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International Journal of Diabetology & Vascular Disease Research (IJDVR)
ISSN:2328-353X

Pharmacological Properties of *Capparis spinosa* Linn

Review Article

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Abstract

Capparis spinosa Linn. (Capparaceae) was traditionally used for pharmacological purposes and has potential for use in modern cosmetics. This review aims to assess the current available knowledge of *Capparis spinosa* and its constituents for management of several diseases. Bibliographic investigation was carried out by scrutinizing classical text books and peer reviewed papers, consulting worldwide accepted scientific databases (SCOPUS, PUBMED, SCIENCE DIRECT, Google Scholar) to retrieve available published literature. Only articles on pharmacological and phytochemical studies of *Capparis spinosa* have been selected. The main pharmacological activities of caper are antidiabetic, antihypertensive, hypolipidemic, antioxidant, antimutagenic, anti-allergic, hepatoprotective, antibacterial, antiviral, antifungal, immunomodulatory, anti-apoptotic and anti-inflammatory activities. Phytochemicals studies of this plant revealed the existence of many bioactive components such as the saccharides and glycosides, flavonoids, alkaloids, terpenoids and volatile oils, fatty acids, vitamin C, vitamin E and steroids. We conclude that *Capparis spinosa* is beneficial for the treatment of many pathologies supporting then its use in human nutrition and healthcare.

Keywords: *Capparis Spinosa*; Ethnopharmacology; Phytochemistry; Pharmacological Activities.

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Received: May 21, 2015
Accepted: June 16, 2015
Published: June 19, 2015

Citation: Moufid A, Farid O, M. Eddouks (2015) Pharmacological Properties of *Capparis Spinosa* Linn. *Int J Diabetol Vasc Dis Res*, 3(5) 99-104. **doi: http://dx.doi.org/10.19070/2328-353X-1500020**

Introduction

Traditional medicine is very important for treating many pathologies such as cancer, diabetes, hypertension, microbial and viral contamination, AIDS, allergy and others. The all genus of *Capparis* have been used extensively in folk medicine by many cultures since ancient times, especially in all countries of the Mediterranean basin (Morocco, Spain, Tunisia, Italy, Turkey) and in Western as well as Central Asia [1]. The relationship between capers and human beings can be traced back to the Stone Age. Remains of *Capparis spinosa Linn.* (Capparaceae family) were unearthed in archaeological sites as early as the lower Mesolithic (9500–9000b.p.) [2]. Recently plant remains of *Capparis spinosa* (*C. spinosa*) have been discovered for the first time in China and the eastern part of Central Asia supporting the use of caper for medicinal purposes from 2800 years b.p [3]. Floral buds of caper are commonly used in the Mediterranean cuisine as flavoring for meat and other foods. Caper has been used as a medicinal plant with many beneficial properties. This review aims to assess the current available knowledge of *C. spinosa* and its phytochemical compounds for management of several diseases.

Methods

Bibliographic investigation was carried out by scrutinizing classical text books and peer reviewed papers, consulting worldwide accepted scientific databases (SCOPUS, PUBMED, SCIENCE DIRECT, Google Scholar) to retrieve available published literature. Only articles on pharmacological and phytochemical studies of *C. spinosa* have been selected. Overall, 100 articles were reviewed and 63 articles were selected for the study.

Description and Ecology

Members of the Capparaceae are trees and shrubs. This family had a medium size with 40-45 genera and approximately 700-900 species and are distributed in warm and tropical, sometimes very arid, regions of both hemispheres of the world [4]. *C. spinosa* has a great economic, cosmetic and medicinal importance. This plant has developed special mechanisms in order to survive in the semi-arid lands conditions and consequently its introduction may help to prevent the disruption of the equilibrium of those fragile ecosystems and the soil degradation. Caper grows spontaneously on the steppes of northern Africa and Mediterranean countries, but recently caper is cultivated and exported. Morocco is the main

producer and the first exporter of the caper fruits in the world.

Several studies have reported that *C. spinosa* possess several pharmacological activities including anti-inflammatory, anti-allergic, antidiabetic, hypolipidemic, hepatoprotective, antimicrobial, antiviral, immunomodulatory, antioxidant, anti-apoptotic, stimulating melanogenesis, antimutagenic, antiparasitic, antihypertensive, antiproliferative, antifungal, anti-HIV, anti-*Helicobacter pylori* and anti-complement effects (Table 1).

Anti Diabetic and Hypolipidemic Activities

In the folk medicine many plants are used to control diabetes [5-7]. *C. spinosa* had a large importance for the treatment of some diseases such as diabetes. Although insulin treatment and other chemical therapies can control many aspects of diabetes, numerous complications and undesirable effects such vascular dysfunctions, nephropathy, neuropathy and retinopathy appear when the disease is not well controlled [8-10]. Some studies have reported the potent hypoglycaemic effect of *C. spinosa* [7]. In Morocco this plant is traditionally used in diabetes control and treatment and is considered as the most commonly aromatic in the Moroccan kitchen [6, 11].

