

Olive and Turmeric Oils: Nutraceutical Effectiveness against Paracetamol-Induced Hepatotoxicity in Experimental Rats

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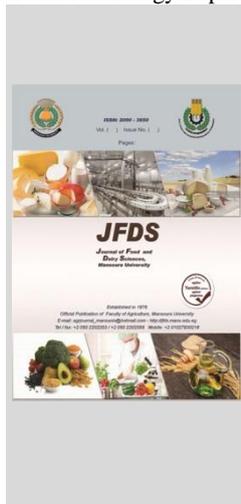


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ABSTRACT

Olive and turmeric oils have numerous health benefits by preventing hepatotoxicity, moreover, each gives benefits that go beyond reducing risk factors of liver diseases. This investigation aimed to estimate the nutraceutical Effectiveness of olive and turmeric oils against paracetamol-induced hepatotoxicity in experimental rats. Twenty Sprague-Dawley male albino rats weighing 200 ± 10 g each, were randomly divided into four groups; five rats each as follows; the first group was control negative (C -ve), the second group induced with liver intoxicated by paracetamol then fed on basal diet (C +ve), the third group induced with liver intoxicated by paracetamol then fed on basal diet concurrently with orally administered of olive oil at a dose of 1 ml/kg body weight., and the fourth group induced with liver intoxicated by paracetamol then fed on basal diet concurrently with orally administered of turmeric oil at a dose of 1 ml/kg body weight. At the finale of investigational period 28 days, blood samples were collected for determination the following parameters; TC, TG, HDL, LDL VLDL, AI, glucose, TP and Alb. Moreover, BWG, FI and FER were calculated. The findings showed that all rats in the experimental groups orally injected with olive oil and turmeric oil at a dose 1 ml/kg body weight, each displayed a notable decline in TC, TG, LDL VLDL, AI, glucose, TP and Alb. Moreover, increasing in HDL, BWG, FI and FER. This study demonstrated that olive oil and turmeric oil had noticeable nutraceutical effectiveness against paracetamol-induced hepatotoxicity in experimental rats.

Keywords: Olive oil, turmeric oil, nutraceutical effectiveness, hepatotoxicity, rats



INTRODUCTION

The metabolism of both endogenous and foreign chemicals depends heavily on the liver, and hepatic damage is linked to a distortion of these processes. Xenobiotics or infections typically decrease liver function. Untreated cases of chronic or severe xenobiotic exposure eventually result in cirrhosis or malignant lesions. Hepatic damage brought on by alcohol, drugs, and infections affects many individuals today. As a result, acute and chronic liver illnesses continue to be major global health issues. According to research by Liu *et al.* (2011), some natural substances, including silymarin and glycyrrhizin, have been shown to be protective against liver disorders. One of the most often used medications is paracetamol (acetaminophen), which has a wealth of experience clearly establishing it as the standard antipyretic and analgesic for mild to moderate pain conditions. It may be found in over 100 products either alone or in combination with other treatments. One of the most frequent side effects from acute paracetamol overdose is likely liver toxicity. More than 56 000 trips to the emergency room are due to paracetamol overdose, these accounts for 50% of all cases of acute liver failure in the nation (Kraemer and Maurer, 2014). An example of an oil is olive oil, which is made from the olive tree's fruit, the olive. The manufacturing procedure is easy. Although olives can be pressed to obtain their oil, contemporary techniques entail crushing the olives, combining them, then centrifuging the mixture to separate the oil from the pulp. Olive oil has a significant amount of monounsaturated fats and only trace amounts of vitamins E and K. Extra virgin olive oil has a

distinct flavor and scent in addition to being high in anti-inflammatory and disease-fighting antioxidants, which are linked to a variety of potential health benefits (Fernando, 2021). Also, Badawy and Saleh (2018) indicated that the main fatty acids of olive oil were the unsaturated oleic acid (72.1 %), the linoleic (9.5%), linolenic acid (4.1%), the palmitic (7.3 %) and stearic acid (4.4 %). Turmeric's culinary spice, curcumin, is a polyphenolic molecule that has a variety of pharmacologic, comprised of anti-inflammatory, antioxidant, anti-proliferative, and antiangiogenic properties (Anand, 2007). Due to their anti-inflammatory and antioxidant qualities, curcumin and turmeric essential oil have been discovered to slow the progression of numerous disease processes (Das *et al.*, 2010). Accordingly, this study aimed to estimate the nutraceutical effectiveness of olive and turmeric oils against paracetamol-induced hepatotoxicity in experimental rats.

