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ACUTE TOXICITY EVALUATION AND ANTIDYSLIPIDEMIC POTENTIAL OF RETAMA SPHAEROCARPA AERIAL PARTS IN TRITON WR-1339 INDUCED HYPERLIPIDEMIC RATS

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ABSTRACT

Background: Dyslipidemia constitutes a major risk factor for cardiovascular diseases. Although conventional lipid-lowering therapies are effective, their prolonged use is associated with adverse effects, highlighting the need for safer natural alternatives. Species of the genus *Retama*, including *Retama sphaerocarpa*, have been reported to possess various pharmacological properties, including antioxidant, hepatoprotective, anti-inflammatory, and hypoglycemic activities. However, no study to date has evaluated the antidyslipidemic potential of *R. sphaerocarpa*. This study was conducted to evaluate both the acute oral toxicity and the antidyslipidemic effect of the *Retama sphaerocarpa* aqueous extract (RSAE) in a Triton WR-1339-induced hyperlipidemic rat model. **Methodology:** The acute toxicity study of RSAE was conducted in accordance with OECD Guideline 423. RSAE was administered orally as a single dose of 2000 mg/kg, and the rats were monitored for any signs of toxicity or mortality. Hematological and biochemical parameters were assessed 24h post-administration of RSAE. The antidyslipidemic effect of RSAE (400 mg/kg) was studied in Triton WR-1339-induced dyslipidemia in Wistar albino rats. **Results and discussion:** Results showed no mortality or clinical signs of toxicity following RSAE administration; hematological and biochemical parameters remained unaltered after 24 hours post-treatment. The RSAE demonstrated antioxidant activity (IC_{50} = 241.45 µg/mL). For the lipid-lowering assessment, RSAE pretreatment significantly reduced plasma TC levels by 51.1% ($p<0.01$), TGs by 60.2% ($p<0.01$), and LDL-c by 73.5% ($p<0.01$), while increasing HDL-c levels ($p<0.01$). **Conclusion:** Results from the present study highlight the potential of *Retama sphaerocarpa* in the prevention and management of dyslipidemia.

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INTRODUCTION

Dyslipidemia is a metabolic disorder characterized by elevated levels of serum total cholesterol (TC), triglycerides (TGs), or low-density lipoprotein cholesterol (LDL-c), and reduced levels of high-density lipoprotein cholesterol (HDL-c) [1]. It constitutes a major public health problem and is recognized as a primary risk factor for the development of cardiovascular diseases, such as coronary heart disease, ischemic stroke, and peripheral vascular disease [2], which collectively represent the leading causes of death worldwide [3]. Epidemiological estimates suggest that approximately 12 million people in the world die each year from cardiovascular disease [4]. Conventional lipid-lowering drugs, such as statins, modulate lipid metabolism through different mechanisms. Despite their proven efficacy, their use is often associated with numerous adverse effects [5]. Consequently, the development of lipid-lowering drugs derived from natural substances has emerged as a promising alternative and increasingly attractive strategy in the management of dyslipidemia.

A large number of plants have been employed in traditional medicine for the prevention and treatment of different cardiovascular diseases. Furthermore, information from various ethnobotanical studies indicates that herbal medicines are widely used to control dyslipidemia [6]. *Retama sphaerocarpa* (L.) Boiss (Fabaceae), also called yellow retama, is known in the south-east of Morocco as "Algou". It is a leguminous shrub distinguished by its deciduous leaves and small yellow flowers appearing between April and May. It is mainly distributed in the Iberian Peninsula and the Mediterranean region of Northeast Africa [7]. In traditional medicine, the decoction of the roots of Retama sphaerocarpa has been used to treat diabetes and diphtheria [8-9]. Beyond its traditional uses, several scientific investigations have demonstrated that it possesses cytotoxic and antimicrobial activities [10,11]. However, despite this growing ethnobotanical & pharmacological interest, no scientific study has, to date, explored its antidyslipidemic potential. Accordingly, this present investigation aimed to assess, for the first time, the antidyslipidemic activity of the aqueous extract of *Retama sphaerocarpa* on Triton WR-1339-induced hyperlipidemia in rats.

