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Evaluation of the biological activity of the aqueous extract of *Teucrium Polium* on some biochemical parameters in *Oryctolagus cuniculus* male rabbits

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Abstract---The current study aims to know the protective effects of the aqueous extract of the plant *Teucrium Polium* to reduce the toxic effects of the liver caused by sodium benzoate in male rabbits of the type *Oryctolagus cuniculus* by studying some biochemical parameters, whereas the results of the current study showed that animals dosing with sodium benzoate at a concentration of (250)mg/kg of body weight for 30 days led to a significant increase at ($p < 0.05$) in the concentration of liver enzymes (AST, ALT, ALP) and a significant decrease in the concentration of oxidative enzymes (GSH, CAT) at ($p < 0.05$) in the blood serum of the animals of the positive control group when compared with the animals of the negative control group. Whereas, animals were dosed with cold aqueous extract of *Teucrium Polium* at concentrations (150, 200, 250mg/kg) of body weight for a period of 30 days, and then they were dosed with sodium benzoate at a concentration (250) to reduce the toxic effects of sodium benzoate through a significant decrease in the concentration of Liver enzymes (AST, ALT, ALP) in addition to a significant increase in the concentration of oxidative enzymes (GSH, CAT) at the level of ($p < 0.05$) so that their concentrations became as close as possible to the normal limits when compared with the negative control group, which allows the recommendation to consider the extract of the plant from the preventive against Various toxic effects to the body.

Keywords---sodium benzoate, perennial plant, pathological changes.

Introduction

Medicinal plants

The plant (*Teucrium Polium*) belongs to the Lamiaceae family and has many uses as a food and medicine. It has antioxidant properties. About 27 active compounds have been diagnosed in it that have increased effects on the concentrations of antioxidant enzymes. It also has antispasmodic effects, and digestive diseases. It is used in developing countries. It is widely used for the treatment of many different diseases, including liver problems, blood pressure, antipyretic, rheumatism, parasitic diseases, and it is an antimicrobial, and its importance lies in the fact that it contains many antioxidant elements, as many active compounds have been diagnosed in it that have inhibitory effects on the effect of free radicals In the body (1) (2) . The *Teucrium Polium* plant is a small herbaceous plant that is widely spread in the Mediterranean regions in rocky areas, hills, deserts and dry places (3)

The scientific name of the plant is *Teucrium Polium*, which is derived from the Greek term Teucrum, which is associated with the ancient king of Troy, who was the first to use this plant for medicinal purposes as for the word Polium, it means grayish-white, and this is a reference to the color of the flowers (4). *Teucrium Polium* plant contains many biologically active compounds, the most important of which are Alkaloids, including Stkadrin and Sisteron, in addition to essential oils and flavonoids, which are phenolic compounds and other active substances that have an important role in reducing the risk of disease, They act as an anticoagulant and reduce oxidative stress resulting from It generates free radicals and protects the body from cancer and heart diseases, The plant also contains many volatile oils, which have a major role in treating various infections, in addition to its role in increasing the body's immunity. The plant also contains carbohydrate compounds such as Fructose, Glucose, Sucrose, Ramenose, Ravenose and other sugars, which They are polyhydroxy compounds, which makes them of great importance in animal and plant organisms as they store and transfer energy in addition to being part of cellular components such as chitin in animals and cellulose in plants. (5) (6) (4).

Food additives

Food additives are defined as materials that are not consumed as food in themselves and are not used as an essential ingredient of food, whether they have nutritional value or not, but are intentionally added to food for a technological purpose or for preservation during transportation or storage. These additives or their by-products may become one of the components of this food. (7) (8).

Food additives are one of the important materials because they are linked to human health and safety, as many of them are linked to serious and chronic diseases, and the food industry has become linked to the addition of these materials, and food manufacturers use these materials to present their goods with a delicious taste, attractiveness and beautiful texture for the purpose of increasing their profits, and as a result of increased concentrations These substances in food, food has become a threat to human health and safety(9).

