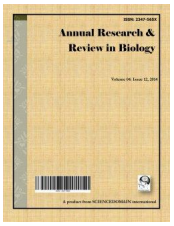

*Annual Research & Review in Biology*

*25(3): 1-12, 2018; Article no.ARRB.40410*
*ISSN: 2347-565X, NLM ID: 101632869*

# Hepatoprotective and Anti-inflammatory Activities of Algerian *Capparis spinosa.* L

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***Authors' contributions***

*This work was carried out in collaboration between all authors. Author RA designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Authors LA, AB and NC managed the analyses of the study. Author NB managed the literature searches. All authors read and approved the final manuscript.*

***Article Information***

DOI: 10.9734/ARRB/2018/40410
Editor(s):
(1) George Perry, Dean and Professor of Biology, University of Texas at San Antonio, USA.
Reviewers:
(1) Errafiy Nadia, Mohammed VI University of Health Sciences, Morocco.
(2) Norma Aurea Rangel Vazquez, Mexico.
(3) Vetriselvan Subramaniyan, MAHSA University, Malaysia.
Complete Peer review History: http://www.sciencedomain.org/review-history/23914

***Original Research Article***

***Received 13th January 2018***
***Accepted 22nd March 2018***
***Published 31st March 2018***

## ABSTRACT

The aim of this study was to evaluate anti-inflammatory and hepatoprotective effects of methanolic extracts from fruits and leaves of *Capparis spinosa*. For hepatoprotective activity, liver injury was induced in male Wistar mice by administration of $CCl_4$ (1 ml / kg of $CCl_4$ 30% in olive oil,), while *C. spinosa* leaf extract (CSLE) and fruit extract (CSFE) were administered orally to the experimental animals. Haematoxylin and Eosin based histology was performed to evaluate the histological changes in the liver. *In vitro* anti-inflammatory activity was evaluated using albumin denaturation assay and membrane stabilization inhibitory activity at different concentrations. The methanol extracts showing effective *in vitro* anti-inflammatory activity were also tested for *in vivo* anti-inflammatory activity by carrageenan-induced paw edema in mice model. At a dose of 400 mg / kg, both extracts showed significant reduction of edema in the early and late phases of acute inflammation with a maximal effect at 6 hours after induction of the inflammation. Also and at the concentration of 400 µg / ml, the CSFE and CSLE exhibited significant protection of erythrocyte

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membrane against the lysis induced by heat (35.4% and 28.4%, respectively) and induced hypotonicity (58.9% and 72.8%, respectively). They also showed a significant protective effect, with a maximum percent of inhibition of the denaturation of albumin of 61.78% and 61.12%, respectively. Moreover, both extracts showed significant hepatoprotective activity that was evident by enzymatic examination and histopathological study. These findings proved that CSFE and CSLE have an anti-inflammatory and hepatoprotective activities, although slightly better for the leaf extract.

*Keywords: Hepatoprotection; anti-inflammatory; Capparis spinosa; methanolic extracts.*

## 1. INTRODUCTION

The use of plants as medicines goes back to early man. Certainly the great civilisations of the ancient Chinese, Indians, and North Africans provided written evidence of man's ingenuity in utilising plants for the treatment of a wide variety of diseases [1]. Currently, natural products are important sources of medicines, and Over 60% of the world's population, uses plant medicines as an initial pharmaceutical remedy [2]. Algeria, a country known for its natural resources, has a singularly rich and varied flora which is widely used in traditional system of medicine. There are approximately 3000 plant species of which 15% are endemic and belong to several botanical families [3].

Caper (*Capparis spinosa* L.) is native to the Mediterranean region, like Algeria, and is also widely grown in the dry regions in west and central Asia. Its immature flower buds, unripe fruits, and shoots are consumed as foods or condiments in cooking [4]. Different parts of this plant, including the flower buds, fruits, seeds, shoots, and bark of roots, were traditionally used as folk medicines in the treatment of disorders, such as rheumatism, stomach problems, headache and toothache [5]. In spite of the very wide-spread use of *Capparis spinosa*, few studies were carried out on leaves and fruits to support its ethno pharmacological use. Pharmacological studies have demonstrated that *C. spinosa* known to possess hypoglycemic [6] antibacterial [7] antifungal [8] anti-inflammatory [9] anti hepatotoxic [10], broncho-relaxant [11], and immunomodulatory activities [12,13]. These biological activities could be attributed to the presence of secondary metabolites present in caper such as carotenoids [14] sterols [15,16] alkaloids [17] flavonoids and phenolics [18] .