MATERIALS AND METHODS

Plant collection and identification

Aerial parts of *Retama sphaerocarpa* were collected in the vicinity of Goulmima in the Tafilalet region (Gps:31.736612, -4.876526) in May 2023, then air-dried at 40 °C. The plant was taxonomically identified and authenticated by the Department of Botany, Faculty of Sciences and Techniques, Errachidia, and a reference specimen was prepared and deposited in the faculty herbarium under the number RS2.

Preparation of the aqueous extract

1 g of powdered aerial plant material was mixed with 100 mL of distilled water and boiled for 10 min. The mixture was then cooled at room temperature for 15 minutes. To remove solid particles, the solution was filtered through a 0.2 mm Millipore membrane filter (Millipore, St Quentin en Yvelines, France). The filtrate was then lyophilized, yielding a dried extract of 6.5% (w/w) [12]. Based on preliminary dose screening experiments, the dose of 400 mg/kg of *Retama sphaerocarpa* aqueous extract (RSAE) was selected as the optimal effective dose that produced significant antidyslipidemic activity

Determination of total polyphenol, total flavonoid, and tannin contents

The total phenolic content of the aqueous extract of *Retama sphaerocarpa* was measured as previously described [13]. The total flavonoid content was determined by the method of Kim *et al*. [14], whereas the tannin content was assessed according to the method of Broadhurst *et al*. [15].

Evaluation of the anti-free radical activity

The antioxidant potential of RSAE was evaluated by the 2,2-diphenyl-1-picrylhydrazyl (DPPH) free radical scavenging assay. A DPPH solution (4 mg/100 mL in methanol) was prepared and kept in the dark for 3 hours. Serial dilutions of RSAE and the positive control, butylhydroxytoluene (BHT), were made from stock solutions (5 mg/10 mL) to obtain the following concentrations: 31.25, 62.5, 125, 250 & 500 µg / mL. For each concentration, 2.5 mL of sample was mixed with an equal volume of DPPH solution in a glass tube, stirred, and incubated at room temperature in the dark for 30 minutes. The control consisted of 2.5 mL of methanol mixed with 2.5 mL of DPPH solution. Absorbance was measured at 515 nm using a UV/Vis spectrophotometer [16].

Experimental animals

Adult albino rats of the Wistar strain, weighing between 120 and 200 grams, were selected for the study. The animals were kept under controlled laboratory conditions, with temperature maintained at 23 ± 1 °C, relative humidity at 55 ± 5%, and a 12-

hour light/dark cycle. All animals had unrestricted access to drinking water and were fed a standard laboratory chow diet ad libitum. All experiments involving animals were conducted in strict accordance with institutional ethical standards for the care and use of laboratory animals established by the Pharmacological Research Committee of FSTE, Moulay Ismail University (FSTE/2015).

Evaluation of acute oral toxicity

The assessment of acute oral toxicity for the aqueous extract of *Retama sphaerocarpa* (RSAE) was conducted in accordance with OECD guideline No. 423 [17]. Adult female rats (weighing 150–250 g), were fasted overnight, weighed before extract administration, and randomly assigned to two experimental groups (n=5 per group). The control group received physiological saline, whereas the treated group was administered a single oral dose of RSAE at 2000 mg/kg body weight. All rats were observed for 6 hours following the administration of the extract, and then once daily for 14 days, to monitor changes in general behavior, clinical signs of toxicity, and mortality. Body weights were recorded at baseline (Day 0) and on days 7 and 14. After 24 hours of fasting, rats were anesthetized, and blood samples were collected from the retro-orbital sinus to determine hematological and biochemical parameters.

For hematological analysis, blood is collected in EDTA tubes and analyzed for red blood cell count (RBC), white blood cell count (WBC), hemoglobin concentration (Hb), hematocrit value (HCT), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), and platelet count. Hematological parameters were measured using an automated hematology analyzer (Sysmex KX-21, Japan). For the biochemical analysis, serum was used to determine the following parameters: blood urea, blood creatinine, alanine aminotransaminase (ALT), aspartate aminotransaminase (AST), TC, TGs, HDL-c, and LDL-c. All biochemical analyses were carried out on an automated analyzer, ERBA XL-600, Germany.

