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The Effects of Flavonoid Extract from *Capparis spinosa* L. on Some Biological Parameters in Adult Male Albino Rats

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Abstract

This study aimed to explain the effect of the flavonoid extract of *Cappairs spinosa* on the body weight, lipid profile, glucose, and kidney functions of male rats. We extracted the plant material using methanol at 85% in the Soxhlet apparatus for 8 hours and fractionated it with ethyl acetate. Twenty adult male rats were used in this study, which was divided into four groups (5 rats/group); the first group (T1) received 10 mg/kg. The second group (T2) received 20 mg \kg. The third group (T3) received 40 mg\kg orally for 30 days, and the 4th group (control) received orally distal water. At the end of the experiment, we collected blood samples by cardiac puncture to measure blood sugar level, lipid profile, and kidney function parameters. The levels of blood cholesterol, triglycerides, and very-low-density lipoprotein (VLDL) all went down significantly in all treated groups. On the other hand, the level of high-density lipoprotein (HDL) went up significantly compared to the control group. The blood sugar result explained a significant reduction in all treated groups compared with the control group. When kidney function parameters were measured, the amounts of urea, creatinine, and uric acid were significantly lower in animals that were given the flavonoid extract compared to those that were not. The result shows that extracts affect a significant decrease in body weight compared with control rat**s.** These results of biological parameters explained that there were significant ($P \leq 0.05$, $P \leq 0.01$).

Keywords: Capparidaceae, caper, lipid profile, glucose, kidney functions.

1. Introduction

Medicinal plants have been used since the earliest times as therapeutic agents for treating diseases because they have health-promoting properties and contain bioactive components [1]. The *Capparis* genus, including the species of *Capparis spinosa* L., called in Arabic "Kabbar," is considered one of the most important economical species belonging to the *Capparidaceae* family and has a wide range of diversity (700–900 species). It is native to the Mediterranean basin and widely distributed, from Morocco to Crimea, Armenia, Iraq, and Iran. The Sumerians, Greeks, and Romans used it because of its therapeutic qualities. Different parts of this plant, including fruits and roots, have been used as a traditional herbal medication since ancient times for their beneficial effects on human diseases [2,3]. Ancient Egypt consumed the roots of *C. Spinosa* to treat liver and kidney diseases; the Romans used *C. Spinosa* to treat paralysis. In Iraq, *C. Spinosa*

has been used in traditional medicine to treat gout and rheumatoid arthritis [4- 6]. The literature provides plentiful information about the health benefits and chemical composition of *Capparis spinosa* L. leaves; for instance, they are well known for their antimicrobial and antioxidative properties, attributed to lipophilic and hydrophilic compounds including carotenoids, polysaccharides, amino acids, and flavonoids [5,7]. Previous studies investigated the phytochemical components of caper extracts. They showed the presence of many bioactive compounds from different chemical families, such as phenolic acids, flavonoids, alkaloids, fatty acids, vitamins, and glucosinolates [8]. Many studies have indicated the bioactive compounds of different parts of *C. Spinosa,* such as leaves [3]. In the species *C. Spinosa*, Polyphenols, phenolics, and flavonoids were demonstrated to possess strong antioxidant activity with free radical scavenging efficiency. They have received considerable attention for their pharmacological functions as antitumor, antimutagenic, and antioxidant activities [9-11]. Natural antioxidants play an important role in inhibiting reactive oxygen species and scavenging free radicals, thus avoiding degenerative and chronic diseases such as cholesterol rates, cardiovascular disease, and aging [12]. Despite the documented *Capparis spinosa* L. fruits, leaves, and roots, data on the other organs remains disparate. In this study, we focused our work on the flower of *C. Spinosa* in Iraq, which was investigated for its phytochemical contents and antioxidant potential. We studied the effect of these extracts on lipid profile, kidney function parameters, blood sugar, and weight.

2. Materials and Methods

2.1.Plant material

Fresh flowers of *C. Spinosa* were collected from Rawa City, western Iraq. The specialist from the Department of Biology, College of Sciences for Women, University of Baghdad, authenticated and identified the flowers. The flower was cleaned and washed with tap water and dried under shade at room temperature.

