ARTICLE / INVESTIGACIÓN

Synergistic effect of Rosemary and Lemon extractions on some physiological and biochemical parameters of CCl_4-Stressed male rats

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Abstract: This study was carried out to examine the preventive impact of marine extracts of rosemary and lemon individually or together in adult-male rats with liver injury induced by carbon tetrachloride. The extracts were prepared and tested on 40 male rats distributed into groups by collecting blood samples and conducting some hematological and biochemical parameters. CCl_4-induced significant increases in the weight of the liver and heart, while rosemary and lemon extracts alone were not able to restore the liver weight, but the effect was in the synergy. As well, the extracts alone or in combination had a significant impact on reducing heart weight. Additionally, CCl_4 caused a substantial reduction in RBC, Hb, PCV, MCV, MCHC and lymphocytes, whereas WBC, monocyte and granulocyte increased. While extracts exhibited an enhancement in these parameters, the best effect was when the two extracts were used together. The biochemical parameters indicated high significance in glucose, AST, ALT and triglycerides; however, total protein, albumin, cholesterol and T-AOC decreased compared to the control group. Both rosemary and lemon worked to restore and remove the oxidative effect.

Key words: Rosemary(A plant that grows in mountainous regions), Lemon, Carbon tetrachloride, Stress, Rats.

Introduction

Carbon tetrachloride (CCl_4) is a synthetic chemical. It does not occur naturally but is present in the environment because it does not decompose easily and has built up over time from human activities. CCl_4 is a colorless gas found in the air. It is used to produce refrigerant fluid, cleaning fluid, pesticides, degreasing agents, fire extinguishers and in stain removers[1]. It is generally used to induce free radical toxicity in various tissues of experimental animals such as the brain, heart, lung, testis, liver, kidney, and blood[2]. On the other hand, CCl_4 is a potent hepatotoxic, and a single exposure to it can rapidly lead to severe centrifugal necrosis and steatosis[3].

Free radicals cause injury that leads to peroxidative oxidation of biofilms and DNA that leads to tissue damage, and as a result, causes many diseases. Antioxidants come from the impacts of free radicals and might prevent the body from many diseases[4].

Rosemary is a sweet-smelling evergreen herb with leaves like needles of pine, used as a flavor for cooking. Rosemary is grown in Asia, and the Mediterranean lives for long periods and tolerates drought. The plant is 1.5-2 cm in height and beyond. The leaves are high and broad (2-5 mm), green and white downward, and have thick fine hairs. The flowers come in many colors, like white, dark blue, pink and purple. The gastrointestinal tract can absorb rosmarinic acid. *Rosmarinus officinalis* is a medicinal plant used in the treatment of a variety of disorders. It contains phytochemical compounds like rosmarinic acid, caffeic acid, ursolic acid, betulinic acid, camphor, carnosic acid and antioxidants. Rosemary is rich in several vital activities like antioxidant factors[5,6].

The pathophysiological mechanisms for a chemical that stimulates hepatotoxicity are still not completely understood. Still, it is mainly related to the conversion metabolism of xenobiotics to reactive oxygen species (ROS) that motivate oxidative stress and then destroy cell macromolecules[7].

Herbal medicine is based on the assumption that plants consist of natural substances which reduce disease and promote health. Many herbs can help lower high cholesterol, and blood sugar, activate the immune system and provide some protection against cancer[8].

Rosemary has been authenticated to have several curative applications in medicine to treat or manage various ailments like digestive and respiratory disorders and inflammatory diseases[9]. Oxidative stress is a natural activity due to a glitch between producing free radicals and antioxidants. It is one of the most critical problems that affect animals and causes serious problems that affect health and production[10].

Additionally, fruit extracts rich with antioxidants, like Lemon juice, have been used as active agents in reducing the ROS concentration within cells and protecting the functions of lipids, DNA and mitochondria from damage caused by free radicals[11].

