



STUDY OF THE COMBINED EFFECT OF THE DRUG PROPYLTHIOURACIL AND THE AQUEOUS EXTRACT OF THE LICORICE PLANT ON SOME HORMONAL AND HISTOLOGICAL VARIABLES IN ALBINO RATS

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Article history:	Abstract:
Received: 14 th May 2023 Accepted: 10 th June 2023	This study was conducted at the University of Tikrit, College of Education for Pure Sciences, Department of Biology, in 2024, on the licorice plant, to study the synergistic effect of the drug Propylthiouracil and the aqueous extract of the licorice plant, to reveal the effective biological active compounds contained in this plant and the effect of these compounds on the level of T3 thyroid hormones And T4 and TSH the active compounds detected in the aqueous extract of the licorice plant, which are phenols, flavonoids, alkaloids, glycosides, and tannins. In this study, 10 rats were divided into two groups. The first group was the control group, and the second group was the group treated with the drug Propylthiouracil and the aqueous extract of the licorice plant Treatment with propylthiouracil and aqueous extract of licorice led to a significant decrease ($P \leq 0.05$) in the level of T3 and T4. The same treatment also caused an increase in TSH levels. with propylthiouracil and aqueous licorice extract did not witness any negative side effects on kidney and liver tissues.

Keywords: Propylthiouracil, Licorice Plant, Hormones, Histological

INTRODUCTION

For more than 70 years, thionamide compounds have been used to treat hyperthyroidism. There are three available Thionamide antithyroid drugs are methimazole, carbimazole, and propylthiouracil (Brix *et al*;2020). Propylthiouracil, known as PTU, is an anti-thyroid drug that prevents the creation of thyroid hormones by inhibiting the peroxidase system in the thyroid gland. It is used clinically to treat cases of hyperthyroidism in all age groups (Amisha and Rehman, 2022). It first began to be used in 1940 and was classified One of the most important, effective and safest drugs (Groot *et al.*, 2016). Propylthiouracil was used as an alternative to the drug methimazole in Graves' disease and toxic multinodular goiter and to relieve the symptoms of hyperthyroidism before treatment with radioactive iodine. It is preferable to use it in the first three months of pregnancy It can cause a variety of It has harmful side effects, including liver toxicity and vasculitis (Hiruma *et al.*, 2021).

Licorice is one of the most widespread medicinal plants in the world. It is included in the field of many experiments because of its medicinal importance in ancient and modern times. It is one of the perennial wild plants that belong to the plants of the leguminous family. It is called by several names, including licorice, licorice root, and sweet wood. It grows in many regions of the country. Especially in Mosul, in the alluvial plain, the foothills of the eastern mountains, and in southern Iraq, the marshland region, there are about 30 species of licorice, but fifteen species are under study. Licorice contains a large group of elements, active substances, and nutrients. Iraqi licorice is considered a member of the Glycyrrhizin family, which is one of the... The finest species, as it is characterized by containing the licorice-based substance, which has a sweet taste (Krishnaiah *et al*; 2009).

MATERIALS AND METHODS

This study was conducted for the period from 6/22/2023 until 7/22/2023 in the Animal House Unit / College of Veterinary Medicine / Tikrit University, where the rats were subjected to appropriate environmental conditions in terms of ventilation and temperature of 25 °C and a lighting period of 12 hours. The animals were fed with the standard and mixed ration. From yellow corn 35% wheat 35% soybeans 20% concentrated protein 10%. (Ward,1970).

DISTRIBUTION OF STUDY ANIMALS

The laboratory rats were distributed into two groups, each group containing 5 rats. Each group was placed in a separate cage and provided with water and food in sufficient quantities during the experiment period of 30 days. Each animal was weighed separately before the experiment began, taking into account the similarity in weights between the groups. The weight was then recorded. Weighing them weekly after starting the experiment during the remaining period, the study animals were divided into two groups.

The first group (control): This group was given water and food for 30 days.

The second group (propylthiouracil and licorice group). The animals of this group were given propylthiouracil at a concentration of 50 mg/kg body weight and aqueous extract of licorice at a concentration of 500 mg/kg body weight. It was dissolved in distilled water and dosed orally daily for 30 days.

Estimation of T3 concentration

The concentration of the T3 hormone was estimated by following the steps included with the ready-made analysis kit of the American company Monobind and according to the manufacturer’s instructions for the ELISA technique (Braverman, 1996).