MATERIALS AND METHODS

Materials:

1. Oils:

Olive and turmeric oils, which were used in this experiment, were purchased from a local market in Kafrelsheikh city, Egypt.

2. Rats:

Twenty mature male albino rats weighing 200 ± 10 g. Body weight. were used in this investigation.

3. Basal diet:

According to the procedure outlined by Hegsted *et al.* (1941), the staple foods were casein (12.5%), corn starch

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(up to 100%), maize oil (10%), choline chloride (0.2%), vitamin mixture (1%), cellulose (5%), salt mixture (4%), and sucrose (22%).

4. Paracetamol:

Paracetamol will be obtained from Alnahdi Pharmacy, Holy Makkah, KSA.

Methods:

1. Liver toxicity Induction:

The induction of paracetamol toxicity for rats occurred by oral injection with paracetamol at a dose of 500 mg/kg body weight. (Farghaly and Hussein, 2010).

2. Experimental design:

Twenty Sprague-Dawley male albino rats weighing 200±10 g each were randomly divided into four groups; five rats each as follows;

Group (1): A control negative group (C-ve) was fed a basal diet for 28 days .

Group (2): The control positive group (C+ve) was fed a basal diet for 28 days after having their livers induced with paracetamol intoxication.

Group (3): Paracetamol was used to induce liver intoxication, which was followed by feeding on a basal diet and taking 1 ml/kg body weight of olive oil every day for 28 days.

Group (4): Paracetamol was used to induce liver intoxication, and after being fed a basal diet for 28 days, turmeric oil was given orally at a dose of 1 ml/kg body weight.

3. Biological evaluation:

Body weight was checked once a week for the duration of the feeding session, which lasted 4 weeks. Following the recording of food intake, the body weight gain (BWG) and feed efficiency ratio (FER) were calculated according to Hegazy *et al.* (2021) using the following equation:

$$BWG (g) = \text{Final weight} - \text{initial weight}$$

$$FER = \frac{\text{Gain in body weight (g)}}{\text{Feed intake (g)}}$$

4. Biochemical Evaluation

Following the 28-day study period, blood samples will be collected for serum separation in order to determine the following parameters: Total cholesterol (TC) was calculated according to Allen (1976), total bilirubin (TBIL) was calculated using the method described by Doumas and Wu (1991) triglycerides (TG) was calculated using the method of Fossati and Prencipe (1982), high-density lipoprotein (HDL) and low-density lipoprotein (LDL) were calculated using the method of Herrmann *et al.* (1983), and very low density lipoprotein (VLDL) was calculated as described by Doumas *et al.* (1971) . The albumin was measured using the method, according to Buzanovskii (2017). Additionally, serum glucose levels were evaluated using the method of Kaplan (1984), serum total protein was determined using the method of Buzanovskii (2017).

4. Statistical analysis

Utilizing automated SPSS (Statistic Program Sigma Stat, statistical software, SAS Institute, Cary, NC), the acquired data were statistically evaluated. One-way examination of difference (ANOVA) tests were performed to compare the effects of various treatments, and p0.05 was used to denote significance between different groups (Snedecor and Cochran, 1967).

RESULT AND DISCUSSION

1. Effect of olive and curcumin oils on BWG, FI and FER in paracetamol intoxicated rats:

The data listed in Table (1) demonstrates the preventive effects of olive oil and curcumin oil on total body weight gain (BWG), food intake (FI), and feed efficiency ratio (FER) in rats that have been given paracetamol to induce intoxication.

Table 1. Effect of olive s-and curcumin oil on BWG, FI and FER in paracetamol intoxicated rats

Parameters	BWG (g/7d)	FI (g/7d)	FER
Animal group	Mean±SE	Mean±SE	Mean±SE
Control (-)	4.70±0.01 ^a	28.19± 0.13 ^a	0.17± 0.003 ^a
Control (+)	0.90±0.04 ^d	21.12±0.45 ^d	0.04±0.001 ^d
Olive oil	3.10±0.03 ^c	25.09±0.27 ^{bc}	0.12±0.005 ^{bc}
Curcumin oil	3.40±0.02 ^b	26.90±0.34 ^b	0.13±0.002 ^b
L.S.D	0.22	2.35	0.01

- *SE means standard error.