Lemon juice contains several important chemical components with healing properties like citric acid (vitamin C) and high concentrations of polyphenols. Other micro-nutrients reported in lemon juice is potassium, magnesium, limonoids, xanthoxyletin, folic acid, oils, volatile acids, glycosides and carotenoids. This antioxidant is known for eliminating free radicals and preventing the disease from stress factors by alkalinizing the body through its acidic nature[12,13].

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Citrus flavonoids are effectively used in complementary therapies, as they have antioxidant, anti-cancer, anti-inflammatory and pharmacological properties[14].

The present study is designed as a part of the therapeutic approach to evaluate the antioxidant effect of rosemary and lemon juice extracts on carbon tetrachloride-induced oxidative stress on some hematological and biochemical parameters in rats' males.

Materials and methods

Rosemary extract

50 g of rosemary was soaked in 150 ml boiling water for 3 hours, then filtered with carbon-silica cloth and filter; approximately 45 ml was stored in a refrigerator at 4 C°[15].

Lemon extract

Lemon was obtained from the markets and cleaned with Deionized water. The eaten fraction was weighed and mixed with deionized water (1:1, m/v), the mixture was blended by a homogenizer. Then, it was centrifuged at 5000 rpm for ten minutes, and the supernatant was obtained[16].

Animals

Forty male albino rats weighing 150-200 g were used in the study. The rats were kept under constant conditions of temperature 25 ± 2°C. They were allowed free access to food and water during the experimental period.

Experimental design

The experimental rats were divided into eight groups:

Group 1

Served as control.

Group 2

Were injected intraperitoneally with CCl_4 in olive oil (10% V/V) at a dose of 1ml /kg twice a week for 30 days.

Group 3

Rats were orally administrated with 0.5 ml of rosemary extract by gavage tube.

Group 4

The rats administrate daily lemon extract 10 ml/kg by gavage tube.

Group 5

Were given rosemary and lemon extract orally.

Group 6

The rats were injected intraperitoneally with CCl_4 twice a week and administrated with rosemary extract daily.

Group 7

Rats were intraperitoneally injected twice a week with CCl4 and given daily lemon extract.

Group 8

The rats were injected with CCl_4 and administrated two extracts.

Blood collection

The blood samples were collected from the eye socket of the rats, part of it put into an EDTA tube and the other in non-heparinized tubes. The samples were left for 15 minutes at room temperature; then, the tubes were centrifuged for 15 minutes at 3000 rpm to get serum and kept frozen until use.

Hematological Biochemical Parameters

The hematological factor represented by assessment of complete blood count (CBC) and the biochemical were carried out: glucose, cholesterol, triglycerides, alanine aminotransferase, aspartate aminotransferase, total protein and albumin.

Human Total Antioxidants Capacity Eliza Kit

The kit prepared by Bioassay Technology Laboratory is used to detect total antioxidants capacity (T-AOC) in serum.

Statistical Analysis

SPSS version (26)

The data were performed by using the Duncan test, one-way ANOVA at the value of $P \leq 0.05$ by using SPSS version (26)[17].

Results

The results showed a significant difference in liver and heart weights for 30 days compared with the control group when rats were treated with rosemary and lemon extracts. The study also indicates that CCl_4 increased the importance of the two organs, while rosemary and lemon extracts alone were not able to restore weight of the liver, but the effect was in the synergy between the two extracts. Additionally, the extracts alone or in combination significantly reduced heart weight and returned it to approximately the control group, table (1).

The results, which is agreement with[18,19], confirmed that CCl_4 administration alone induced a pronounced increase in both spleen index and liver index compared with the control group after continued administration 8 weeks. Additionally, the results are in agreement with[20]. They demonstrated that the body weight significantly decreased, whilst liver index and weight increased after receiving 1 ml/kg of CCl_4 orally (diluted in 50% olive oil) twice a week for eight weeks in the model group. Whereas[21] showed upon treatment with CCl_4 for eight weeks, a significant ($P < 0.05$) increase in the absolute and relative weight of the liver was observed with a notable decrease in body weight. In contrast, simultaneous management of silymarin and CCl_4 recovery of the liver and body weight toward control rats. furthermore[22] indicated that left ventricular, whole heart weight and their ratio to body weight for the CCl_4-treated intraperitoneal group were significantly higher than that of the control group.