Estimation of the concentration of thyroxine tetraiodine

The T4 hormone concentration was estimated by following the steps included with the ready-made analysis kit (Kit) of the American company Monobind and according to the manufacturer's instructions for the ELISA technique (Mazzafferi and Gharib, 1998).

Estimating the concentration of thyroid-stimulating hormone

The TSH concentration was measured by following the steps included with the ready-made analysis kit (Kit) of the American company Monobind, and according to the manufacturer’s instructions for the ELISA technique (Fisher, 1996).

Statistical analysis

Statistical analysis of the results was conducted using the ANOVA test, and significant differences were determined according to Duncan's multiple ranges test with a significance level of (0.05). (Steel & Torries, 1980).

RESULTS

The results of the current study, as shown in Table (2), showed a significant decrease ($P \leq 0.05$) in the level of the thyroid hormones tetraiodothyroxine (T4) and triiodothyronine (T3) and a significant increase in the level of thyroid-stimulating hormone (TSH).

Table (2): The level of the thyroid hormones.

NO	Parameters Groups	Mean ± SD		
		T3 ng/ml	T4 ng/ml	TSH ng/ml
1	Control	0.5950±0.1118 ab	3.9420 ± 0.687 a	0.0050±0.0000 c
2	Propyl + Lico	0.2646 ±0.0721 f	0.4388 ±0.0420 f	0.0358± 0.0320 b

The current histological study showed in Figure (1) a histological section of the liver of the group treated with propylthiouracil and the aqueous extract of the licorice plant in a synergistic form, the central vein and the hepatic cells and blood sinusoids in an almost normal form.

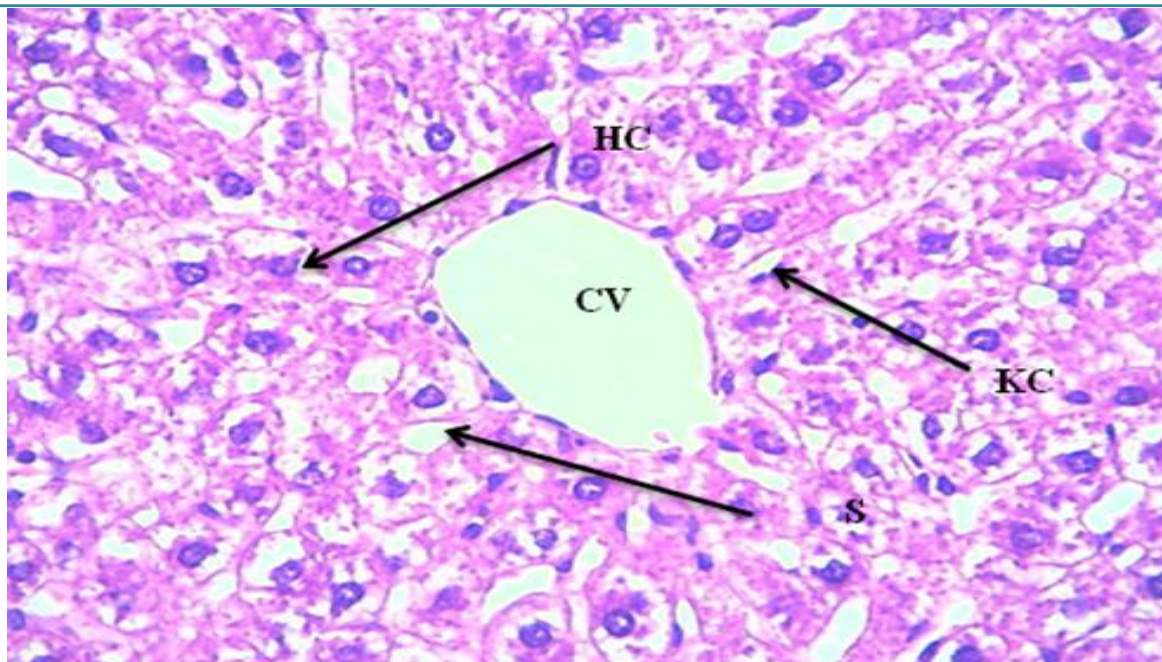


Fig1: A conventional section of the liver of control rats in the first group shows the central vein (CV), hepatocytes (HC), and sinusoids (S). Köffer cells (KC) can also be observed. H & E 400X.