- Letters of (a,b,c,d)in one column significantly differ at p≤0.05.

Rats that had consumed paracetamol (C+ve group) showed that total body weight gain (BWG), food intake (FI), and feed efficiency ratio (FER) were 0.90±0.04 (g/7d), 21.12±0.45(g/7d) and 0.04±0.001 compared to 4.70±0.01(g/7d), 28.19± 0.13(g/7d) and 0.17± 0.003 in (C-ve) normal rats (p<0.05). These results showed that body weight, food intake, and feed efficiency ratio were all-significantly lower in paracetamol-intoxicated rats than in negative control rats. All orally treated animals given a dose of 1mL/kg body weight of olive oil with curcumin oil demonstrated a substantial rise in BWG, FI, and FER as compared to control positive rats. Rats administered olive oil orally demonstrated the highest significant reduction in BWG, FI, and FER when compared to the Curcumin oil group. These outcomes were supported by Hegazy *et al.* (2021) who concluded that paracetamol affects the physiological evaluation by caused a significant decrease in BWG, FI and FER compared to other group. Moreover, Salih (2015) reported that paracetamol affects the Physiological evaluation by caused a significant decrease in the average amount of FI of the injected rats compared to other groups. Meanwhile, Al-Seeni *et al.*, (2016) observed that effect of CCl4 induced hepatotoxicity treatment with olive oil on physiological evaluation (BWG, FI and FER). The proportion physiological evaluation in the positive group significantly decreased because of liver damage compared to the negative control group. Hepatotoxicity treatment in the olive oil group respectively led to a significant increase (P<0.001) compared to the positive control group.

2. Effect of olive and curcumin oils on TC, TG and TBIL in paracetamol intoxicated rats:

Data listed in Table (2) show the protective effect of olive and curcumin oils on total clolesterol (TC), triglycerides (TG), total bilirubin (TBIL) in paracetamol intoxicated rats.

It was observable for paracetamol intoxicated rats (C+ve group) TC , TG , TBIL were 2.18±0.05 (mmol/L), 1.58±0.04 (mmol/L)and 02.40±0.06 (umol/L) compared to 1.65±0.01(mmol/L), 0.60± 0.03(mmol/L) and 1.40± 0.02(umol/L) in (C-ve) normal rats (p<0.05). These results demonstrate that when compared to control rats, rats given paracetamol had considerably higher levels of TC, TG, and TBIL. All rats that received olive oil and curcumin oil orally at a dose of 1mL/kg body weight showed a significant

reduction in TC, TG, and TBIL as compared to control positive animals. When compared to the control negative group and to curcumin oil, rats administered olive oil orally displayed the most significant increase in TC, TG, and TBIL. The most notable increase in TC when compared to the Olive oil group and the control negative group, as well as an increase in TG and TBIL when compared to the latter (C-ve), was seen in the oral administration of curcumin oil, nevertheless. These data agreed with Soliman, *et al.*, (2014) and Almajwal and Elsadek (2015) who concluded that paracetamol in overdose caused a significant change in lipid profile (reduction in reduced glutathione and antioxidant enzymes) as indicated by the increased levels of TC, TG and TBIL in the blood compared with all group. Additionally, according to Ghorbel *et al.* (2015) and Cullinan (2006), adding olive oil to the diet may help reduce liver damage by improving the antioxidant balance and cellular oxidative stress, as shown by the lower levels of TC, TG, and TBIL in the blood when compared to the optimistic group.

Table 2. Effect of olive and curcumin oil on TC, TG and TBIL in paracetamol intoxicated rats

Parameters Rats group	TC (mmol/L)	TG (mmol/L)	TBIL (umol/L)
Control (-ve)	1.65±0.01 ^d	0.60±0.03 ^d	1.40±0.02 ^d
Control (+ve)	2.18±0.05 ^a	1.58±0.04 ^a	2.40±0.06 ^a
Olive Oil	1.95±0.03 ^c	1.10±0.02 ^b	2.10±0.03 ^b
Curcumin Oil	2.03±0.02 ^b	0.70±0.01 ^c	1.80±0.02 ^c
L.S.D	0.07	0.05	0.20

- Letters of (a,b,c,d) in one column significantly differ at p≤0.05 and± SE.