Al-Attar[23] noticed that the liver/body weight ratio values did not change statistically in normal rats supplemented with olive leaves extract, rosemary leaves extract, or with olive and rosemary leaves extracts in addition to thioacetamide.

The results of table (2) confirmed that rats intraperitoneally injected with CCl_4 caused significant erythrocytopenia reduction in Hb, PCV, MCV, MCHC and lymphocytes in comparison with the control group. As well as a substantial leukocytosis increase in a number of monocyte and granulocyte. Rosemary also showed significant differences

Groups	Liver	Heart
Control	2.96 ± 0.11 ^{a}	0.29 ± 0.00 ^{a}
CCl_4	5.89 ± 0.00 ^{c}	0.51 ± 0.01 ^{e}
Rose	3.05 ± 0.26 ^{a}	0.39 ± 0.03 ^{d}
Rose + CCl_4	5.50 ± 0.20 ^{c}	0.38 ± 0.01 ^{cd}
Lemon	4.03 ± 0.04 ^{b}	0.32 ± 0.00 ^{abc}
Lemon + CCl_4	4.12 ± 0.08 ^{b}	0.31 ± 0.03 ^{ab}
Rose + Lemon	3.28 ± 0.02 ^{a}	0.37 ± 0.00 ^{bcd}
Rose + Lemon +CCl_4	3.39 ± 0.02 ^{a}	0.39 ± 0.03 ^{d}

* 3 replicates were used for each treatment.
** Based on the Duncan test, the vertically different letter indicates a significant difference between treatments at $P \leq 0.05$.

Table 1. Effect of rosemary and lemon extract on liver and heart weight of white rats.

	Control	CCl_4	Rose	Rose + CCl_4	Lemon	Lemon + CCl_4	Rose + Lemon	Rose + Lemon+CCl_4
	Mean ± SE	Mean ± SE	Mean ± SE	Mean ± SE	Mean ± SE	Mean ± SE	Mean ± SE	Mean ± SE
RBC	7.32 ± 0.04^{c}	6.04 ± 0.01 ^{a}	8.23 ± 0.08 ^{e}	7.23 ± 0.13 ^{c}	6.93 ± 0.09 ^{b}	8.00 ± 0.08 ^{e}	7.67 ± 0.05 ^{d}	7.41 ± 0.07 ^{c}
Hb	13.8 ± 0.11 ^{cd}	10.9 ± 0.34 ^{a}	13.8 ± 0.35 ^{cd}	12.9 ± 0.28 ^{b}	13.4 ± 0.17 ^{bc}	14.2 ± 0.10 ^{d}	13.9 ± 0.11 ^{cd}	13.7 ± 0.12 ^{cd}
PCV	37.6 ± 0.51^{def}	31.4 ± 0.41 ^{a}	38.4 ± 0.00 ^{f}	34.1 ± 0.29 ^{b}	36.3 ± 0.34 ^{c}	37.4 ± 0.30 ^{de}	38.3 ± 0.15 ^{ef}	36.9 ± 0.05 ^{cd}
MCV	51.5 ± 0.62 ^{d}	46.7 ± 0.17 ^{b}	52.0 ± 0.57 ^{d}	47.3 ± 0.20 ^{b}	52.5 ± 0.40 ^{d}	44.7 ± 0.28 ^{a}	50.0 ± 0.26 ^{c}	49.8 ± 0.56 ^{c}
MCH	18.8 ± 0.11 ^{cd}	16.7 ± 0.17 ^{a}	18.0 ± 0.29 ^{b}	17.8 ± 0.00 ^{b}	19.3 ± 0.12 ^{d}	16.9 ± 0.51 ^{a}	18.1 ± 0.20 ^{bc}	18.4 ± 0.11 ^{bc}
MCHC	37.6 ± 0.21 ^{cd}	35.9 ± 0.28 ^{b}	34.7 ± 0.00 ^{a}	37.8 ± 0.11 ^{d}	36.9 ± 0.17 ^{d}	37.9 ± 0.11 ^{d}	36.2 ± 0.23 ^{bc}	37.1 ± 0.17 ^{d}
WBC	9.69 ± 0.18 ^{b}	11.8 ± 0.07 ^{d}	9.29 ± 0.09 ^{a}	9.34 ± 0.00 ^{a}	9.18 ± 0.02 ^{a}	10.64 ± 0.06^{c}	9.64 ± 0.09 ^{b}	10.55 ± 0.75 ^{c}
Lymph	8.05 ± 0.04 ^{f}	6.64 ± 0.08 ^{c}	6.48 ± 0.02 ^{bc}	5.92 ± 0.10 ^{a}	7.15 ± 0.08 ^{d}	6.26 ± 0.13 ^{b}	7.74 ± 0.05 ^{e}	7.03 ± 0.04 ^{d}
Mono	1.04 ± 0.02 ^{a}	2.50 ± 0.11 ^{f}	1.97 ± 0.01 ^{e}	1.71 ± 0.03 ^{d}	1.17 ± 0.07 ^{a}	1.61 ± 0.05 ^{cd}	1.36 ± 0.01 ^{b}	1.52 ± 0.01 ^{c}
GRA	0.60 ± 0.05 ^{a}	2.67 ± 0.01 ^{d}	0.84 ± 0.02 ^{b}	1.71 ± 0.04 ^{c}	0.86 ± 0.02 ^{b}	2.77 ± 0.01 ^{d}	0.54 ± 0.00 ^{a}	1.80 ± 0.06 ^{c}