However, fruits and leaves of *C. spinosa* specie grown in Est of Algeria have never been screened for hepatoprotective and anti-inflammatory activity. Likewise, in the previous work conducted in our laboratory, we have demonstrated that all parts of *Capparis spinosa* have good antioxidant potential capacity and free radical scavenging. These effects may be attributed to the contents of polyphenols [19]. Therefore; the present study was performed to investigate methanolic extracts of both leaves (CSLE), and fruits (CSFE), for their hepatoprotective and antiinflammatory activities.

## 2. MATERIALS AND METHODS

### 2.1 Plant Material

The fruits and leaves of *Capparis spinosa* were collected on May and June 2014 from the region of Beni-Aziz, Setif (northeast of Algeria; 36° 28′ North and 5º39′ East). The samples were transported to the laboratory to be cleaned manually and identified by Prof H. Laouer and a voucher specimen was deposited at the Department of vegetal biology and Ecology, University Ferhat Abbas, Setif 1, Algeria. The extracts were prepared as reported previously [19].

### 2.2 Animals

Male Wistar albino mice weighing between 30 and 33 g were used in all experiments. The animals obtained from 'Institut Pasteur d'Algérie', were maintained under standard laboratory conditions: temperature of 25ºC and a photoperiod of 12 h and received standard mouse food and water *ad libitum.* The animal studies were conducted after obtaining clearance from Institutional Animal Ethics Committee (Ref LBA2017), and the experiments were conducted in strict compliance according to ethical principles and provided by Committee for the Purpose of Control and Supervision of Experiments on Animal (CPCSEA).

### 2.3 Erythrocyte Membrane Stabilization Assay

The inhibition of hemolysis test of the red blood cells is carried out with the method of [20] and [21] with some modifications.

#### 2.3.1 Preparation of red blood cells (RBCs) suspension

The Blood was collected from healthy volunteer human who has not taken any Non-steroidal Anti-Inflammatory Drugs (NSAIDs) for 2 weeks prior to the experiment and transferred to the centrifuge tubes. The tubes were centrifuged at 2200 rpm for 10 min and were washed three times with equal volume of normal saline. The volume of blood was measured and reconstituted as 10% (v/v) suspension with normal saline.

#### 2.3.2 Heat induced haemolysis

A volume of 5 ml of the isotonic buffer containing 200 and 400 µg /ml of methanolic extracts of *C. spinosa* were put into centrifuge tubes. The vehicle, in the same amount, was added into another tube as control. Erythrocyte suspension 50 µl was added to each tube and mixed gently by inversion. The tubes were incubated at 54°C for 20 min in a water bath. At the end of the incubation, the reaction mixture was centrifuged for 3 min at 1300 g and the absorbance of the supernatant was measured by spectro-photometry at 540 using Aqua Mate spectro photometer. Acetyl salicylic acid (ASA) 100 µg/ml was used as a reference. The Percentage of inhibition of haemolysis was calculated as follows:

$$\text{Percentage inhibition} = 100\ (Abs_{control} - Abs_{sample}) / Abs_{control}$$

#### 2.3.3 Hypotonicity-induced haemolysis

The hypotonic solution (distilled water, 5 ml) containing methanolic extract of fruits or leaves (200 µg / ml and 400 µg / ml) is prepared (for each dose) in centrifuge tubes. The control tubes contained 5 ml of distilled water or acetylsalicylic acid (0.5 mg / 5 ml). The red blood cells human (50 µl) are added to each tube. After gentle stirring, the mixtures were incubated for 1 h at room temperature. After incubation, the reaction mixture is centrifuged for 3 min at 1300 g and the absorbance of the supernatant is measured at 540 nm using an AquaMate spectrophotometer, then the % of haemolysis inhibition were calculated as follows: Inhibition of hemolysis % = 100 (A1 – A2) / (A1), where A1: Absorbance of the control sample, A2: Absorbance of treated sample/ standard

### 2.4 Albumin Denaturation Assay

The anti-inflammatory activity of *C.spinosa* was studied by using inhibition of albumin denaturation technique which was studied according to [22,23] with minor modifications. The reaction mixture consists of tested extracts and 1% aqueous solution of bovine serum albumin (BSA), the pH of the reaction mixture was adjusted using small amount of 1N HCl. The sample were incubated at 37ºC for 20 min then heated to 54ºC for 20 min. After cooling the samples the turbidity was measured at 660 nm. The Percentage of inhibition of protein denaturation was calculated using the relation:

$$\% \text{ Inhibition} = 100\ (A_{Control} - A_{Sample}) / A_{Control}.$$

### 2.5 Carrageenan-induced Paw Edema in Mice

Acute inflammation was induced using Carrageenan-induced mice paw edema model as previously described [24]. Mice (n = 6/group) were treated orally using 200 and 400 mg / kg of CSFE or CSLE, one hour before carrageenan injection. At the same time, control group was given 10 ml / kg of normal saline and the reference group was given 10 mg/kg of an aqueous solution of indomethacin. The carrageenan was injected to induce paw edema 1 h after the last dose on the third day. The right hind paw of each mouse was subcutaneously injected with 10 µL of freshly prepared carrageenan (1.0%, w/v) in physiological saline. The thickness of the edema was determined using an electronic calliper (Mastercraft, Canada) immediately before and 1, 2, 3, 4, 5, and 6 h after carrageenan injection. The inhibitive rate of *C. spinosa* extracts on the paw edema was calculated following the formula:

Inhibition % = 100 (T0 -Tt) / T0, where Tt = thickness of the paw edema of the treated group at a given time (t), T0 = thickness of the paw edema of the control group at the same time.

### 2.6 Hepatoprotective Activity

The present study was done according to the method previously described by [25] with a few modifications. The hepatoprotective activity was evaluated in Wister albino mice using $CCl_4$ (30% mixed with olive oil, 1ml/kg) induced liver injury. Mice were divided into seven groups (n=7); Group-1 served as control (normal saline), Group II served as hepatotoxic ($CCl_4$), Group III, served as positive control treated with Silymarin. Group IV & V served as CSFE (200 and 400 mg/kg bw) treated groups, while Group VI & VII served as CSLE (200 and 400 mg/kg bw) treated groups.

Animals were sacrificed, under light ether anesthesia, 24 h after the last dose. Blood samples were collected into tubes. After blood collection, animals were sacrificed and the liver was excised, fixed in 10% buffered formalin for histopathological assessment of liver damage. Blood was centrifuged at 3500 rpm for 10 min and the serum was tested for liver markers; Aspartate aminotransferase (AST), Alanine aminotransferase (ALT), Alkaline phosphatase (ALP) and bilirubin.

## 2.7 Statistical Analyzes

Statistical study was carried out by Graph Pad Prism 5 statistical software. The results are represented as mean ± standard deviation and the differences were considered significant at $P \leq 0.05$. Group comparisons were performed by ANOVA analysis. Significance between the control group and the experimental groups was evaluated by the Dunnet test and differences at $p \leq 0.05$ were considered significant.

## 3. RESULTS AND DISCUSSION

## 3.1 *In vitro* Anti-inflammatory Activity

### 3.1.1 Membrane stabilizing activity

In the study of membrane stabilizing activity, the both extracts of Capparis spinosa at different concentrations (100, 200 and 400 µg/mL) were tested against the lysis of human erythrocyte membrane induced by hypotonic solution as well as heat, and compared with the standard acetyl salicylic acid (ASA) Table 1. For hypotonic solution induced haemolysis, at a concentration of 400 µg/ mL, CSLE inhibited 72.8% haemolysis of RBCs as compared to 70.4% produced by acetyl salicylic acid which is used as a reference drug (100µg/mL). CSFE also revealed good inhibition of haemolysis of RBCs 58.9%. Although, it is less effective than the inhibition caused by the leaf extract. On the other hand, during heat induced condition both extracts CSLE and CSFE demonstrated 35.4% and 28.4% inhibition of haemolysis of RBCs, respectively whereas ASA inhibited 35.01%. The RBC membrane stabilization has been used as a method to study the *in vitro* anti-inflammatory activity because the erythrocyte membrane is analogous to the lysosomal membrane [26,27] and its stabilization implied that the extracts might well stabilize lysosomal membranes. Stabilization of lysosomal is important in limiting the inflammatory response by preventing the release of lysosomal constituents of activated neutrophil, such as bactericidal enzymes and proteases, which causes further tissue inflammation and damage upon extra-cellular release [28]. The lysosomal enzymes released during inflammation produce a various disorders. CSLE and CSFE inhibited both heat and hypotonicity-induced lysis. These extracts may possibly inhibit the release of lysosomal contents of neutrophils at the sites of inflammation. Anti-inflammatory activity of extracts is comparable to that of acetylsalicylic acid. Although, the precise mechanism of this membrane stabilization is to be elucidated, it is possible that the extracts produced this effect by interacting with membrane proteins to induce cyto protection of the membrane of red blood cells against lysis induced by the heat. Lyses induced by hypotonicity are probably caused by the narrowing of cells due to intracellular osmotic loss of electrolyte and fluid components. The inhibition of hypotonic lysis clearly involves the processes that prevent the migration of these intracellular components out of the cell. It has been shown that cell deformability and erythrocyte cell volumes are closely related to their intracellular calcium content [21]. Thus, the effect of stabilization of the membrane by these agents may be due to the alteration of the calcium influx in the erythrocytes [21].