3. Effect of olive and curcumin oils on HDL, LDL, VLDL and A.I in paracetamol intoxicated rats:

The effects of olive and curcumin oils on HDL, LDL, VLDL and atherosclerosis index AI were demonstrated by data from Table (3) in rats that had consumed paracetamol.

Table 3. Effect of olive and curcumin oils on HDL, LDL, VLDL and A.I in paracetamol in toxicated rats

Parameters Rats group	HDL (mmol/L)	LDL (mmol/L)	VLDL (mmol/L) AI
Control (-ve)	0.80±0.01 ^a	0.73±0.03 ^d	0.12±0.01 ^d 1.06±0.02 ^d
Control (+ve)	0.60±0.03 ^d	1.26±0.04 ^a	0.32±0.03 ^a 2.63±0.05 ^a
Olive s Oil	0.65±0.02 ^c	1.08±0.02 ^c	0.22±0.02 ^b 2.00±0.03 ^b
Curcumin Oil	0.70±0.01 ^b	1.19±0.03 ^b	0.14±0.01 ^c 1.90±0.01 ^c
L.S.D	0.04	0.05	0.01 0.05

- Letters of (a,b,c,d) in one column significantly differ at p≤0.05 and± SE.

LDL, VLDL, and AI were increased in rats that had consumed paracetamol (C+ve group) as shown : 1.26±0.04(mmol/L), 0.32±0.03(mmol/L) and 2.63±0.05 compared to 0.73±0.03(mmol/L), 0.12±0.01(mmol/L) and 1.06±0.02 in (C-ve) normal rats (p<0.05). These results demonstrate that paracetamol-intoxicated rats exhibited a significant decrease in HDL and a rise in LDL, VLDL, and AI when compared to a negative control rats. In contrast, positive control rats, all orally preventable animals supplied olive oil and curcumin oil at a dose of 1mL/kg b wt showed a substantial rise in HDL and decrease in LDL, VLDL, and AI. When compared to the group receiving curcumin oil, rats given olive oil orally showed the greatest significant reduction in LDL. In contrast to both the control positive group and the olive oil group, orally preventable given with curcumin oil showed the largest significant rise in HDL and reduction

VLDL and AI. These findings matched with the findings of Almajwal and Elsadek (2015) who injected with paracetamol caused a significant change in lipid profile, as indicated by the decreased levels of HDL and improved levels of VLDL, LDL in the blood. Also, Al-Seeni *et al.* (2016) treating the CCl4 made hepatotoxicity in male rats with olive oil decreased the mean values of LDL and VLDL and increased HDL. Meanwhile, Naga and Bakr, (2015) found significant increase in AI in liver intoxicated rats. Once the lipid profiles change due to triglyceride buildup, inhibition of bile acid synthesis from cholesterol produced in the liver or taken from plasma lipids, which results in an increase in cholesterol levels (Oyagbemi and Odetola, 2010).

4. Effect of olive and curcumin oils on Glucose, TP and Alb., in paracetamol intoxicated rats:

The data presented in Table (4) demonstrates the preventive effects of olive and curcumin oils on glucose, total protein (TP), and albumin (Alb) in rats that had been given paracetamol to get them drunk.

Table 4. Effect of of olive and curcumin oils on Glucose, TP and Alb., in paracetamol intoxicated rats

Parameters Animal group	Glucose (mmol/L)	TP (mmol/L)	Alb. (U/L)
Control (-)	3.90±0.05 ^d	69.10±0.03 ^b	30.90±9.11 ^d
Control (+)	6.98±0.08 ^a	72.60±0.05 ^a	39.00±5.32 ^a
Olive Oil	4.80±0.04 ^c	67.80±0.02 ^{cd}	33.80±3.62 ^b
Curcumin Oil	5.59±0.03 ^b	68.60±0.03 ^{bc}	35.10±2.51 ^c
L.S.D	0.25	1.98	1.09

- Letters of (a,b,c,d) in one column significantly differ at p≤0.05 and± SE.