* RBC ($\times 10^6/\mu l$) - Hb (g/dl) - PCV and PDW (%) - MCV (fl) - MCH (pg) - MCHC (g/L) - WBC, Lymph, Mono and GRA ($\times 10^3/\mu l$).

** 3 replicates were used for each treatment.

*** Based on the Duncan test, the horizontally different letter indicates a significant difference between treatments at $P \leq 0.05$.

Table 2. Effect of rosemary and lemon extract on hematological parameters of white Rats.

in most treatments compared to the rosemary and CCl_4 groups. Additionally, to a significant presence between the lemon and lemon with CCl_4 group. The best effect was when the two extracts were used together.

The reduction in RBC count and its indices may condole to the oxidative-stress force by CCl_4[24]. At the same time, the increases in WBC may be due to the immune defense mechanism[25].

Our results agreed with Ubhenin[26], they tackled a significant increase in WBC count with a similar reduction in RBC count and difference compared to the control when given CCl_4 at the day 14 and 28 pretreatments with *Pleurotus ostreatus* for 28 days. Also[27], They demonstrate a significant ($P<0.01$) decrease in the RBC, Hb, PCV, MCV, MCH and platelet count. At the same time, MCHC was higher ($P<0.01$) in the rats exposed to CCl_4 without treatment with *Cnidoscolus aconitifolius* extract. While[28] revealed a depletion of RBC and a decrease in PCV and Hb in addition to an elevation in the levels of WBC caused by CCl_4 compared to control samples after 28 days.

Regarding the effect of rosemary and lemon extracts on some biochemical variables in the serum of rats induced with CCl_4, the results demonstrated that the injection of it caused significant increases in glucose, AST, ALT and triglycerides. In contrast, total protein, albumin and cholesterol decreased compared to the control group. Both rosemary and lemon extracts, either alone or in combination, restored glucose and removed the oxidative effect of CCl_4. The results also showed significant differences in AST, ALT enzymes, total protein, albumin, cholesterol and triglycerides in all groups treated with these extracts compared to the control group (Table 3).