We have previously demonstrated that the aqueous extract of *C. spinosa* decreased blood glucose, plasma triglycerides and plasma cholesterol levels in both normal and diabetic rats after oral and repeated administration [12]. The results showed that this plant extract had a clear preventive effect on the hypertriglyceridemia related to development of insulin resistance and glucose intolerance. In addition, we have demonstrated the potent hypolipidemic and anti-obesity effects of caper in high fat diet mice as well as the beneficial effect on insulin resistance [13]. Recently a controlled human study has determined the efficacy of *C. spinosa* in the treatment of hyperglycemia in Type 2 diabetic patients. Interestingly no liver, kidney and other side effects were observed in these patients when treated by 400 mg caper fruit extract three times a day for two months [14].

Cardiovascular Activty

Hypertension is a serious public health problem worldwide; more than 20% of the world's population suffers from high blood pressure. Among the new choices for preventing or treating these disorders the natural products isolated from medicinal plants are taking an important place. *C. spinosa* is widely used in the folk medicine for its diuretic and antihypertensive effects [6, 15, 16] and vasorelaxant effect [15]. These studies have demonstrated the beneficial effect of *C. spinosa* causing a significant reduction in arterial blood pressure by acting on heart rate, the Nitric oxide synthesis pathway as well as the angiotensine converting enzyme inhibition. In addition, we have reported the furosemide-like effect of *C. spinosa* in normal and anaesthetized rats and a significant increase of glomerular filtration rate, urinary volume and electro-

Table 1. Main pharmacological properties of *Capparis spinosa*.

Pharmacological activity	Animal model	Part of the plant	References
Treatment of rheumatism and inflammatory disorders	Kun Ming mice, wistar rats, human chondrocytes	Fruits, Flower buds	[16, 21, 24, 37, 42, 43]
Antiallergic and antihistaminic	Male guinea-pigs and allergic patients	Flower buds and fruits	[4, 44, 45]
Antidiabetic and hypolipidemic	C57BL/6J mice and Type 2 diabetic patients	Fruits	[12-14, 46, 47]
Antihepatotoxic	Wistar rats, mice	Aerial parts, roots	[4, 32]
Antimicrobial	Deinococcus radiophilus, Gram-positive & negative bacteria	Whole plant and roots	[31, 48, 49]
Antiviral and immunomodulatory	Herpes simplex virus (Type HSV-2)	Flower buds	[50, 51]
Antioxidant	Swiss albino rats	Aerial parts and Fresh buds	[52, 53]
Anti-apoptotic	Human dermal fibroblasts	Fruits	[25]
Stimulating melanogenesis	B16 murine melanoma cells	Leaves	[53]
Antimutagenic	*In vitro*	Flower buds	[27]
Antiparasitic	Plasmodium falciparum	Aerial parts	[54]
Diuretic effect	Wistar rats	Fruits	[17]
Antiproliferative	Human hepatoma HepG2 , colon human cancer HT29, human breast cancer MCF-7	Seeds	[41]
Antifungal activity	Valsa mali fungi	Seeds	[41]
HIV-1 reverse transcriptase inhibitory	DNA molecule	Seeds	[41]
Hypotensive	Rats and Spotaneously hypertensive rats	Fruits	[15, 18, 55]
Anti-Helicobacter pylori	clinical isolates of Helicobacter pylori	Plant crude extracts	[56]
Anti-complement	*In vitro*	Fruits	[39]

lyte output without modifications in the plasma angiotensin converting enzyme and renin activities [17, 18]. These studies support the beneficial role of caper in the management of hypertension.