2.2. Extraction

100 g of dry powder of flowers was packed in a thimble of soxhlet and extracted with 85% methanol for 8 hours. The extracts were filtered and concentrated by a rotary evaporator under reduced pressure at approximately 40°C. Fractionating the extract with ethyl acetate resulted in the evaporation of the filtered end. Weighing this fraction is necessary for further analysis [10].

2.3. Primary qualitative phytochemical analysis

Chemists used standard procedures to identify the active constituents by conducting chemical tests on the methanolic extracts from plants. The alkaloid test is done with Mayer’s and Wagner's reagents. Tests about flavonoids were achieved by the lead acetate test and the NaOH test. The Saponins tests were done by foam tests and $HgCl_2$ tests. Tannins were achieved by using the $FeCl_3$ solution test. The terpenoids test was done by chloroform and H_2SO_4 [13].

2.4. Determination of total flavonoid content

The aluminum chloride colorimetric method used the total flavonoid content of the crude extract. In brief, 50 µL of crude extract (1 mg/ 1 M ethanol) was made up to 1Ml with methanol, mixed with 4 ml of distilled water, and then 0.3 ml of a 5% $NaNO_2$ solution and 0.3 mL of a 10% $AlCl_3$ solution were added after 5 min of incubation, then the mixture was allowed to stand for 6 min. Then, 2 mL of 1 mol/ L NaOH solution was added, and the final volume of the mixture was brought to 10 mL with double-distilled water. The mixture was allowed to stand for

15 minutes, and absorbance was measured at 510 nm. The total flavonoid content was calculated from the calibration curve, and the result was expressed as mg rutin equivalent per gram dry weight [14].

2.5. High-performance layer chromatography analysis (HPLC)

The sample was analyzed by a high-performance liquid chromatography (HPLC) model (SYKAM, Germany) to identify different constituents found in fractions. Pump model: S 2100 Quaternary Gradient Pump, autosampler model: S 5200, detector: U.V. (S 2340), and column oven model: S 41145. The mobile phase is (methanol, D.W., formic acid) (70:25:5), the column is C18-ODS (25 cm x 4.6 mm), and the detector is UV-280 nm at a flow rate of 1.0 ml/ min [14].

2.6. Animal and experimental design

Twenty adult male rats weighing 130–200 g and aged 6–8 weeks were housed in metal cages under the controlled temperature condition of 25 °C. We divided the rats into four groups, with five rats in each group. Animals in the first group (T1) were intubated daily with a dose of 10 mg/kg of *Capparis spinosa* extract for 30 days. Rats of T2 were intubated orally with 20 mg\kg of *Capparis spinosa* extract. The T3 received 40 mg\kg *Capparis spinosa* for 30 days. Rats in the control group received an oral dose of distilled water for 30 days.

2.7. Blood sample preparation

After 30 days of the experiments, the albino male rats were weighed by a sensitive balance, blood samples were collected (5CC) from animals by the cardiac puncture technique, and a part of the blood (1CC) was kept in a tube containing EDTA (volume of 3 ml) anticoagulant for a complete blood picture. Another part of the blood (3–4 CC) was placed in a gel-activated tube. Then, the serum was separated by centrifugation for 10 minutes at 4000 RPM and stored in Eppendorf tubes at -20 °C for biochemical analysis (lipid profile, kidney function parameters, and blood sugar). COBAS C111, a fully automated device from Roche Company, did all biochemical tests.

2.8. Blood sample preparation

After 30 days of the experiments, the albino male rats were weighed by a sensitive balance, blood samples were collected (5CC) from animals by the cardiac puncture technique, and a part of the blood (1CC) was kept in a tube containing (EDTA) (volume 3ml) anticoagulant for complete blood picture, another part of the blood (3-4 CC) was placed in gel activated tube. Then, the serum was separated by centrifugation for 10 minutes at 4000 RPM and stored in Eppendorf tubes at -20C for biochemical analysis (lipid profile, kidney function parameters, and blood sugar). COBAS C111, a fully-automated device from Roche Company, did all biochemical tests.