Effect of *Retama sphaerocarpa* aqueous extract on Triton WR-1339-induced hyperlipidemic rats

To investigate the antidyslipidemic activity of RSAE on Triton WR-1339-induced hyperlipidemic rat model. Hyperlipidemia was induced by a single intraperitoneal injection of Triton WR-1339 (200 mg/kg; Sigma-Aldrich, St. Louis, MO, USA), dissolved in phosphate-buffered saline (pH 7.4). The experimental design and procedures were performed according to previously published studies [18].

After an overnight fast, animals were randomly assigned to four experimental groups (n = 6 per group). Group I served as the normal control and received a standard diet and distilled water. Groups II, III, and IV received Triton WR-1339 intraperitoneally to induce hyperlipidemia. Group II served as the hyperlipidemic control and received distilled water. Group III received RSAE at a dose of 400 mg/kg/day via oral gavage. Group IV was treated with atorvastatin (10 mg/kg/day, aqueous suspension). Atorvastatin was used as a positive control in the study. Treatments were given once daily for seven consecutive days. On the 7th day, following an 18-hour fast, Triton WR-1339 (200 mg/kg, dissolved in 0.9% saline) was administered intraperitoneally 1 hour after the last oral administration to induce experimental hyperlipidemia. After 24 hours, blood samples were collected under light anesthesia. Samples were immediately centrifuged (5000 rpm/10 min) and serum was used for lipid analysis (Total cholesterol, Triglycerides, LDL-c and HDL-c levels) using an automated biochemical analyzer (ERBA XL-600, Germany).

Statistical analysis

All experimental data were expressed as mean values ± SEM. Student's t-test was used to compare two groups (acute toxicity study). To evaluate antidyslipidemic activity, one-way analysis of variance (one-way ANOVA), followed by Bonferroni's post hoc test, was used to compare the means of the hyperlipidemic groups with those of the treated groups and the normolipidemic control groups. Statistical analyses were conducted using GraphPad Prism version 7. A *p*-value of less than 0.05 was considered statistically significant.

RESULTS AND DISCUSSION

Total phenolic, flavonoid, and tannin contents

The total phenolic compounds in the aqueous extract of *Retama sphaerocarpa* were determined to be 289.57±8.41 mg gallic acid equivalents per 1 gram of the extract (289.57±8.41 mg GAE/1 g RSAE), using gallic acid as a standard for the calibration curve. The total flavonoid content in the same extract was estimated to be 174.35±7.54 mg of the equivalent of Rutin per one g of the extract (174.35±7.54 mg RE/ 1 g RSAE), using Rutin as the standard flavonoid to establish the calibration curve. While the tannins of the extract were estimated at 20.32 ± 3.29 mg catechin

equivalents (CE) per gram of RSAE, with catechin serving as the reference standard for calibration.

Antioxidant activity

The findings of this study revealed that RSAE exhibited a concentration-dependent antioxidant activity across the tested concentrations (31.25, 62.5, 125, 250, and 500 µg/mL). The following percentages of inhibition (I%) were revealed (16.49, 25.45, 38.41, 52.29, and 84.34%, respectively) (Figure 1). Concerning the synthetic antioxidant agent BHT, inhibition percentages of 49.17%, 52.89%, 59.67%, 68.66%, and 82.87% were recorded at the tested concentrations. The IC_{50} value was determined using linear regression analysis. The RSAE exhibited an IC_{50} equal to 241.45 µg/mL, whereas the standard antioxidant, butylated hydroxytoluene (BHT), showed an inhibitory concentration (IC_{50}) equal to 13.63 µg/mL.