CCl_4 is converted to trichloromethyl free radical, and then in the presence of oxygen, trichloromethyl free radical is converted to trichloromethyl peroxide. These free radicals cause oxidative stress, destruction of plasma membrane and damage to liver tissues[29].

Saba[27] observed that there was hepatocellular damage caused by CCl_4 toxicity, caused serum AST, ALT and ALP to be significantly increased in the group exposed to CCl_4 alone. In contrast, CCl_4 caused a decrease in total serum protein, which may be due to the reduced number of hepatocytes caused by the liver's inability to synthesize protein. Additionally, a reduction in serum albumin might be associated with biliary liver damage and active cirrhosis[30].

The results of Zhou, T[16] point out that rats were given 1 ml /kg b. wt. CCl_4 scored severe liver damage compared to the control, evidenced by a marked increase in serum liver enzyme levels: ALP, AST and ALT, whereas total protein was decreased. Hira S[31] shown that treatment with CCl_4 led to significant increases in the serum levels of liver biomarker enzymes ALP, ALT and AST. In contrast, the total serum protein level was reduced relative to the normal control mice. They also indicated that liver biomarkers are present in the mitochondria of hepatocytes. However, CCl_4 damages the hepatocyte membrane, leading to loss of structural integrity and leakage of liver enzymes from the mitochondrion into the blood circulation.

Almundarij[32] noticed that total protein and albumin levels were significantly decreased in injection substantially CCl_4-treated rats. The CCl_4 toxicity has 3 or 4 distinguished phases. The first two weeks are mainly characterized by ne-

	Glucose	AST	ALT	T. P	ALB	CHO	TRI
	Mean ± SE	Mean ± SE	Mean ± SE	Mean ± SE	Mean ± SE	Mean ± SE	Mean ± SE
Control	70.0 ± 1.15 ^{a}	73.0 ± 0.57 ^{b}	28.0 ± 1.15 ^{ab}	7.10 ± 0.23 ^{a}	3.30 ± 0.05 ^{ab}	84.0 ± 2.30 ^{cd}	66.0 ± 0.00 ^{ab}
CCl_4	114.0 ± .57 ^{e}	117.9 ± 1.71 ^{a}	61.9 ± 4.27 ^{d}	5.80 ± 0.00 ^{d}	2.90 ± 0.06 ^{c}	58.0 ± 3.46 ^{a}	73.0 ± 7.50 ^{b}
Rose	89.0 ± 6.92 ^{bc}	102.0 ± 0.50 ^{e}	26.0 ± 1.16 ^{ab}	6.80 ± 0.17 ^{abc}	3.50 ± 0.05 ^{a}	86.0 ± 5.77 ^{d}	57.0 ± 6.64 ^{a}
Rose + CCl_4	103.0 ± 1.73 ^{bc}	94.0 ± 2.30 ^{d}	34.0 ± 1.73 ^{c}	6.50 ± 0.28 ^{abcd}	3.15 ± 0.08 ^{bc}	78.0 ± 2.88 ^{cd}	58.0 ± 0.60 ^{a}
Lemon	80.0 ± 3.46 ^{ab}	84.0 ± 2.31 ^{c}	24.0 ± 0.50 ^{a}	6.20 ± 0.11 ^{bcd}	3.20 ± 0.06 ^{b}	75.0 ± 0.00 ^{bc}	66.0 ± 2.30 ^{ab}
Lemon + CCl_4	106.0 ± 8.08 ^{de}	74.0 ± 1.73 ^{b}	27.0 ± 1.10 ^{ab}	6.10 ± 0.23 ^{cd}	3.15 ± 0.08 ^{bc}	65.0 ± 1.15 ^{ab}	67.0 ± 1.15 ^{ab}
Rose + Lemon	94.0 ± 2.30 ^{cd}	93.0 ± 1.70 ^{d}	32.0 ± 0.60 ^{bc}	6.90 ± 0.40 ^{ab}	3.25 ± 0.14 ^{b}	85.0 ± 5.19 ^{cd}	66.0 ± 5.77 ^{ab}
Rose+Lemon+C Cl_4	87.0 ± 0.56 ^{bc}	88.0 ± 0.60 ^{c}	30.0 ± 1.17 ^{abc}	6.50 ± 0.12 ^{abcd}	3.15 ± 0.04 ^{bc}	66.0 ± 0.57 ^{ab}	61.0 ± 0.57 ^{ab}