2.9. Statistical analysis

The Statistical Analysis System- SAS (2018) program was used to detect the effect of different factors on study parameters. The least significant difference –the LSD test (Analysis of Variation-ANOVA), was used to compare between means in this study with the control [15].

3. Results and Discussion

Phytochemical screening of *C. Spinosa* flower extracts showed alkaloids, saponins, flavonoids, tannins, and terpenoids. This result can be compared with previous studies of qualitative analysis for aerial parts of *C. Spinosa* methanolic extract, which showed glycoside, alkaloids, tannins, phenol, and triterpenoids, while alkaloids, steroids, carbohydrates, tannins,

flavonoids, phenol and flavonoids in aqueous extract [16].

Many studies investigated the presence of different secondary metabolites in all parts of *C. Spinosa*, such as roots, leaves, and buds. They mentioned that *C. Spinosa* leaf extract has flavonoids, phenols, alkaloids, tannins, and glycosides [17]. Many researchers mentioned that bioactive compounds vary from one plant to another, which belongs to the same genus and occurs in different parts of the same species. This is due to factors like environment, soil texture, depth, and moisture, which create variations in the chemical compounds even in the same country [13

3.1. Total flavonoid contents

We used the aluminum chloride colorimetric method to measure the flavonoid content and reported it as rutin equivalents per dry weight**.** *Capparis Spinosa* has 24.28 mg/ gm of methanolic flower extract. This result is an approach to [18], who mentioned that caper flower contained 34 different flavonol compounds **Figure 1**.

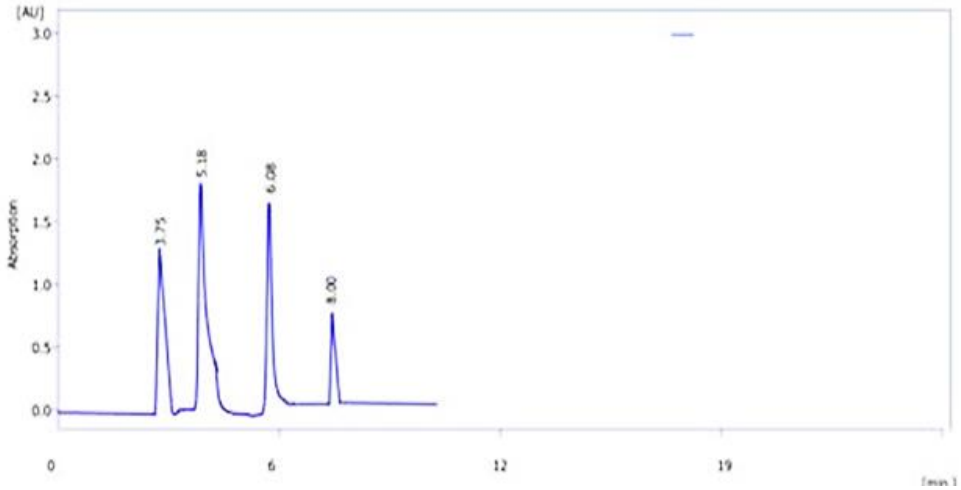

Figure 1. Chromatogram rutin, quercetine, Luteolin and keampferol of *Caparis spinosa* flavonoid extract**.**

3.2. High-performance layer chromatography analysis (HPLC)

The identification of compounds in the flavonoid extract of *C. Spinosa* flowers was done by HPLC analysis, which revealed the presence of four peaks: rutin, quercetin, Luteolin, and kaempferol **Figure 2.** and their chromatograms are shown in the following figure compared with standards **Figure 1.** It was noticed that quercetin compounds were highly available in the extract. Phytochemical studies have shown the presence of rutin, kaempferol, quercitin, stigmasterol, tocopherols, campesterol, and carotenoids. Quercetin considerable attention is due to his impact on health. It has one of the most potent antioxidant, antiviral, antibacterial, and anti-inflammatory effects. The antioxidant activity of quercetin is due to its ability to scavenge antioxidant and transition metal ions [13,19].