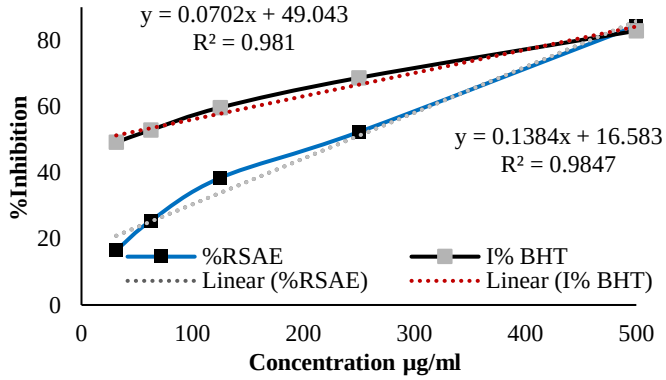

Figure 1: DPPH radical scavenging activity of *Retama sphaerocarpa* aqueous extract *(*RSAE). BHT: butylhydroxytoluene; DPPH: 2,2-diphenyl-1-picrylhydrazyl.

ACUTE TOXICITY STUDIES

Clinical observations and determination of LD_{50}

Single oral administration of RSAE at 2000 mg/kg did not cause any signs of toxicity or mortality in rats compared with the vehicle-treated group during the 14-day study period, although a slight loss of appetite was observed on the first day; the animals then returned to their normal state. The lethal dose 50 (LD_{50}) is therefore presumed to be greater than the dose tested (2000 mg/kg).

Effect of RSAE on body weight

Single oral administration of RSAE at 2000 mg/kg did not significantly affect body weight during the 14-day monitoring period compared with the control group (Figure 2).

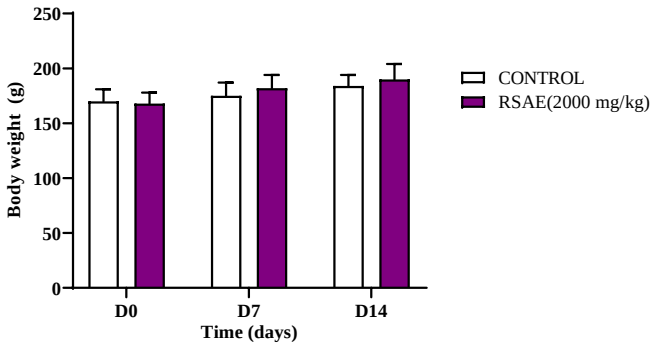

Figure 2: Body weight changes during the oral toxicity study of RSAE. Values are expressed as mean ± SEM (n = 5).

Effect of RSAE on hematological and biochemical profile

Hematological parameters were assessed 24 hours after a single oral administration of RSAE (2000 mg/kg), and the results are presented in Table 1. Our findings showed that a single oral dose of RSAE (2000 mg/kg) in rats did not produce any significant alterations in hematological parameters compared with the control group. Similarly, the effects of RSAE on biochemical parameters, summarized in Table 2, revealed no statistically significant differences in any biochemical parameter compared with the control groups.

Effect of RSAE on Triton WR-1339-induced hyperlipidemic rats

Table 3 summarizes the effects of RSAE on plasma lipid profile parameters (TC, TGs, HDL-c, and LDL-c). Compared with the normolipidemic control group, injection of Triton WR-1339 markedly increased plasma TC, TG, and LDL-c levels. However, Triton WR-1339 did not significantly increase high-density lipoprotein cholesterol (HDL-c) levels compared with the normolipidemic control group.

Compared with the hyperlipidemic control group, pretreatment of hyperlipidemic rats with RSAE (400 mg/kg) for seven days before Triton injection significantly attenuated plasma levels of TC ($p<0.01$), TGs ($p < 0.001$), and LDL-c ($p < 0.0001$). Moreover, pretreatment with RSAE (400 mg/kg) for 7 consecutive days significantly increased plasma HDL-c levels ($p < 0.01$) compared with the hyperlipidemic control group.

Similarly, treatment of rats with atorvastatin significantly reduced plasma levels of TC ($p<0.001$), TGs ($p<0.0001$), and LDL-c ($p<0.0001$), without producing any significant elevation in plasma HDL-c levels.

