin and decreasing its concentration in the blood serum<sup>42</sup>. Forty-seven indicated that treating animals suffering from hypothyroidism with olive oil and the solid residues of olives rich in polyphenols improves the secretion of the thyroid gland. Or because it contains selenium, which is necessary for deiodinase activity, and its deficiency leads to a lack of activity of the latter and thus to a decrease in the activity of the thyroid gland<sup>45, 46</sup>. The significant decrease in the concentration of TSH, T<sub>3</sub> and T<sub>4</sub> hormone in the fattening group compared to the rest of the groups was consistent with what was stated by<sup>48</sup>, as it was shown that the TSH hormone was lower in obese people than in people of normal weight, as well as<sup>49</sup> pointed out the relationship between obesity and low secretion of thyroid hormones, this may be attributed to the fact that obesity leads to cell hypertrophy as a result of fat accumulation as well as hypoxia and the generation of systemic oxidative stress in fatty tissues such as OH, O, H<sub>2</sub>O<sub>2</sub> etc., although T<sub>3</sub> and T<sub>4</sub> hormone synthesis is stimulated by thyroid peroxidase and needs ROS, especially H<sub>2</sub>O<sub>2</sub>, are an essential component in the early stages of thyroid hormone production during iodine oxidation, and due to thyroid function, they are particularly vulnerable to oxidative damage<sup>50, 51</sup>. Also, the oxidative stress leads to a decrease in the levels of thyroid hormones from iodothyronin 5- monodeiodination which is a prohormone for T<sub>4</sub> hormone, when reduced, it leads to a decrease in the level of T<sub>4</sub> hormone and indirectly leads to a decrease in the level of T<sub>3</sub> hormone, because T<sub>3</sub> hormone consists of transforming T<sub>4</sub> hormone by stimulating enzymes by removing one atom of iodine<sup>52</sup>.

## CONCLUSION

They investigate the effect of lemon juice on the concentration of glucose, insulin, leptin, adiponectin, thyroid-stimulating hormone, thyroxine and thyroxine in experimentally fattened white male New Zealand rabbits.

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