These results agree with [19], who mentioned that quercetin is one of the important components of this plant; flowers containing the highest quercetin content reached 12.8 mg/g. While [20] reported that the leaves of *C. Spinosa* were a good source of quercetin, kaempferol, rutin, and isoharmintin**.**

The results of the current study showed that there was a significant decrease ($P \leq 0.05$) in the level of blood cholesterol (from 45.26 ±2.02 to 56.46±2.77 Mg\dl) in treated groups as compared with the control group (61.94±61.94 mg\dl), and a significant decline ($p \leq 0.01$) in the levels of

triglyceride (21.88±1.07, 54.58±7.95, 57.64±7.49 mg\dl) in groups that received flavonoid extract compared with control group(101.54±21.45mg\dl), as shown in **Table 1.** The result of low-density lipoprotein (LDL) level showed a non-significant decrease (22.44±1.03, 27.62±2.54, 29.02±0.96 mg\dl) in animals treated with flavonoid extract of *C. spinosa* compared with the control group (29.04±4.42 mg\dl).

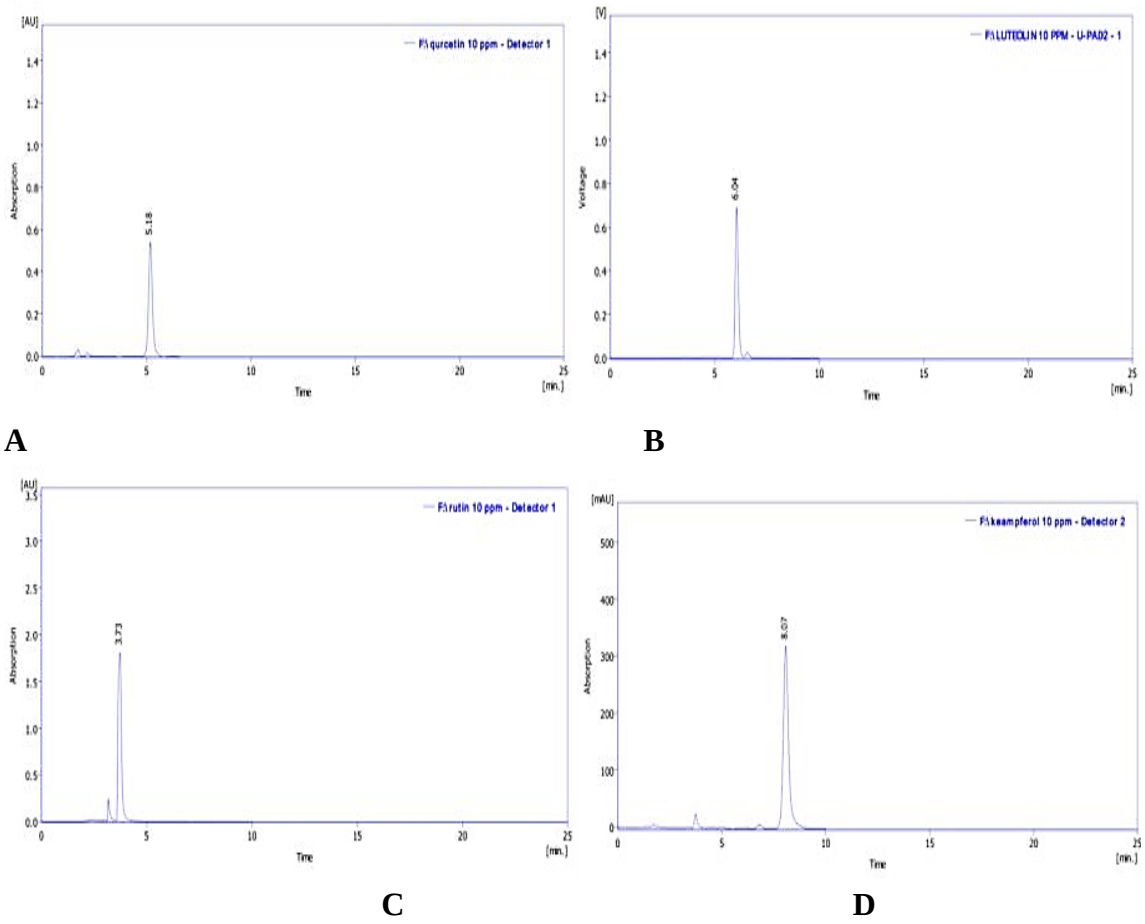

Figure 2. Chromatogram A: rutin, B: quercetine, C: Luteolin and D: keampferol standard