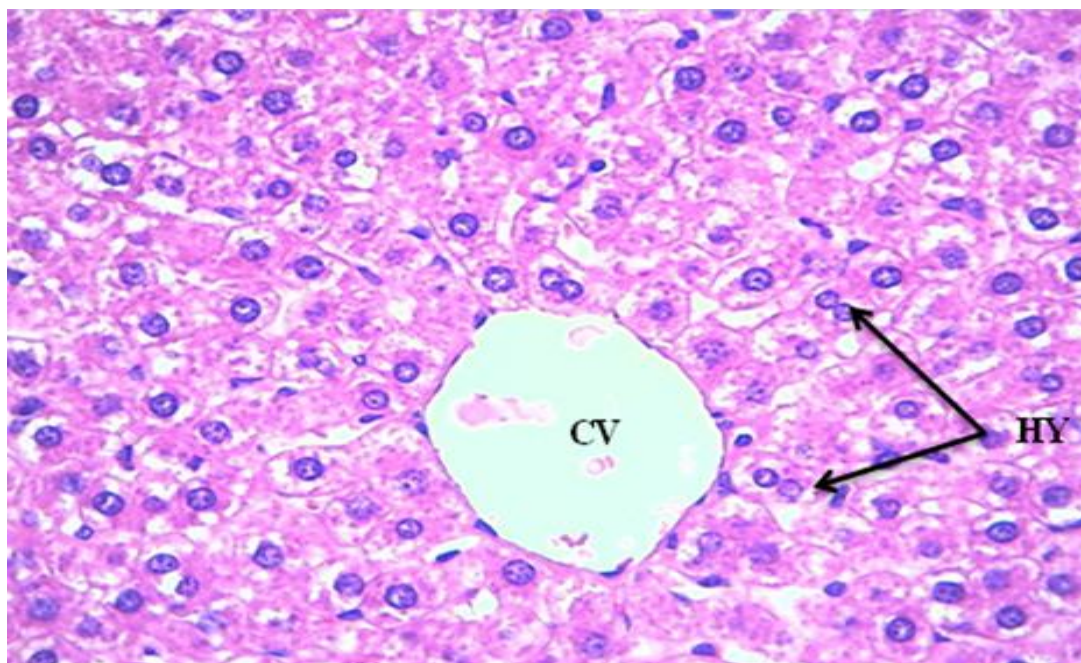


Fig2: A cross- section of the liver of rats of with propylthiouracil second group treated the and aqueous extract of the licorice plant shows the central vein (CV)hepatocytes (HC) and blood sinusoids (s) almost normal. H&400X

DISCUSSION

Synergistic effect occurs when two or more substances work together to produce a combined effect. Many studies have indicated that plant extracts contain biologically active compounds that affect the synthesis, secretion, and function of thyroid hormones. These compounds have a synergistic effect with the drug propylthiouracil in the synthesis of thyroid hormones in various ways. One of these studies is a study conducted by Wang and his group (2023) which showed that the drug affects the process of manufacturing thyroid hormones through several mechanisms, including inhibiting the enzyme thyroperoxidase and inhibiting the process of converting thyroxine T4 to thyronine T3 by inhibiting the enzyme deiodinase. Propylthiouracil reacts with selenium iodide (selenium iodide). This reaction results in the synthesis of the selenium sulfur compound, which inhibits the process of converting T4 to T3 (Jamiu *et al.*,2022).

The reason for the decrease in thyroxine T4 and thyronine T3 is that the drug propylthiouracil inhibits the action of the enzyme thyroperoxidase, which is an essential enzyme in the process of manufacturing thyroid hormones by inhibiting the process of iodine oxidation and the process of coupling iodine absorbed in the thyroid gland with tyrosine (Kahaly *et al.*, 2018).

Phenolic and flavonoid compounds affect the metabolism of thyroid hormones in peripheral tissues by affecting many reactions, including the deiodination reactions by deiodination enzymes. Changes in these metabolic pathways may significantly affect the metabolism of thyroid hormones. In addition, phenolic compounds inhibit the activity of the thyroperoxidase enzyme, which plays a fundamental role in the production of thyroid hormones by oxidizing iodine and binding it to tyrosine (Dos Santos *et al.*, 2011) .

Glycosides are active compounds present in different proportions in the aqueous extract of licorice plant. Glycosides are converted by enzymatic decomposition of intestinal enzymes or by enzymes present in the plant itself into cyanates and then into thiocyanates. They have an antithyroid effect, as it has been proven that thiocyanates inhibit the absorption process of iodide in thyroid tissues, as thiocyanates and iodide compete for the carrier through which iodine is transported into thyroid cells iodide/sodium (DiDalmazi and Giuliani, 2021).

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