Table 1: Effect of acute oral treatment with *Retama sphaerocarpa* aqueous extract on hematological parameters

Parameters	Control	RSAE (2000 mg/kg)
White blood cell ($x10^9$/L)	8.75±0.42	8.47±0.32
Red blood cell ($x10^{12}$/L)	6.86±0.62	7.10±0.57
Haemoglobin (g/dL)	12.89±0.45	13.36±0.49
Mean corpuscular volume (fl)	48±3.47	55±3.38
Hematocrit %	37.54±1.60	39.19±1.45
Mean cell haemoglobin (pg)	19.45±0.22	19.40±0.25
Mean cell haemoglobin conc. (g/dl)	40.1±0.77	38.1±0.80
Platelets ($x10^9$/L)	522±24.12	540±22.75

All Data are expressed as mean ± SEM (n= 5 animals per group). No significant differences were observed between the treated groups and the control at p < 0.05.

Table 2: Effect of acute oral treatment with *Retama sphaerocarpa* aqueous extract on biochemical parameters

Parameters	Control	RSAE (2000 mg/kg)
Urea (mmol/L)	3.99±0.060	3.66±0.055
Creatinine (µmol/L)	33.15±0.412	34.29±0.428
AST (U/L)	300±22.931	296±18.879
ALT (U/L)	98±5.78	111±5.91
TC (mmol/L)	2.06±0.183	1.98±0.169
TGs (mmol/L)	0.42±0.078	0.38±0.091
HDL-c (mmol/L)	1.31±0.123	1.24±0.119
LDL-c (mmol/L)	0.59±0.063	0.54±0.057

Data are expressed as mean ± SEM, with n= 5 animals per group. All values were not significantly different from the control at p<0.05.

Table 3: Effect of *Retama sphaerocarpa* aqueous extract (400 mg/kg) on the lipid profile in Triton WR-1339-induced hyperlipidemic rats.

Groups	TC (mmol/L)	TGs (mmol/L)	HDL-cholesterol (mmol/L)	LDL-cholesterol (mmol/)
Normolipidemic group	2.15 ± 0.11	0.70 ± 0.09	1.59 ± 0.09	0.36 ± 0.01
Hyperlipidemic control	10.37 ± 0.40 # # # #	21.94 ± 2.67# # # #	2.06 ± 0.52	4.60 ± 0.34# # # #
Hyperlipidemic+ Atorvastatin (10 mg/kg)	4.04± 0.91***	5.07 ± 1.99****	1.27 ± 0.19	1.42 ± 0.14 ****
Hyperlipidemic+ RSAE (400 mg/kg)	5.07 ± 0.67**	8.74 ± 0.72***	4.44 ± 0.97**	1.22 ± 0.23****

*Values are expressed as mean ± SEM (n = 6). ** p<0.01, *** p<0.001 and **** p<0.0001 when compared to the hyperlipidemic group. ####p < 0.0001 when compared to normolipidemic control group.*

DISCUSSION

Several experimental studies have widely used Triton WR-1339 (Tyloxapol) to induce acute hyperlipidemia in experimental animal models to evaluate the potential of natural and synthetic lipid-lowering agents [19] and to investigate the lipid metabolism [20]**.** Its mode of action involves the activation of 3-hydroxy-3-methylglutaryl-CoA (HMG-CoA) reductase, thereby increasing hepatic cholesterol biosynthesis, and inhibition of lipoprotein lipase activity, the enzyme responsible for triglyceride hydrolysis, thereby reducing their absorption by tissues [21].