Table 1. Effect of flavonoid extract from *C. spinosa* on Lipid profile and glucose in rats

Group	Mean ± SE					
	Cholesterol Mg\dL	**Triglyceride Mg\d**	**HDL Mg\dL**	**LDL Mg\dL**	**VLDL Mg \dL**	**Glucose Mg\Dl**
Control D.W	61.94 ±6.34 a	101.54 ±21.45 a	29.76 ±2.66 b	29.04 ±4.42 a	18.30 ±2.12 a	258.52 ±9.39 a
T1 10 mg\kg	45.26 ±2.02 b	21.88 ±1.07 b	34.46 ±4.99 ab	27.62 ±2.54 a	5.22 ±0.29 c	247.74 ±12.98 a
T2 20 mg\kg	56.46 ±2.77 ab	57.64 ±7.49 b	41.38 ±1.70 a	29.02 ±0.96 a	11.54 ±1.51 b	87.20 ±11.29 b
T3 40 mg\kg	46.14 ±1.99 b	54.58 ±7.95 b	43.74 ±2.29 a	22.44 ±1.03 a	11.02 ±1.68 b	235.18 ±17.50 a
LSD value	11.21 *	36.12 **	9.506 *	7.947 NS	4.669 **	39.40 **

Means having with the different letters in same column differed significantly.
* (P≤0.05), ** (P≤0.01).

As illustrated in this study, there was a significant decrease (P≤0.01) in the levels of urea in

treated groups compared (from 47.96 ±2.32 to 56.34 ±2.64 mg\dl) as compared with the control group (60.16 ±1.96 mg\dl), as shown in **Table 2**. Significant drop (P≤0.05) in creatinine level (from 0.2886 ±0.03 to0.396 ±0.02 mg\dl) compared with control (0.440 ±0.06 mg/dl) and uric acid (from 1.06 ±0.12 to 3.68 ±0.68 mg/dl) compared with control animals (3.72 ±1.19 mg\dl).

Table 2. Effect of flavonoid extract from *C.spinosa* on Kidney functions in rats.

Group	Mean ± SE		
	Urea (mg\dL)	Creatinine (mg\dL)	Uric acid (mg\dL)
Control D.W	60.16 ±1.96 a	0.440 ±0.06 a	3.72 ±1.19 a
T1 10 Mg\kg	49.76 ±2.09 bc	0.396 ±0.02 ab	1.14 ±0.05 b
T2 20 Mg\kg	47.96 ±2.32 c	0.292 ±0.01 b	3.68 ±0.68 a
T3 40Mg\kg	56.34 ±2.64 ab	0.286 ±0.03 b	1.06 ±0.12 b
LSD value	6.821 **	0.123 *	2.082 *

Means having with the different letters in same column differed significantly. * (P≤0.05), ** (P≤0.01).

As shown in **Table 3.** and **Figure 3,** explaining the effect of the extract on body weight, a significant increase (P≤0.01) in body weight was observed in the control group from the first day to the end of the experiments, it was while significantly lower (P≤0.05) (from 210.00 ±6.49 to 236.80 ±11.54 gm) in the treated groups compared with the control group (249.00 ±6.78 g). This plant may slow food digestion reducing carbohydrate absorption rate and clearing the postprandial glucose load [21].

The result agrees with [22], who revealed a significant reduction in body weight in treated animals with *C. spinosa* extract and mentioned that the potential of the extract is connected with inhibition of pancreatic lipase activity, adipocyte differentiation, and enhancement of antioxidant activity by phytonutrients that are present in the extract.

Table 3. Effect of total flavonoid extract from *C. Spinosa* on weight in male rats.