At the present time, many preservatives have been added to food, because the development in the marketing of the various foods offered requires making food in one place and processing it in another place, and then exporting it later to many other countries. Food from spoilage, rotting and unwanted changes that may occur in it (10) Aim of the study: The current study aims to demonstrate the protective effects of the cold aqueous extract of *Teucrium Polium* against the toxic effects of sodium benzoate on some biochemical parameters in male rabbits.

Materials and Methods

In this study, used 40 male rabbits, whose weight ranged from (1000-1500) grams, and their ages ranged between (7-11) months, approximately, they were raised in the animal house of the College of Pharmacy / University of Karbala for the period from October 2021 to December 2021, the animals were placed in special plastic cages covered with metal covers, their floors were brushed with fine sawdust, the cages were cleaned, the floors were constantly changed and sterilized with disinfectants, as well as care Continuous cleaning of perfusion bottles, and the accommodation room, and all the experimental animals were subjected to appropriate laboratory conditions in terms of temperature of 25°C and the duration of lighting and ventilation, the animals were provided with water and a standard diet *Ad libitum* was freed for the duration of the research, and the animals were left for two weeks to adapt to the conditions before conducting the experiment and to ensure that they were free of diseases.

Preparing the of Aqueous Extract of *Teucrium Polium*

The leaves of the *Teucrium Polium* plant were washed with running water, then dried and crushed using a grinder, then mixed (20) g of dry powder with (400) ml of distilled water using an electric mixer and left for (24) hours at room temperature, then filtered the mixture using several layers of medical gauze To get rid of the plankton, then centrifugation at a speed of (3000) revolutions / min for a period of (10) minutes, then filter the extract using mesh filter papers (NO.0.1) type whatman to obtain a clear solution, then dry the extract using an electric oven at 40°C Keep in a cool place until use (11)

Experiment design

The animals were divided into eight groups with five animals for each group. The first group was considered a negative control group and was dosed orally with tap water only, and the second group was a positive control group and was orally dosed with sodium benzoate at a dose of (250 mg/kg) body weight, and the third, fourth and fifth groups were considered extract groups and all dosed with aqueous extract for *Teucrium Polium* plant at a dose of (150,200,250mg/kg) of body weight, as for the sixth, seventh and eighth groups, they were considered protective groups and all dosed with aqueous extract for *Teucrium Polium* plant at a dose of (150,200,250mg/kg) of body weight for the last three groups in addition to sodium benzoate in the same previous dose, respectively, and after the end of the experiment period of (30) days, the animals were brought to the laboratory, after the animals were anesthetized with chloroform Withdrawing blood from the heart directly by Heart Puncture (12) Using a sterile medical

syringe with a capacity of 5 ml, then placing the blood in plastic tubes (Gel-tube) and separating the serum (serum) from it using a centrifuge at a speed of (5000 RPM) for a period of (5 min) and then withdrawing the serum (serum) using a variable micropipette and placed in Ibendrove tube and the serum was kept at (-20)° C for the purpose of conducting biochemical tests and oxidation parameters in blood serum.

Result

First: Study the effect of treatment with sodium benzoate on some biochemical parameters: The results of the current study showed that there are significant differences at the probability level ($P < 0.05$) in the concentration of the studied parameter, where the concentration of liver enzymes (ALT, AST, ALP) increased in addition to a decrease in the concentration of oxidative enzymes (GSH, CAT) in the blood serum of the group of animals dosed with sodium benzoate at a concentration of (250) mg / kg of body weight for 30 days when compared with negative control group Table (1).

Table (1) shows the concentration of liver and oxidation enzymes in the negative and positive control group

Parameter Groups	CAT	GSH	ALP	AST	A LT
Negative control group(G1)	42.41±0.34 A	6.20 ±0.10 A	98.40±0.67 A	31.80±0.48 A	29.80±0.37 A
Positive control group (G2)	32.26±0.25 B	3.73±0.07 B	120.20±0.20 B	40.80±0.37 B	42.60±0.67 B
LSD($P < 0.05$)	0.8244	0.2955	1.4112	1.179	1.2474

Means ± SE

*Different letters mean that there is a significant difference at ($P < 0.05$).