Antioxidant, Anti-Allergic and Anti-Inflammatory Activities

Numerous investigations support the relationship between the Mediterranean diet and low incidence of several diseases, such as cardiovascular diseases and cancer; and they recommended an increase of the consumption of fruits and vegetables. Some plants are known in phytomedicine around the world as anti-oxidative and contain often wide variety of antioxidant molecules, such as phenolic acids, flavonoids and other natural antioxidants distributed in different parts of the plants. Several compounds have been identified in *C. spinosa* including flavonoids, saponins, tannins and tocopherol. These flavonoids display a remarkable role in various pharmacological activities including anti-allergic, anti-inflammatory and antioxidant effects. The important presence of alpha tocopherol in the caper parts makes a new choice for protecting cell membranes from oxidative damage [19, 20]. Cappariside is one of new antioxidant isolated from the *C. spinosa* fruit [19]; this cappariside (4-hydroxy-5-methylfuran-3-carboxylic acid) can be used against multiple types of cancer cells [21]. Similarly more than eleven organic acids isolated from *C. spinosa* possess similar beneficial effects. Recently, a study has revealed that an N-butanol extract of caper induced apoptosis through mitochondrial pathway [22]. In addition, hydro-ethanolic extract obtained from C. spinosa leaves has been demonstrated to exhibit antioxidant activity in both chemical and biological tests [23]. In Male Chinese Kun Ming mice, an acute inflammation in mice hind paws by subcutaneously injection of Carrageenan has been induced, and the anti-inflammatory effects of *C. spinosa* aqueous extract was evaluated with calculating of the paw edema "or inhibition rate" [23]. After oral administration *C. spinosa* extract induced a significant anti-inflammatory activity against carrageenan-induced edema. Additionally, the methanolic extract of the flowering buds of *C. spinosa* possess a chondroprotective effect on human articular chondrocytes. These results could be explained by the high density of flavonoids in methanolic extract of the flowering buds of *C. spinosa* which play an anti-apoptotic or cytoprotective action and prevented cell death caused by reactive oxidative substances (ROS). These flavonoids not only play a direct role as ROS scavengers but also inhibit the enzymes involved in the production of these oxidative substances protecting the DNA against the toxic effects of these compounds [16]. In a recent study the significant inhibitory effect of stachydrine isolated from *C. spinosa* has been demonstrated to be similar to a standard analgesic and anti-inflammatory drug; Diclofenac sodium [24]. This study has demonstrated experimentally that *C. spinosa* extract possess an anti-rheumatoid and anti-arthritic effect, reduced tissue swelling and decreased the edema in both Carrageenan induced paw oedema and Xylene induced ears edema in Male wistar rats. Moreover the ethanolic extract of *C. spinosa* has been demonstrated to protect against apoptosis and cell death induced by oxygenic water H_2O_2 in normal and systemic sclerosis fibroblasts and reduced the levels of reactive oxygen species in systemic sclerosis fibroblasts [25]. Furthermore *C. spinosa* extract has been shown to stimulate melanogenesis in B16 murine melanoma cells, and the increase in the melanin was accompanied by an upregulated expression of tyrosinase [26]. In another study, the genotoxic and antimutagenic effects of caper flower buds aqueous extract on the Allium cepa L root tip meristem cells have been demonstrated [27]. The results of this study suggest that *C. spinosa* buds aqueous extract is non-genotoxic and reveals that this extract has antimutagenic potential against ethyl methane sulfonate induced chromosomial and mitotic aberrations in terms of lagging chromosomes. Moreover, the determination of the protective effects was evaluated against oleaceae antigen challenge induced and histamine-induced bronchospasm in male guinea pigs, and the histamine skin prick test was performed on human volunteers. The methanolic fraction of *C. spinosa* has been demonstrated to exert an inhibitory effect against histamine-induced skin erythema on humans and a good protective effect against the bronchospasm induced by antigen challenge in sensitized guinea-pigs [28].

Antimicrobial Acivity

The antimicrobial activity of *C. spinosa* aqueous extract has been tested against some dermatophytes, this extract prevented completely the growth of two species of fungi: Misrosporum canis and Trichophyton violaceum [29]. On the other hand the petroleum ether and hexanic extracts of *C. spinosa* aerial parts showed a similar activity of inhibition against both gram-positive and gram-negative bacterial species tested such as Helicobacter pylori, Escherichia coli and Bacillus cereus [30, 31].

Hepatoprotective Effect

An important compound named p-Methoxy benzoic acid has been isolated from an aqueous extract of *C. spinosa* and its anti-hepatotoxic activity has been evaluated against hepatotoxicities in wistar rats after intraperitonial injection of the carbontetrachloride CCl_4 and paracetamol successively [32]. This compound prevented toxic effects of both CCl_4 and paracetamol in hepatocytes both *in vivo* and *in vitro* tests. These results are comparable to the known antihepatotoxic agent named Silymarin [32, 4].