* Glucose(mg/dl), AST-Aspartate transaminase(U/L), ALT-Alanine transaminase(U/L), T.P-Total Protein(g/dl), ALB-Albumin (g/dl), CHO- Cholesterol(mg/dl), TRI-Triglycerides(mg/dl).
** 3 replicates were used for each treatment.
*** Based on Duncan test, a vertically different letter refers to a significant difference between treatments at $P \leq 0.05$.

Table 3. Effect of rosemary and lemon extract on some biochemical parameters of white rats.

crosis, the increased activity of specific liver enzymes. Over the next two weeks, a significant accumulation of hepatic fat occurs, the triglycerides levels and AST rise in the blood dramatically, whereas liver function decreases. Phase III persistently increased AST, and elevated triglyceride levels were found. Finally, hepatic depression and atrophy were noted. This could be coupled with a significant decrease in serum albumin[33].

(34) notice that the intense macro and micro lipid vacuoles in the cytoplasm of hepatocytes might cause by alterations of glucose and lipid metabolism; the increase in glucose could result from a decreased insulin secretion and amylase activities from interference in metabolic pathways of carbohydrates with CCl_4-induced hepatotoxicity. Additionally, (35) shows that high concentrations of glucose and fatty acids may promote hepatic fatty acid and triglyceride uptake and synthesis and impair β-oxidation. Whereas[36] talked about the increases in triglyceride may result from reduced lipase activity, which can lead to a decrease in triglyceride hydrolysis.

The results of the study agreement with Labban[37] they demonstrated a significant rise in the levels of ALP, ALT, AST, total bilirubin, cholesterol, glucose and triglyceride; well there was significant reduction in the TP and ALB levels in comparison with the control group after CCl4 subcutaneous injection of 0.5 ml/ kg body weight for 4 weeks.

As a result of using rosemary extracts, the condition has been restored to what it was before using CCl_4, thus the results are in agreement with[38] they indicate that treatment with rosemary leaves powder at doses (2, 5 and 10 g/ day) significantly reduced glucose for all participants for eight weeks; also they reported that it regenerated pancreatic β-cells. Insulin excretion from surviving beta cells reduces the glucose level in the blood by stimulating insulin secretion from the remaining or regenerated β cells. Additionally, in agreement with El-Hadary, (38) they suggest that after eight weeks of administration of cold-pressed *rosemary officinalis* oil, total lipids and triacylglycerol levels were decreased and reduced activity of ALT, AST and ALP, as well as markers of kidney function. It has a hepatoprotective effect against CCl_4 motivation toxicity, which may be mediated by its antioxidant properties or its high levels of phenolics and tools.

On the other hand, the resulting agreement with Olukanni, (39) they observed at the end of the fifth week of lemon oral administration in wistar rats a significant decrease in total cholesterol, LDL cholesterol and triglyceride when compared with the control group in addition to an increase, but not significant in the total protein during the same period was also recorded. Other researchers[40] proved that lemon juice has curative properties in case of liver injury due to drinking alcohol. Lemon juice improves liver function by scavenging free radicals, raising the level of total protein and reducing serum ALT and AST levels[11], indicating that H_2O_2 has a detrimental influence on biochemical parameters in female mice, whereas the addition of lemon juice decreases these negative impacts and improves the function of the liver.

Chen[14] showed that the oral treatments with fermented lemon juice reduced the level of plasma ALT, AST, and hepatic lipid peroxidation, significantly in rats, as well as decreasing hepatic damage by increasing the content of soluble protein, albumin and glutathione in the liver.