### 3.1.2 Effect of plant extracts on albumin denaturation

In this study, in vitro anti-inflammatory effect of *Capparis spinosa* is evaluated against the denaturation of albumin. The results are summarized in Table 2. At concentrations of 200 and 400 µg / ml, the methanolic extract of fruit incubated with albumin showed a significant inhibition of albumin denaturation (41.59% and 61.78%, respectively), While that of leaves exerted an inhibition of 39.99% and 60.12%, respectively. For both extracts, the protection of albumin at 400 µg / ml is comparable to the reference product (acetylsalicylic acid), which has a protection rate of 64.85%. Reduction in protein denaturation is another method of showing the anti-inflammatory capacity. Proteins denaturation is a process in which proteins lose their secondary and tertiary structure when exposed to an external (heat) or chemical (acid or strong base) stress [29]. The effect of the plant extracts on protein denaturation was evaluated using bovine serum albumin. Denaturation of protein is one of the causes of rheumatoid

arthritis that was well documented. Production of auto-antigen in certain arthritic diseases may be due to denaturation of protein [30]. Any product or substance preventing the denaturation of proteins is entitled to be an effective anti-inflammatory agent [31]. Its ability to reduce denaturation of proteins has been proven by comparing to similar action by the standard drug. The mechanism of denaturation probably involves alteration of electrostatic hydrogen, hydrophobic and disulfide bonding [32]. From the obtained data, both tested extracts of *C. spinosa* inhibited the precipitation of protein comparable to acetylsalicylic acid.

#### 3.1.3 *In vivo* anti-inflammatory effects of extracts

Since methanolic extracts showed significant *in vitro* anti-inflammatory activity they were selected for the evaluation of *in vivo* anti-inflammatory activity by carrageenan-induced paw edema model in mice. The anti-inflammatory effects of the *C. spinosa* extracts and standard drug are presented in Table 3 and 4. Subplantar injection of carrageenan produced a local edema that increased progressively to reach a maximal intensity 6 hours after injection. The oral administration of methanolic extracts significantly ($p<0.001$) inhibited inflammatory response at 400 mg/kg. The most important inhibition of 60.7 % of CSLE and 57.14 % of CSFE were observed at the $6^{th}$ hour Table 4. The acute inflammatory response induced by carrageenan is characterized by a biphasic response early or first phase and late or second phase [33]. Early phase characterized with marked edema formation resulting from the rapid production of several inflammatory mediators such as histamine, serotonin and bradykinin, while the late phase is associated with the release of prostaglandins. Cyclooxygenase and lip-oxygenase enzymes play roles in the formation of carrageenan-induced edema. The suppression of the first phase may be attributed to inhibition of the release of early mediators, such as histamine and serotonin and action in the second phase may be explained by an inhibition of cyclooxygenase(s) [34]. The result of the present study indicates that CSLE and CSFE at 200 mg/kg were unable to reduce inflammation induced by carrageenan. At 400 mg /kg, both extracts showed significant anti edematogenic activity in both phases after carrageenan injection. This result, however, reaffirms the anti-inflammatory potential of the *Capparis spinosa* extracts. The effective anti-inflammatory activity in vitro and in vivo of *C. spinosa* extracts may be attributed to the presence of bioactive compounds like saponins, alkaloids, steroids, polyphenls and flavanoids [35].

### 3.2 Hepatoprotective Activity of *C.spinosa* Extracts

#### 3.2.1 Effect of *C. spinosa* pre-treatment against $CCl_4$ toxicity on body weight of mice

Comparing the body mass of each group of mice before and after treatment with CSLE and CSFE revealed no significant changes in animal weights (Fig. 1). The relative liver weights of mice treated with carbon tetrachloride (intoxicated batch) were significantly increased, compared to control ($p<0.01$). This increase is not reversed or prevented by pretreatment neither with leaf / fruit extracts at 200 and 400 mg / kg doses nor with silymarin at 50 mg / kg (Fig. 2). The changes associated with $CCl_4$-induced liver damage are comparable to that of acute viral hepatitis [36]. Therefore, $CC1_4$-mediated hepatotoxicity was employed as the experimental model for liver injury. Administration of $CCl_4$ (30%, 1 ml / kg) to mice did not cause death to animals and did not affect physical properties (body weight and general behavior). The significant increase in livers weight after treatment with $CCl_4$ is due to the infiltration of fatty acids and glycerols into hepatocytes via their damaged cell membranes. This liver abnormality is a phenomenon reported by many authors following $CCl_4$ aggression [37].