Phytochemistry

Several phytochemical studies have tried to elucidate the phytocompounds of *C. spinosa*. The constituents of *C. spinosa* include the saccharides and glycosides, flavonoids, alkaloids, terpenoids and volatile oils, fatty acids and steroids [33]. The major compounds found in *C. spinosa* are flavonoids, indoles, and phenolic acids [21]. Interestingly, a study has revealed the presence of both α- and γ-tocopherol in buds of *C. spinosa* as well as an appreciable level of vitamin C [20]. Lutein and Violaxanthin are the main carotenoids and the principal form of tocopherol detected in leaves was alpha-tocopherol [34]. Other investigations have demonstrated that *C. spinosa* contains in large amounts many secondary metabolites like flavonoids (rutin, quercetin, quercetin-3- rutinoside, kaempferol-3-rutinoside) phenloic components, different alkaloids (capparispine, capparispine 26-O-β-d-glucoside and cadabicine 26-O-β-d- glucoside hydrochloride) and organic acids [21, 35]. Caper infusion has identified rutin, kaempferol 3-O-rutinoside, and isorhamnetin 3-O-rutinoside as dominant flavonoids in addition to isoginkgetin, ginkgetin and sakuranetin which have demonstrated to exert an anti-inflammatory activity by inhibiting the nuclear factor-kappa B [36, 37]. Moreover, the different glucosinolates found in *C. spinosa* were glucocapparin, mercaptoglucocapparin, 4-hydroxyglucobrassicin and glucobrassicin and glycinyl-glucocapparin [38]. In addition, a homogalacturonan polysaccharide was obtained from the fruits of *C. spinosa* and had

a strong inhibitory effect on the activation of complement system through the classic pathway than that of heparin [39]. A recent study has revealed the presence of high levels of oleic acid and α-Tocopherol in *C. Spinosa* seeds [40]. Finally, a lectin has been isolated from *C. spinosa* and potently inhibited HIV-1 reverse transcriptase and proliferation of both hepatoma HepG2 and breast cancer MCF-7 cells [41]. Table 2 summerizes the known phytochemial components of *C. spinosa.*

Conclusion

This review summarizes the main pharmacological activities of *C. spinosa* including antidiabetic, antihypertensive, hypolipidemic, antioxidant, antimutagenic, anti-allergic, hepatoprotective anti-

Table 2. Main phytocontituents of *Capparis spinosa.*

Phytochemical Compounds	Part of the Plant	References
Flazin Guanosine Capparine A Capparine B 1H- indole-3-carboxaldehyde 4-hydroxy-1H-indole-3-carboxal- dehyde Chrysoeriol Apigenin Kaempferol Thevetia- flavone 5-hydroxymethylfuraldehyde Vanillic acid Cinnamic acid	Fruits	[21]
Cappariside or 4-hydroxy-5-methylfuran-3-carboxylic acid 5-hydroxymethylfurfural 5-hydroxymethyl furoic acid 2-furoic acid	Whole plant	[35]
Protocatechuic aldehyde E-butenedioic acid Ethyl 3,4-dihydroxybenzoate Syringic acid Protocatechuic acid Vanillic acid Succinic acid 4-hydroxybenzoic acid α-tocopherol	Fruits	[35]
β -sitosterylglucoside-6'-octadecanoate 3-methyl-2-butenyl-beta-glucoside	Roots	[57]
Capparispine Capparispine 26-O- β -D-glucoside	Roots	[58]
Cadabicine 26-O- β -D-glucoside hydrochloride		
P-hydroxy benzoic acid 5-(hydroxymethyl) furfural Bis (5-formyl furfuryl) ether Daucosterol α-D-fructofuranosidesmethyl Uracil Stachydrine or 1,1-dimethylpyrrolidinium-2-carboxylate	Fruits	[24]
Rutin Quercetin 3-O-glucoside Quercetin 3-O-glucoside-7-O-rhamnoside	Aerial parts	[59]
Glucocapparin glucobrassicin and 4-hydroxyglucobrassicin	Whole plant	[38]
Isoginkgetin, ginkgetin and sakuranetin	Fruits	[37]
Rutin, tocopherols, carotenoids and vitamin C	Leaves and flower	[20]
Cappariside	Fruits	[35]
beta-carotene, lutein, neoxanthin, violaxanthin and tocopherols	Leaves, buds, and flowers	[34]
Rutin	Leaves, fruits and flowers	[60]
Fatty acid, sterol, and tocopherol	Seeds	[61]
Homogalacturonan	Fruits	[39]
Rutin, kaempferol 3-O-rutinoside, and isorhamnetin 3-O-rutinoside	Whole plant	[62]

bacterial, antiviral, antifungal, immunomodulatory, anti-apoptotic and anti-inflammatory effects. These beneficial effects support the use of this plant for human healthcare from ancient time. However, the underlying mechanisms of these pharmacological activities are not totally elucidated and few clinical trials have been performed until now. In addition, few data are available about the safety of *C. spinosa*. Moreover, the phytochemical studies revealed clearly that the main constituents of this plant are the saccharides and glycosides, flavonoids, alkaloids, terpenoids and volatile oils, fatty acids, vitamin C, vitamin E and steroids. More studies dealing with the relationship between the active principle and pharmacological activity are still needed to develop new complementary active principles able to enrich the therapeutical arsenal especially for treatment of chronic diseases like diabetes and cardiovascular disorders.

Acknowledgment and Grants

This work was supported by the CNRST under the grant number PPR/2015/35.

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