In this study, acute hyperlipidemia was induced by intraperitoneal injection of Triton WR-1339, which resulted in a significant increase in plasma lipids (TC, TGs, and LDL-c) at 24 hours compared with normolipidemic groups, while there was no significant alteration in HDL-c levels in rats after Triton WR-1339 injection. Increased blood cholesterol levels, especially the LDL fraction (bad cholesterol), represent the major risk factor for coronary heart disease [22]. Our findings showed that pretreatment with the aqueous extract of Retama sphaerocarpa for 7 consecutive days before Triton injection prevented increases in total cholesterol and the LDL-c fraction compared with hyperlipidemic controls. The observed decrease in total cholesterol level was accompanied by a considerable reduction in the LDL fraction. This finding suggests that the hypocholesterolemic activity of RSAE may be attributed to enhanced LDL-c catabolism, possibly mediated by increased expression of hepatic LDL-c receptors[23]. Additionally, the decrease in total cholesterol levels may be attributed to inhibition of HMG-CoA reductase, a key enzyme in cholesterol biosynthesis [24]. HDL-c, commonly known as "good cholesterol", has a protective role in coronary heart disease. It transports excess cholesterol from the blood vessels to the liver for processing and elimination, thereby helping prevent the formation of atherosclerotic plaques in the arteries. HDL-c is therefore a key factor in preventing the development of atherosclerosis and reducing the risk of coronary heart disease [25,26].

Importantly, pretreatment with RSAE (400 mg/kg) for 7 consecutive days before induction of hyperlipidemia exhibited a

protective effect by significantly increasing the level of HDL-c, this observed effect may be attributed to the increased activity of lecithin-cholesterol acyl transferase, which facilitates the mobilization of cholesterol and triglycerides from the serum to the liver by a pathway called "reverse cholesterol transport" where it is catabolized and eliminated from the body [25]. Triglycerides play a crucial role in regulating lipoprotein interactions and maintaining normal lipid metabolism [6]. Hypertriglyceridemia is a common lipid disorder that has been associated with an increased incidence of atherosclerotic cardiovascular disease [27].

It should be noted that administration of RSAE (400 mg/kg) for seven consecutive days prior to Triton WR-1339 injection significantly attenuated the rise in plasma triglyceride levels, this observed effect may be attributable to an increase in the activity of the lipoprotein lipase, leading to the hydrolysis of triglycerides into fatty acids [28], or possibly due to increased uptake of triglycerides from plasma by skeletal muscle and adipose tissue [29]. It is important to note that the mechanistic explanations proposed in this study are hypothetical and were not experimentally evaluated. Further mechanistic investigations are warranted to elucidate the precise pathways underlying the observed antidyslipidemic effects. While the present findings demonstrate that RSAE exerts significant antidyslipidemic activity in the Triton WR-1339-induced hyperlipidemia model, this approach reflects a short-term experimental condition that differs from the chronic human dyslipidemia. Therefore, further studies using chronic (e.g., high-fat diet-induced dyslipidemia dietary models are warranted to better assess the sustained therapeutic relevance of RSAE. Our findings are consistent with those reported by Maghrani *et al*. [30], who demonstrated that repeated oral administration of the aqueous extract of *R. raetam* leaves resulted in a significant reduction in plasma cholesterol & triglyce- rides levels in streptozotocin (STZ)-induced diabetic rats. Many investigations reported a link between dyslipidemia and oxidative stress. Dyslipidemia can contribute to oxidative stress by promoting the production of reactive oxygen species (ROS); conversely, oxidative stress can contribute to dyslipidemia by promoting the oxidation of LDL-cholesterol, thereby contributing to atherosclerosis [31]. Consequently, we can conclude that controlling oxidative stress levels may be effective in managing dyslipidemia and its associated health problems. In this regard, an interesting antioxidant activity of *Retama sphaerocarpa* was observed, with the concentration of RSAE required to reduce 50% of the DPPH radical (IC_{50}) determined to be 241.45 µg/mL. Several rigorous clinical studies have demonstrated that bioactive compounds derived from medicinal plants are safe and effective for the management of dyslipidemia [32]. In this context, the observed antidyslipidemic effect in our study of Retama sphaerocarpa is likely attributable to its rich content of various bioactive metabolites. In this regard, our study findings revealed the richness of *Retama sphaerocarpa* in polyphenols, flavonoids, and tannins, all of which are known to modulate lipid metabolism [33]. Several studies have reported that polyphenols can modulate lipid metabolism through multiple mechanisms. Several studies suggest that certain polyphenolic compounds may inhibit HMG-CoA reductase activity, thereby reducing endogenous cholesterol synthesis. Additionally, polyphenols have been reported to enhance LDL receptor expression and promote LDL-c clearance from circulation [34-37]. Nevertheless, further advanced phytochemical studies (e.g., HPLC-MS) are needed to determine the chemical composition of the aqueous extract of *Retama sphaerocarpa* and to identify and isolate the specific active compounds responsible for the observed antidyslipidemic effect.