#### 3.2.2 Biochemical parameters

The effect of CSLE, CSFE and silymarin pre-treatment on serum enzymes of $CCl_4$ intoxicated mice is shown in Table 5. The administration of a single dose of $CCl_4$ (30%, 1 ml/kg) significantly increased the levels of AST ($p<0.01$) and ALT ($p<0.01$), compared to the control. Treatment with extracts and silymarin significantly reduces these parameters. This decrease resulted in values close to those of the control group. The hepatic injury induced by $CCl_4$ also caused an increase in the basal level of bilirubin and alkaline phosphatase (PAL). However, pre-treatment with the both extracts at 400 mg / kg and silymarin showed significant protection against lesions caused by the toxic agent. Pretreatment with *Capparis spinosa* of mice intoxicated with $CCl_4$ significantly reduced

elevated levels of ALAT, ASAT, ALP and bilirubin with $p<0.01$. The decreased levels of serum enzymes can be attributed to the stabilizing effect of the photochemical components of the plant and the various active substances on the plasma membrane of the hepatocytes [38]. Bilirubin levels are related to liver cell function [39]. A high concentration of bilirubin in serum is an indication of the rate of degradation of erythrocytes due to liver damage in hepatotoxin therapy Singh et al. Pre-treatment with *C. spinosa* extracts restored the level of bilirubin to values close to normal indicating the hepatoprotective effect of these extracts. The results suggest that the unbalanced antioxidant system in the liver by carbon tetrachloride is normalized by the protective effect of methanolic extracts of the plant. Many studies have shown that the hepatoprotective effect of plant extracts may be related to its antioxidant ability to trap reactive oxygen species [40,41]. Foods rich in polyphenols and flavonoids have beneficial effects on human health [42]. Of the plants containing natural antioxidants, *Capparis spinosa* has attracted particular interest because of its high content of biologically active compounds. It has been considered to play an important antioxidant role in the prevention of oxidative damage [18].

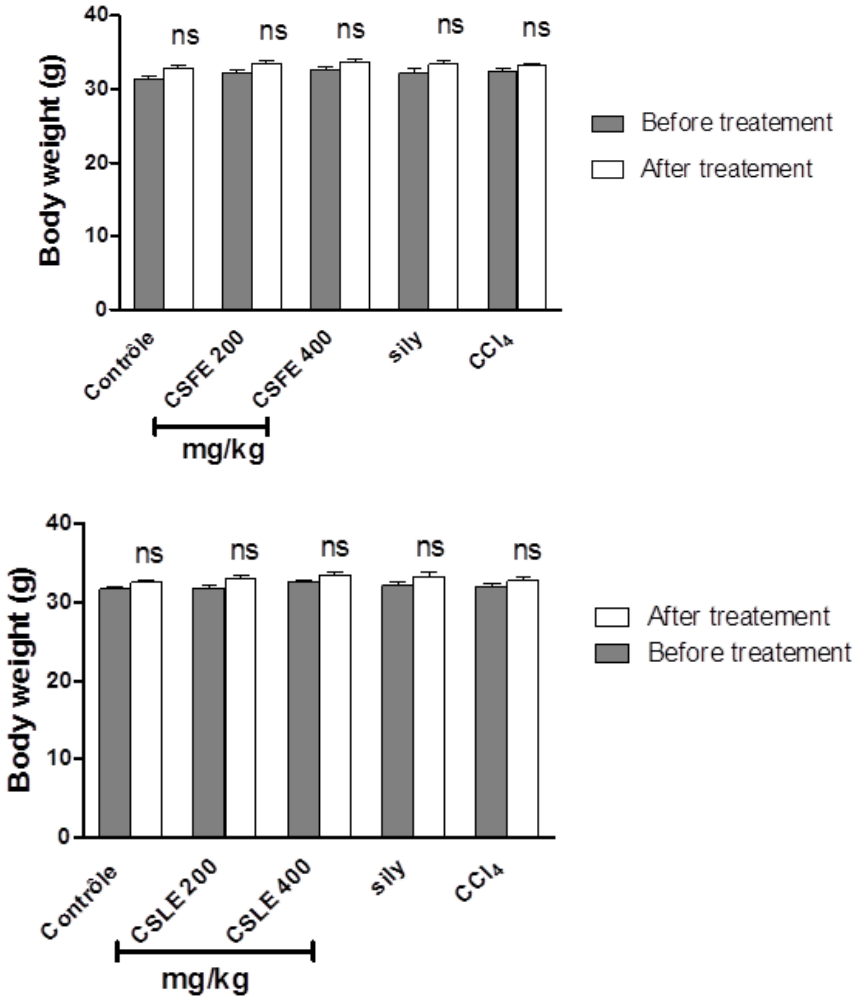


**Fig. 1. (A) Effect of CSFE pre-treatment against $CCl_4$ intoxication, on body weight of mice. (B) Effect of CSLE pre-treatment against $CCl_4$ intoxication, on body weight of mice. Values are expressed as means± SEM (n=7). ns: nonsignificant values**