Yang[41] confirmed that lemon seed flavonoids are a mixture of flavonoids, and their active substances have a protective impact on CCl_4-induced liver damage in mice. CCl_4 can prevent abnormality in serological parameters, including liver function signals, and restore the oxidation and inflammation indices to normal.

Regarding the synergistic treatment, it effectively reduced the damage caused by CCl_4. Thus, our results agreed with Essawy[42]; they reported that both ginger and rosemary increase protection against CCl_4-induced liver injury, which can be an impeccable combination of treatment approaches when compared to each individual treatment.

Albasha[43] concluded that cadmium harms the liver; therefore, aqueous extracts of various natural substances such as cinnamon, fenugreek and rosemary could mitigate these effects alone or when used every two sections in the treatment. While Hashem[10] mentioned that licorice and rosemary licorice extracts have a protective role in mitigating the harmful effects of lead on hepatic and renal functions, antioxidant activities and immunity in rats.

The CCl_4 group of table (4) showed a significant reduction in total antioxidant capacity compared to the control group; in addition, the treatment with rosemary and lemon gives significant repair whether it is the compound alone or with the other.

Groups	Values
Control	11.58 ± 0.16^{c}
CCl_4	9.45 ± 0.09^{a}
Rose	13.00 ± 0.05^{e}
Rose + CCl_4	11.00 ± 0.13^{b}
Lemon	12.35 ± 0.23^{d}
Lemon + CCl_4	11.10 ± 0.58^{b}
Rose + Lemon	11.80 ± 0.11^{c}
Rose + Lemon +CCl_4	11.40 ± 0.07^{bc}

* 3 replicates were used for each treatment.
** Based on Duncan-test, vertically different letter refers to a significant difference between treatments at $P \leq 0.05$.

Table 4. Effect of rosemary and lemon extract on total antioxidant capacity.

Discussion

The study of El-Hadary[38] reported that rosemary extracts significantly reduced contents of malonaldehyde and also act as a cell protective agent when it reverses the scavenging activity of free radicals that caused extensive injury to cell components like membrane lipids, increased normal cells vitality, the antioxidant enzymes activity glutathione reductase and superoxide dismutase.

The result agrees with Almatroodi[44,45]. They mentioned that the levels of antioxidant enzymes were considerably reduced in CCl_4-induced animals relative to the control. Moreover, garlic and olive fruit pulp extract treatment cause a significant increase in these enzymes level. The study of Abdalla[46] refers that rat treatment with CCl_4 reduced the antioxidant capacity of the liver as indicated by the decreased activities of superoxide dismutase, glutathione reductase, glutathione level and T-AOC. Additionally, artichoke processing prevented a decrease in these parameters and consequent oxidative damage to the liver.

On the other hand, (47) they point out the intra-peritoneal administration of CCl_4 induced substantial reductions in the amount of superoxide dismutase, glutathione reductase and T-AOC, accompanied by considerable increases in malonaldehyde activities that indicated lipid peroxidation and oxidative stress injury in hepatocytes. Conversely, the administration of Arabic gum significantly elevated hepatic T-AOC and others. It decreased the stages of lipid peroxidation by elevating the synthesis of antioxidant compounds or scavenging the free radicals.

Conclusions

Rosemary reduced and inhibited the CCl_4 stimulate liver toxicity in rats by Breaking molecular bonds or preventing the free radical formation produced through CCl_4 metabolism. These enhanced effects of rosemary can be attributed to the bioactive Ingredients that moderated the detrimental influence of CCl_4 by scavenging or the antioxidant features that prevent lipid peroxidation, stabilize the reactive radicals, maintain cellular integrity and restrict the riskiness of CCl_4. Additionally, the administration of lemon increased serum T-AOC levels suggesting that this may exert its antioxidant effect. Finally, aqueous extracts of rosemary and lemon alleviated the CCl_4 in rats, especially when administered in combination.

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Conflicts of Interest

The authors declare no conflict of interest.

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