For a long time, medicinal plants have played an important role in the treatment of many diseases [38]; however, it is imperative to investigate their potential toxicity before their use in various disease models [39]. Acute toxicity assessment of medicinal plants provides primary insight into their mechanism of toxic action [40]. Our findings indicate that acute administration of the aqueous extract of *Retama sphaerocarpa* produced no observable toxicity or adverse effects in rats. Moreover, no mortality was observed following the single oral dose of 2000 mg/kg over a 14-day monitoring period, suggesting that the lethal dose (LD_{50}) is greater than 2000 mg/kg. According to Diezi's (1989) [41] classification, the aqueous extract of *Retama sphaerocarpa* is relatively toxic. Our results are consistent with previous studies that estimated the LD_{50} of Retama sphaerocarpa to be greater than 1000 mg/kg, supporting its low acute toxicity and suggesting a favorable safety profile [42]. The analysis of blood parameters is extremely important for determining the anomalies induced by plant extracts [43]. It also provides information about the mechanism of toxicity/safety of a therapeutic agent [40]. The hematopoietic system, which is responsible for the production and development of blood cells, is extremely sensitive to toxic molecules; alterations in this

system provide a greater predictive value for human toxicity [44]. Evaluation of hematological parameters provides important insight into the local and systemic manifestations of intoxication induced by plant extracts [45]. Based on the hematological evaluation results obtained in this study, no significant changes were observed in any hematological indices after 24 hours of single oral administration of RSAE (2000 mg/kg) compared with the control group.

It can be concluded that the extract has no harmful effect on circulating white and red blood cells or on platelets. Additionally, acute oral treatment of rats with the aqueous extract of *Retama sphaerocarpa* did not induce any significant alterations in ALT, AST, urea, or creatinine levels, which are commonly considered reliable markers of liver and kidney function. Furthermore, RSAE did not exhibit any significant impact on the lipid profile (total cholesterol, triglycerides, HDL-cholesterol, and LDL-cholesterol) after a single 24-hour administration compared to the control group, suggesting that the extract does not adversely affect lipid metabolism. Based on the results of the acute toxicity study, we concluded that RSAE was not toxic and could be used for pharmacological and therapeutic purposes; however, more advanced toxicity studies, such as chronic toxicity investigations, including detailed biochemical, hematological, and histopathological evaluations, are needed to predict the potential toxic effects of this plant.

CONCLUSION

In conclusion, the present study demonstrated that the aqueous extract of *Retama sphaerocarpa* prevented elevations in total cholesterol, triglycerides, and LDL-c levels, while promoting an increase in HDL-c levels in Triton WR-1339-induced hyperlipidemic rats. These findings suggest a promising hypolipidemic potential of the *Retama sphaerocarpa*, highlighting its relevance as a therapeutic candidate for the management of dyslipidemia. Furthermore, acute toxicity assessment indicated that the aqueous extract of *Retama sphaerocarpa* is potentially safe and non-toxic at a single oral dose of 2000 mg/kg. Nevertheless, further comprehensive studies are required to confirm its efficacy and safety profile.

ETHICAL CONSIDERATIONS

All applicable institutional guidelines for the care and use of animals were followed, as approved by the local committee of the Faculty of Sciences & Techniques Errachidia, Morocco, with ethical approval number FSTE/2015.

FINANCIAL ASSISTANCE

NIL

CONFLICT OF INTEREST

The authors declare no conflict of interest.

AUTHOR CONTRIBUTION

Adil Qabouche conceived and designed the study and drafted the manuscript. Ismail Bouadid contributed to the realization of experimental techniques and laboratory manipulations. Ayoub Amssayef contributed to the analysis and interpretation of the data. Mohamed Eddouks and Ahmed El-Haidani supervised this work and contributed to the critical revision and correction of the manuscript. All authors read and approved the final manuscript.

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