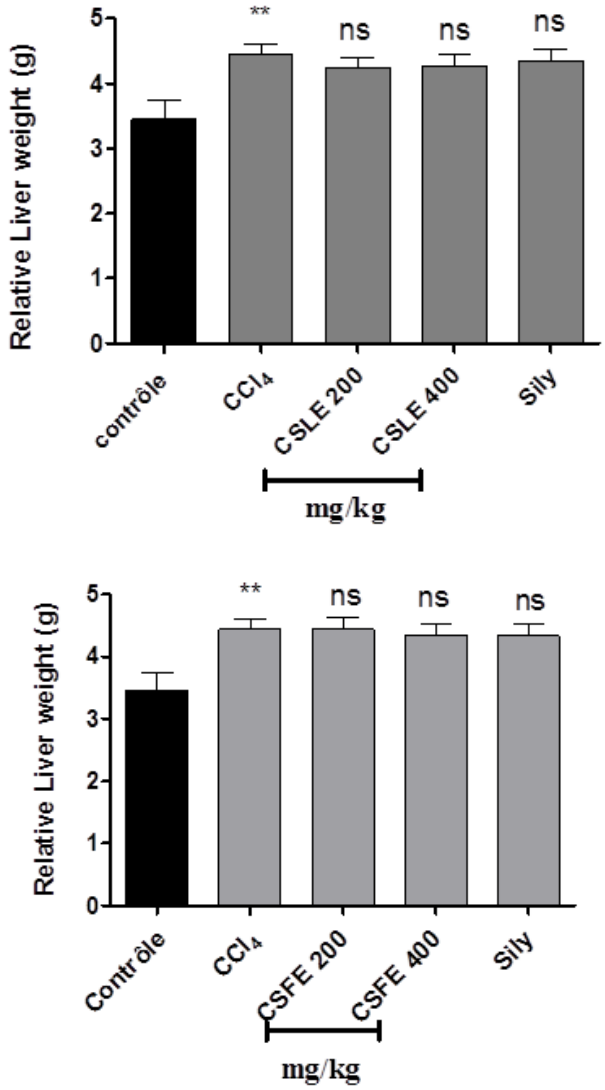


**Fig. 2. (A) Effect of, CSLE pre-treatment against $CCl_4$ intoxication, on relative liver weight of mice. (B) Effect of, CSFE pre-treatment against $CCl_4$ intoxication, on relative liver weight of mice. Values are expressed as means± SEM (n=5). Animal were treated with extract or silymarin for three days before they were treated with $CCl_4$ p.o. * p<0.01 as compared with negative control group. ns compared with intoxicad $CCl_4$ group**

### 3.3.3 Effects of pre-treatment with CSLE and CSFE on histopathological aspect of liver

Liver sections in the control group have normal hepatic cells, visible central veins and thin sinusoids (Fig. 3A). On the other hand, carbon tetrachloride caused a very marked foyer of mononuclear infiltration in the hepatic parenchyma, sinusoid and around central vein, with disorganization of the hepatic structure (Fig. 3B). Pre-treatment with leaf extract at 400 mg / kg body weight showed normal liver cells, a central vein and sinusoids with a weak foyer of mononuclear infiltration without necrosis (Fig. 3C). Similarly, pre-treatment of the liver section with 400 mg / kg of the fruit extract (CSFE) showed liver cells very close to normal, except for the presence of a minimal mononuclear infiltration foyer at the periphery (Fig. 3D). Silymarin drug also showed normal hepatic architecture (Fig. 3E). The protection of liver $CCl_4$ intoxication seems to be dose dependent since the two extracts at 200 mg / kg showed no sign

of protection. Histological studies confirmed the hepatoprotective effect of fruit extract and leaf extracts of *Capparis spinosa*. Liver sections of mice treated with $CCl_4$ showed fatty degeneration of the hepatocytes and necrosis of the cells. Treatment with methanolic extracts (400 mg / kg) almost normalized these effects in the histological architecture of the liver. Therefore, both extracts could be promising hepatotoxic agents against intoxication of liver.