Second: Study the biological activity of the aqueous extract of *Teucrium Polium* plant compared with the negative control group The results of the current study showed that there were no significant differences at the probability level ($P < 0.05$) in the concentration of liver enzymes (ALT, AST) in the blood serum of animals dosed with cold aqueous extract of *Teucrium Polium* plant at concentrations (150,200,250mg/kg) of body weight for a period of 30 days respectively, when comparing the negative control group with the *Teucrium Polium* plant extract groups, while it was noticed that there was a significant difference at the probability level ($P < 0.05$) in the concentration of (ALp) enzyme, as its concentration decreased in the extract groups, in addition to a significant increase at the same level of probability above in the concentration of enzymes Oxidative stress (GSH, CAT) in the extract groups when compared with the negative control group Table (2).

Table (2) shows the concentration of liver and oxidation enzymes in the negative and extract group

Parameter \ groups	CAT	GSH	ALP	AST	A LT
Negative control group (G1)	42.41±0.34 A	6.20 ±0.10 A	98.40±0.67 A	31.80±0.48 A	29.80±0.37 A
first concentrate extract group(G3)	43.62±0.33 B	6.61±0.13 B	96.40±0.50 B	32.00±0.70 A	30.60±0.24 A
Second Concentrate Extract Group(4)	43.15±0.21 B	6.75±0.02 B	96.80±0.20 B	32.80±0.24 A	30.20±0.37 A
Third Concentration Extract Group(5)	43.89±0.03 B	6.68±0.19 B	96.40±0.67 B	32.40±0.24 A	30.10±0.37 A
LSD(P<0.05)	0.8244	0.2955	1.4112	1.179	1.2474

Means ± SE

*Different letters mean that there is a significant difference at (P<0.05).

Third: The protective efficacy of the aqueous extract of *Teucrium Polium* plant compared with the positive control group: The results of the current study showed that there were significant differences at the level (P<0.05) in the concentration of liver enzymes and oxidative enzymes (ALT, AST, ALP) (GSH, CAT) when comparing the positive control group and the protective groups (G3, G4, G5). which was dosed orally with aqueous extract of *Teucrium Polium* plant at concentrations (150,200,250) mg / kg of body weight and then dosed with sodium benzoate at a concentration of (250) mg / kg of body weight for 30 days in respectively where the concentration of liver enzymes decreased and the concentration of oxidative enzymes increased in the extract groups when compared with the positive control group Table (3).

Table (3) shows the concentration of liver and oxidation enzymes in the negative and protective group

Parameter \ groups	CAT	GSH	ALP	AST	A LT
Positive control group (G2)	32.26±0.25 A	3.73±0.07 A	120.20±0.20 A	40.80±0.37 A	42.60±0.67 A
protective group Concentration first	34.52±0.32 B	4.91±0.03 B	117.80±0.37 B	40.80±0.37 B	40.40±0.50 B
protective group Concentration Second	36.83±0.42 B	4.81±0.08 B	118.40±0.50 B	39.00±0.31 B	39.00±0.44 B
protective group Concentration third	38.64±0.14 B	5.04±0.03 B	117.60±0.50 B	39.00±0.31 B	37.00±0.31 B
LSD(P<0.05)	0.8244	0.2955	1.4112	1.179	1.2474

Means ± SE

*Different letters mean that there is a significant difference at (P<0.05)

Discussion

Firstly: The results of the current study showed a clear increase in the concentration of liver enzymes in the blood serum of animals treated with sodium benzoate at a concentration of (250) mg / kg of body weight, along with a significant decrease in the concentration of oxidative enzymes..

The results of the current study are in agreement with the results of the researcher's study (13) which indicated the high concentration of enzymes (ALT, AST) in the blood plasma of the group dosed with sodium benzoate, which had a detrimental effect on all parts of the body, including the liver, being the first center for the treatment of toxins in the body. The release of these enzymes into the bloodstream as a result of destroying the walls of the liver cells, thus increasing their concentration in the serum.