It detected for paracetamol intoxicated rats (C+ve group) that Glucose, TP and Alb were 6.98±0.08(mmol/L), 72.60±0.05(mmol/L) and 39.00±5.32 (U/L) compared to 3.90±0.05 (mmol/L) , 69.10±0.03 (mmol/L) and 30.90±9.11(U/L) in (C-ve) normal rats (p<0.05). These results demonstrate that albumin glucose, and total protein levels are considerably greater in paracetamol-intoxicated rats than in control rats. All orally controllable animals given a dose of 1mL/kg body weight of olive and curcumin oil shown a significant decrease in glucose, TP, and alb as compared to control positive rats. When compared to the control positive group and the group that received curcumin oil, the rats who were given olive oil orally demonstrated the most significant reduction in glucose, total protein, and albumin. These findings are supported by Jaeschke *et al.* (2002), who arrived to the conclusion that a paracetamol overdose results in peroxynitrite, which damages proteins and tissues by scavenging superoxide. The higher total protein and albumin levels compared to the negative control lend credence to this hypothesis. Additionally, Amamou *et al.* (2015) noted that consumption of olive oil could lessen oxidative stress and protect against rat liver injury by enhancing the activities of antioxidant enzymes. This is demonstrated by a decline in glucose, total protein, and albumin levels when compared to the positive control group.

CONCLUSION

The findings showed that all rats in the experimental groups orally injected with olive oil and turmeric oil at a dose 1 ml/kg body weight, each displayed a notable decline in TC, TG, LDL VLDL, AI, glucose, TP and Alb. Moreover, increasing in HDL, BWG, FI and FER. The previous results demonstrated that curcumin and olive oil

had a noticeable improvement of hepatotoxicity with paracetamol in rats with paracetamol liver toxicity.

Conflicts of interest

The authors declare that there are no any conflicts of interest and there is no any financial assistance provided.

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زيوت الزيتون والكرم: الفعالية الغذائية ضد التسمم الكبدي الناجم عن الباراسيتامول في فئران التجارب

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المخلص

يتمتع زيت الزيتون والكرم بفوائد صحية عديدة من خلال منع تسمم الكبد، علاوة على ذلك، فإن كل منهما يعطي فوائد تتجاوز الحد من عوامل الخطر لأمراض الكبد. يهدف هذا البحث إلى تقدير الفعالية الغذائية لزيت الزيتون والكرم ضد التسمم الكبدي الناجم عن الباراسيتامول في فئران التجارب. تم تقسيم عشرين فأراً من ذكور فئران سبراغ داوولي البيضاء ووزن كل منها 200 ± 10 جرام عشوائياً إلى 4 مجموعات؛ 0 فئران لكل منها على النحو التالي؛ المجموعة الأولى مجموعة الكنترول السلبية التي غذيت على العليقة الأساسية (C -ve)، المجموعة الثانية تم تسمم الكبد بالباراسيتامول ثم غذيت على العليقة الأساسية (C +ve)، المجموعة الثالثة تم تسمم الكبد بالباراسيتامول ثم غذيت على العليقة الأساسية المحققة بزيت الزيتون عن طريق الفم بجرعة 1 مل/كجم من وزن الجسم، والمجموعة الرابعة تم تسمم الكبد بالباراسيتامول ثم غذيت على عليقة أساسية بالتزامن مع إعطاء زيت الكرم عن طريق الفم بجرعة 1 مل/كجم من وزن الجسم. كجم بالوزن في نهاية الفترة التجريبية 28 يوماً، تم جمع عينات الدم لتحديد المعايير التالية: تم حساب TG، HDL، LDL، VLDL، AI، الجلوكوز، TP، Alb، علاوة على ذلك، BWG، FI، FER، أظهرت النتائج أن جميع الفئران في المجموعات التجريبية التي تم حقنها عن طريق الفم بزيت الزيتون وزيت الكرم بجرعة 1 مل/كجم ب. بالوزن، أظهر كل منها انخفاضاً ملحوظاً في TG، TC، AI، LDL، VLDL، الجلوكوز، TP و Alb. وعلاوة على ذلك، زيده في BWG، FER. أظهرت هذه الدراسة أن زيت الزيتون وزيت الكرم لهما فعالية غذائية ملحوظة ضد التسمم الكبدي الناجم عن الباراسيتامول في فئران التجارب.