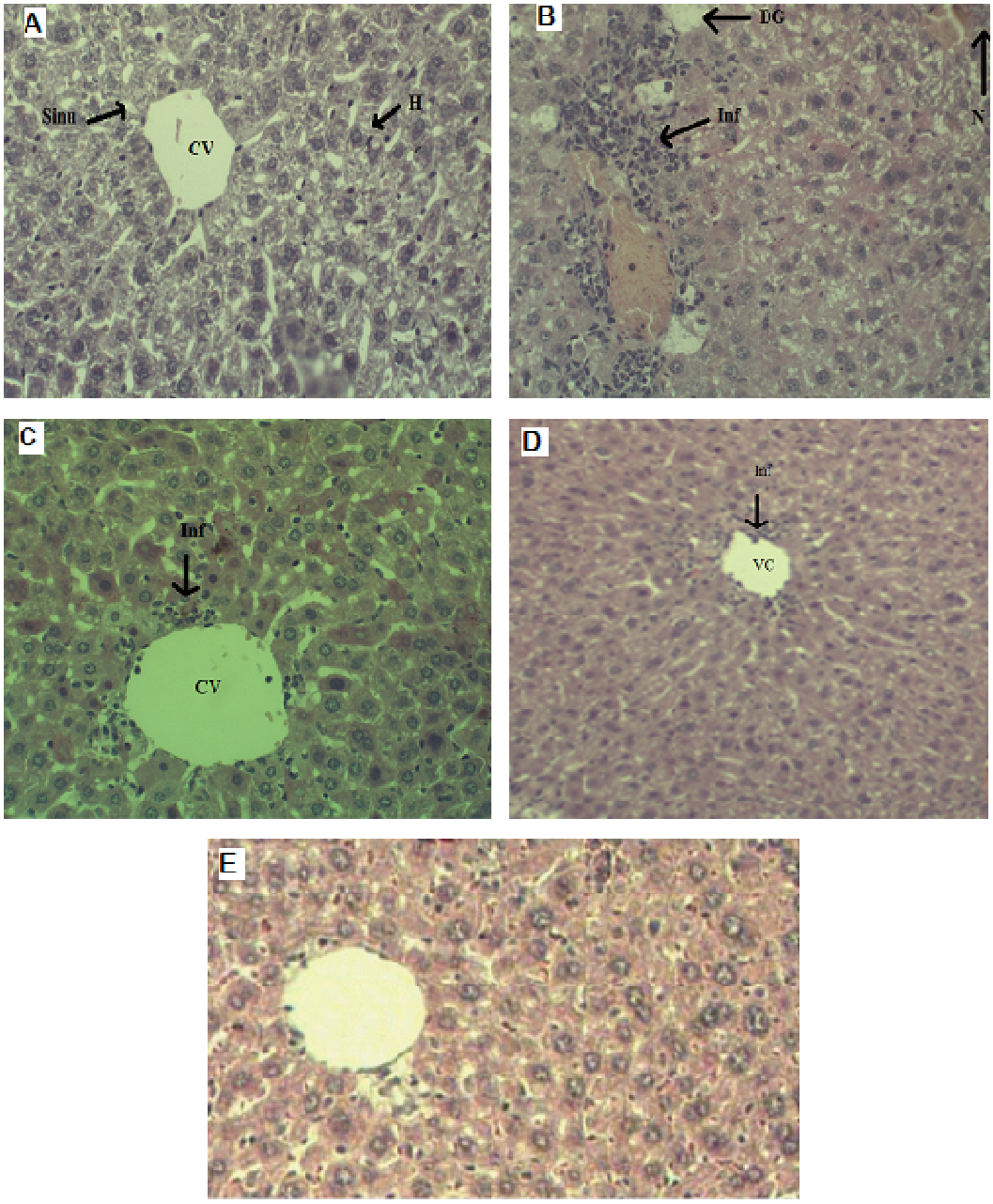


**Fig. 3. Histopathological profile of the livers of mice in *Capparis spinosa* prophylactic treatment with CSLE, CSFE and Silymarin followed by $CCl_4$ intoxication. (A): liver section of normal mice, (B) liver section of $CCl_4$ treated mice, (C): liver of treated mice with 400 mg / kg CSLE, (D): liver of treated mice with 400 mg / kg CSFE, (E): liver of treated mice with Silymarin. DG: Fatty degeneration of the liver; Inf: inflammation by granulocytes; N: Necrosis (× 40)**

**Table 1. Effect of *C. spinosa* extracts on heat-induced and hypotonic solution-induced haemolysis of erythrocyte membrane**

| Treatment | Concentration (µg/ml) | % haemolysis inhibition | |
|---|---|---|---|
| | | Heat-induced | Hypotonic solution-induced |
| Control | - | - | - |
| CSFE | 100 | 6.2±2.94 | 6.8±1.32 |
| | 200 | 5.77± 1.91 | 8.8±2.13 |
| | 400 | 28.4±2.64** | 58.9±4.7*** |
| CSLE | 100 | 8.22±3.02 | 9.6±2.29 |
| | 200 | 7.4±2.13 | 11±2.07 |
| | 400 | 35.4±4.54** | 72.8±2.82*** |
| ASA | 100 | 35.013.73** | 70.4±3.43*** |