The researchers (14) confirmed in the results of their study that there was an increase in the level of liver enzymes in the group of animals dosed with sodium benzoate, and they indicated that this increase was caused by the harmful effect of sodium benzoate on hepatocytes, which causes decomposition Its plasma membrane, which leads to the massive exodus of these enzymes into the bloodstream, or as a result of oxidative stress, which can lead to the breakdown of fats, proteins and DNA in the hepatocytes, leading to their degeneration and then the destruction of those cells and thus the exodus of the contents of these enzymes into the blood.

While the results of the current study agreed with the results of the researchers' study (15), who noticed a rise in the concentration of these enzymes in the bloodstream. He justified this rise to the fact that the liver is one of the largest specialized organs to perform many functions in the body, including removing toxins, which makes It is subject to damage and damage due to these substances and the resulting metabolism of free radicals that cause significant damage to hepatocytes.

The researchers' study (16) confirms the results of the current study, as it indicates a severe rise in the concentration of liver enzymes in the blood serum of animals treated with sodium benzoate. Cell necrosis caused by biochemical changes resulting from liberated free radicals resulting from poisoning the body with these substances. The study (17) indicated a significant increase in the concentrations of liver enzymes in the groups treated with sodium benzoate, as this substance caused toxicity to the liver cells, leading to damage to them, accompanied by the release of these enzymes into the blood at high rates Poor liver function.

The researchers (18) also noted a very clear rise in the concentration of these enzymes in the blood serum when male rats were orally dosed with sodium benzoate in different concentrations for a period of 30 days, and that the reason for the rise of these enzymes is due to the fact that the liver is the main site in the treatment and removal of The toxins resulting from the toxicity of sodium benzoate in the body, as these substances work to liberate free radicals that

would break down the cellular membranes of hepatocytes, thus releasing these enzymes into the bloodstream and raising their concentrations in the serum.

The researcher (19) confirms in his study these results, as he showed that there is a rise in the concentrations of these enzymes (ALT, AST, and ALP) when adult and immature male rats are dosed for different periods with sodium benzoate, and indicates that the reason for the high these enzymes are due to the toxicity of sodium benzoate, which the liver in turn works to reduce or eliminate as toxic substances. Their increase in the liver cells leads to the death of those cells, followed by laceration in their membrane and hemorrhage within the liver tissue, and thus the filtration of high concentrations of liver enzymes into the blood as a result Harm .

With regard to the effect of the duration of administration, the results showed that the longer the period of administration of sodium benzoate increased, this led to an increase in the levels of these enzymes dosage and duration of dose (20). The results of the current study related to the concentration of antioxidant enzymes also agreed with the study (21) that was conducted on mice, which was divided into three groups and then dosed with sodium benzoate at different concentrations (150, 300, 600) mg/kg of body weight. The results showed that there are a clear decrease in the level of glutathione and catalase concentrations. The reason for the decrease may be the presence of damage to liver tissue or the presence of other toxic effects in the body's systems that require an increase in the consumption of glutathione and catalase as a result of the toxic effects of sodium benzoate that affect all organs of the body.

The results of the current study also agreed with the study of (22) who also found a decrease in the concentration of GSH when rats were dosed with different concentrations and for different periods of time with sodium benzoate, and explained the reason for the decrease in GSH concentration due to an increase in its consumption in the treatment of free radicals or a decrease in the process of Build it inside the body. And this is consistent with the results of (23), who indicated that one of the requirements for building glutathione is its dependence on ATP and glycine, and that using glycine to detoxify sodium benzoate may lead to a decrease in the process of building glutathione.

Secondly: The results of the current study showed that the treatment of animals with aqueous extract of the *Teucrium Polium* plant did not cause any significant change in the concentration of liver enzymes (ALT,AST), while a significant decrease in the concentration of enzymes (ALP) was observed at the comparison between the negative control group and the extract group, in addition to a significant increase in the concentration of oxidative enzymes.