Group	Mean ± SE (gm)		LSD value
	Wt. before	Wt. after	
Control D.W	138.00 ±9.55 B a	249.00 ±6.78 A a	32.52 **
T1 10mg\kg	137.80 ±8.86 B a	213.80 ±13.56 A b	25.49 **
T2 20 mg\kg	143.80 ±12.31 B a	210.00 ±6.49 A b	25.05 **
T3 40 mg\kg	139.80 ±11.18 B a	236.80 ±11.54 A ab	31.58 **
LSD value	31.668 NS	30.203 *	---

Means with different small letters in the same column and big letters in the same row are significantly different. * (P≤0.05), ** (P≤0.01).

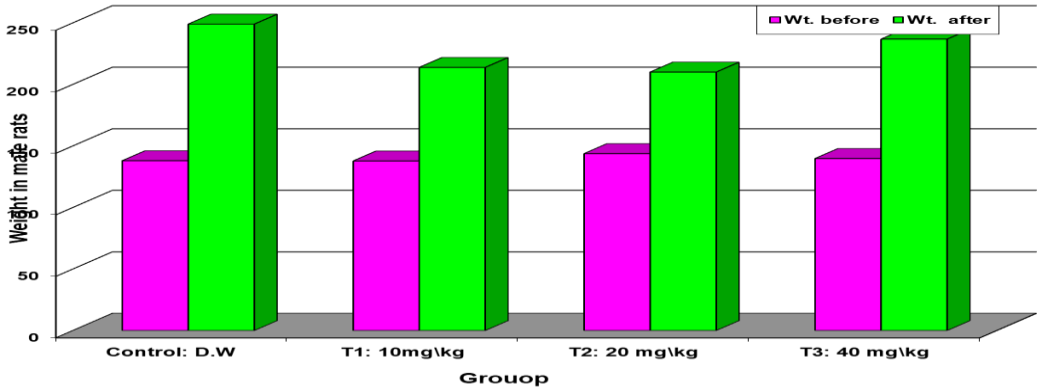

Figure 3. Effect of total flavonoid extract from *Capparis Spinosa* on weight in male rats

The current study's results showed a significant decrease in the levels of blood lipid profile in the groups that received the extract, which agrees with [3, 23, 24] that the *Capparis spinosa* extract has beneficial properties that result in a decreased level of lipid profile. Many reasons can illustrate these results: *Capparis spinosa* contains several compounds, such as phenols, tocopherols, polyphenols, alkaloids, and flavonoids [2]. It contains many antioxidant compounds, such as rutin, quercetin, and kaempferol [18]. These compounds show a remarkable role in different pharmacological activities, including hypolipidemic, cardiovascular, and antidiabetic [2, 25]. As shown in this study, there was a significant decrease in the level of blood glucose in the treated groups. This finding agrees with a previous study by [26, 27], which indicates that capers reduce digestion and absorption of carbohydrates in the gut, which leads to the gradual entry of glucose into the blood to prevent any sudden increase in glucose levels after eating. Other putative mechanisms of capers that lower the blood sugar level are inhibiting the formation of glucose in the liver and enhancing its absorption into the tissues [28, 29]. *Capparis spinosa* is also rich in antioxidants, such as polyphenols, that cause the activation of hypoglycemic properties [21].

Furthermore, the present results revealed a significant decrease ($P \leq 0.01$) in the concentration of urea in treated groups as compared with a control group, and there was also a significant decrease ($p \leq 0.05$) in Creatinine and Uric acid in animals treated with the alcohol extract of *C. Spinosa* as compared with the control group. The result agrees with [30], who showed that rats treated with *Capparis Spinosa* extract significantly decreased urea, Creatinine, and total protein levels.

4. Conclusion

The findings of the current study indicated that flavonoid extracts of *C. Spinosa* containing rutin, quercetin, luteolin, and kaempferol were identified by HPLC analysis, and our results indicate that flavonoid extracts of Capparis spinosa may decrease the levels of blood cholesterol, triglyceride, very low-density lipoprotein, and blood sugar, thus being useful in treating hyperlipidemia and hyperglycemia. Additionally, the flavonoid extracts of Capparis spinosa have the potential to increase the levels of good cholesterol (HDL). Moreover, it has protective effects on the kidneys by reducing Creatinine and uric acid. And it may have anti-obese activity.

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Conflict of Interest

There are no conflicts of interest.

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