*Values are mean ± S.E.M, (n = 6); *p<0.001 and *p<0.01 vs. control.*

**Table 2. Albumin denaturation activity of *Capparis spinosa* extracts**

| Traitement | Concentration (µg/ml) | % d'inhibition |
|---|---|---|
| Contrôle | - | - |
| CSLE | 100 | 13.59 ± 2.2 |
| | 200 | 41.59 ± 8.23*** |
| | 400 | 61.78 ± 9.18*** |
| CSFE | 100 | 16.27 ± 6.48 |
| | 200 | 39.99 ± 5.75*** |
| | 400 | 60.12 ± 3.3*** |
| Acide acétylsalicylique | 100 | 64.85 ± 2.63*** |

****: P<0,001 is considered significant compared to the control.*

**Table 3. Effect of CSLE and CSFE on paw edema (mm) induced by carrageenan in mice**

| Treatments | | Changes in paw thickness (mm) | | |
|---|---|---|---|---|
| Mice (n= 6) | | 1h | 3h | 6h |
| Control | - | 0.72 ± 0.06 | 0.79 ± 0.06 | 0.84 ± 0.04 |
| | 200 mg/kg | 0.66 ± 0.05 | 0.70 ± 0.08 | 0.70 ± 0.03 |
| CSLE | 400 mg/kg | 0.64 ± 0.03 | 0.43 ± 0.03** | 0.33 ± 0.03*** |
| CSFE | 200 mg/kg | 0.67 ± 0.03 | 0.66 ± 0.11 | 0.72 ± 0.03 |
| | 400 mg/kg | 0.63 ± 0.03 | 0.44 ± 0.06** | 0.36 ± 0.05*** |
| Indometacin | 10 mg/kg | 0.51 ± 0.05* | 0.37 ± 0.04*** | 0.28 ± 0.03*** |

*Values are expressed as mean ± SEM (n = 6). *p<0.05; **p<0.01; ***p<0.001*

**Table 4. Inhibition of carrageenan-induced paw edema of mice by oral treatment of CSLE and CSFE**

| Treatment | | Inhibition (%) | | |
|---|---|---|---|---|
| | | 1h | 3h | 6h |
| Control | | - | - | - |
| CSLE | 200 (mg/kg) | 8.33 | 11.39 | 16.6 |
| | 400(mg/kg) | 11.11 | 45.56** | 60.7*** |
| CSFE | 200 (mg/kg) | 6.94 | 16.45 | 14.28 |
| | 400 (mg/kg) | 12.5 | 44.3** | 57.14*** |
| Indometacin | 10 (mg/kg) | 33.33* | 53.16*** | 66.66*** |

*P<0.05 *; P<0.01**; P<0.001****

**Table 5. Effect of leaves and fruits of *Capparis spinosa* extracts on the biochemical parameters of the various groups intoxicated by $CCl_4$**

| Groups | Concentration | ASAT | ALAT | ALP | Bilirubin |
|---|---|---|---|---|---|
| Normal Saline | - | 150,1 ± 1.98 | 134 ± 2,42 | 61,86 ± 4,32 | 0,35 ± 0,02 |
| $CCl_4$ | - | 221 ± 2,43 | 208 ± 3,13 | 167,9 ± 3.2 | 2,12 ± 0,11 |
| CSLE | 200 mg/ kg | 211,8 ± 2,78 | 195 ± 2.86 | 159,1 ± 2.89 | 1,96 ± 0,04 |
| | 400 mg/ kg | 183 ±1,66** | 160,8± 3,29** | 73,57 ± 2,36** | 0,42±0,02** |
| CSFE | 200 mg/ kg | 214,9 ± 3,52 | 189,3 ± 2,78 | 162,1 ± 2,65 | 1,99 ± 0,07 |
| | 400 mg/ kg | 190,7 ± 2,97** | 154,3 ± 2,81** | 79,86 ± 3,58** | 0,48 ± 0,03** |
| Syliramin | 50 mg/ kg | 174,5 ± 4,49** | 147,8 ± 4,17** | 70,16 ± 1,55** | 0,38 ± 0,05** |

*Values are the mean± S.E.M. of seven mice. Significance levels: $p < 0.01$, compared to $CCl_4$ group.*

## 4. CONCLUSION

The two parts of *C. spinosa* used possessed marked anti-inflammatory activity against carrageenan-induced edema and exhibited a liver protective effect against $CCl_4$ induced hepatotoxicity. However, methanolic extracts of leaves of *Capparis spinosa* exhibited more potentiating anti-inflammatory and hepatoprotective activities than that of methanolic extracts of fruits. This may be due to the difference between the levels of the phytochemical constituents present in each extract. Further studies are under way to determine the exact mechanism responsible of the pharmacological effects shown in this paper.

## COMPETING INTERESTS

Authors have declared that no competing interests exist.

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