The results of the current study agreed with the results of the study of researchers (24), who noticed a clear decrease in the concentration of these enzymes in the group of animals dosed with aqueous extract of *Teucrium Polium* plant, which was attributed to the fact that the plant extract in the body prevents the generation of free radicals and this is due to the active compounds that Possessed by the perennial plant, of which flavonoids are the main active contents

in it, which contribute to improving the liver's performance in getting rid of toxic substances entering the body.

On the other hand, the researchers' study indicated (25) that there was a significant decrease in the concentration of liver enzymes in the bloodstream of the collectors who were given the alcoholic extract of the *Teucrium Polium* plant. Enzymes by restoring the structural and functional structure of the liver by preventing the formation of free radicals that destroy the membranes of hepatocytes and thus maintaining the structure of the cells, which leads to the preservation of these enzymes within the hepatocytes.

While the results of the current study did not agree with the study (26) who noticed an increase in the concentration levels of these enzymes in the groups dosed with aqueous extract of *Teucrium Polium* plant when compared with the non-dose group. Shorten the duration of the experiment.

The results of the current study are in agreement with the results of the study (27) which noted an increase in the level of these parameters in groups of mice treated with aqueous extract of *Teucrium Polium* plant. Responsible for the integrity of tissues in all organs of the body, which led to the production of large quantities of these antibiotics, which appeared in high concentrations.

The results of the study come to confirm the results of the study (28), which noted that there was a clear increase in the levels of these antigens in the groups treated with the aqueous extract of the *Teucrium Polium* plant in mice with diabetes induced by (STZ). The wrinkle that is concentrated in the leaves of the plant because it contains phenolic compounds, which are antioxidants, which work to inhibit the oxidation of fats, which leads to the absence of free radicals. Also, prolonging the first stage of the oxidation process delays the formation of peroxides and hydroperoxide, which leads to a decrease in the concentration of MDA, whose quantity is proportional to its quantity. Directly with the formation of free radicals.

Third: The results of the current study showed that animal dosing with the plant extract led to a significant decrease in the concentration of liver enzymes when compared with the positive control group accompanied by a gradual increase in oxidative enzymes. The results of the current study are in agreement with the results of the study (29) who noticed a very clear decrease in the concentration of liver enzymes in the protective groups dosed with aqueous extract of *Teucrium Polium* plant. The blood thus maintains the integrity of the hepatocytes and thus the concentration of those enzymes in the bloodstream decreases.

In the same direction, a study (30) indicated that there was a decrease in the concentration of these enzymes when mice were dosed with different concentrations of aqueous extract of the *Teucrium Polium* plant in the protective groups, and the concentration of these enzymes decreased directly with the concentration of the given dose. Structure and Function of the Liver Due to the fact that the *Teucrium Polium* plant contains potent compounds that are powerful antioxidants that help the liver maintain its normal function by inhibiting the formation of free radicals.

The results of the current study agreed with the results of the study (31) who noticed a gradual increase in the concentration of (GSH, CAT) in the protective groups when compared with the control group dosed with the toxin. Helps to scavenge free radicals, thus gradually increasing the concentration of antioxidants, as well as containing effective antioxidants such as flavonoids, and this inhibits the formation of free radicals as well.

The results of the current study also agreed with the results of the study (32) where a very clear rise in the level of (GSH) was observed in the animals of the protective group, where it increased by about 80% of its percentage in the control groups dosed with the toxin, in addition to a high concentration of (GPX, SOD) respectively, as the reason for that rise is that the plant contains antioxidants such as phenolic substances and volatile oils that are important in treating many infections.

The results of the current study contradicted the results of the study (33) which noted a clear increase in the concentration level of (GSH, CAT) rats with diabetes induced by *Streptozotocin*, which were dosed 0.5 g/kg of body weight of the aqueous extract of the *Teucrium Polium* plant for a period of 30 days. The concentration of (GSH, CAT) increased in the pancreatic tissues. He explained the reason for this increase because the chemical compounds in the plant have a wide range of pharmacological effects, including antioxidants and anti-inflammatory.

Conclusions

The results of the current study show that the cold aqueous extract of the *Teucrium Polium* plant possesses anti-toxic properties.

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