**Herbal Medicines Journal** **2020; 5(4):163-77**
**DOI: 10.22087/herb%20med%20j.v5i4.813** **ISSN:** 2538-2144

Review Article

# Phytochemical, Antidiabetic and Therapeutic Properties of Zygophyllum

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Received: 13.06.2020; Accepted: 25.01.2021

## Abstract

Natural bioactive compounds, isolated from medicinal plants, have an efficient role in the management of various diseases. They have remained sources of new drugs with diversified structural arrangements and interesting biological activities. Among these medicinal plants, species belonging to the genus *Zygophyllum* are efficient sources of bioactive compounds, mainly antihyperglycemic substances. Hence, they are used in traditional medicine against diabetes. It has been indicated that these species could be useful against the skin, stomach and liver diseases. The present review provides phytochemical profiles and in vitro as well as in vivo biological activities of a number of *Zygophyllum* plants with hypoglycemic properties, available through researches from the selected research articles and books published from 1939 to 2017. The sources were collected from various databases.

**Keywords:** Traditional medicine, Antidiabetic plants, Zygophyllaceae, *Zygophyllum Album*, *Zygophyllum gaetulum*, Triterpenoid saponins

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**Please cite this article as:** Mohammadi Z. Phytochemical, Antidiabetic and Therapeutic Properties of Zygophyllum. Herb. Med. J. 2020; 5(4):163-77.

## Introduction

*Zygophyllum* family includes around 285 species in twenty-two genera, growing in arid and semi-arid, tropical and semi-tropical areas. This family comprises small trees, shrubs, and herbs; usually resinous and some are toxic**.** The biggest taxonomic group is the subfamily of Zygophylloideae, with near 185 species, distributed into 4 genera, i.e. *Fagonia*, *Zygophyllum*, *Augea*, and *Tetraena* (1-4).

*Zygophyllum* is found in several coastal and inland saline sandy soils of the world, along the Mediterranean seashores and oases, with high tolerance to a salty and dry environment. Species of this genus are a party of succulent herbs that are resistant against drought. They are salt-tolerant, and live in severe, dry atmospheric conditions. The copiousness of species associated with this genus might be due to their high tolerance to environmental stresses. The growth, expansion, and distribution of *Zygophyllum* species are influence by their dependence on the chemical nature of the soil of their habitats (5-10).

*Zygophyllum* plants have mechanisms to adapt like the buildup of soluble osmolytes for diffusion adjustment, increasing the expression of genes that create channels and anti-porters of cytomembrane to eliminate $Na^+$ and intracellular accumulation of $K^+$, and accretion of

**Figure 1.** Fatty Acids Fraction of *Zygophyllum album* (27).

**Table 1:** Fatty Acids Fraction of *Zygophyllum album* (27).

| Constituent | Relative percentage |
|---|---|
| *Octanoic acid* | 0.69 |
| *Decanoic acid* | 33.46 |
| *Dodecanoic acid* | 5.65 |
| *Myristic acid* | 6.47 |
| *Palmitic acid* | 31.18 |
| *Heptadecanoic acid* | 2.43 |
| *Stearic acid* | 4.51 |
| *Linoleic acid* | 7.32 |
| *Arachidic acid* | 8.29 |

ascorbate peroxidase and superoxide dismutase (SOD) in order to fight reactive oxygen species (ROS). The presence of salt glands in halophytes prevents the buildup of salt within the herb. Additionally, other mechanisms, like proline accumulation, soluble sugars or increase in the activity of antioxidant enzymes are influential in the adaptation of *Zygophyllum* to salt as the rise in stress causes a remarkable increase in proline and raises the relative salt tolerance (11).

The use of plants for health purposes to cure diseases and relieve physical suffering has started since a long time ago. Plants have been sources of significant pharmaceuticals. A wide range of species are listed in herbal medicine and aromatherapy. Research for remedies in nature continues to increase, and new biologically active molecules are continuously identified. Moreover, their use as drugs has been proven in laboratories by various biological and clinical tests. *Zygophyllum* is a genus which includes a large number of species, many of which have been used by indigenous populations as remedies to treat

**Figure 2.** *Zygophyllum gaetulum* (35).

certain diseases. Since the identification of diabetes, these populations have been found in these plants as antihyperglymic treatments.

This paper foregrounds the medicinal significance of some species from the genus *Zygophyllum* and elucidates the phytochemical bioactive compounds responsible for the traditional uses of these species and discusses the pharmacological properties proved experimentally by in vitro and in vivo analyses. To collect the data, we searched publications in various databases and journals using relevant keywords. Information about *Zygophyllum* was obtained from several books and dissertations. After the documentations, interesting files published from 1939 to 2017 were selected and organized in an electronic repertoire. Subsequently, we extracted all the texts which reported botanical, phytochemical, ethnobotanical, biological ant therapeutical properties.

**Systematic and Botanical Description of the Genus *Zygophyllum***

The genus *Zygophyllum* could be a principal genus in the Zygophyllaceae. There are 120 species which is indicative of its abundance in the desert, tropical and semi-tropical, saline and calcareous areas, particularly in Western Asia and Africa. This genus generally contains plants or shrubs having flower buds with unpleasant smell (2,12-13).

**Figure 3.** *Zygophyllum coccineum* (47).

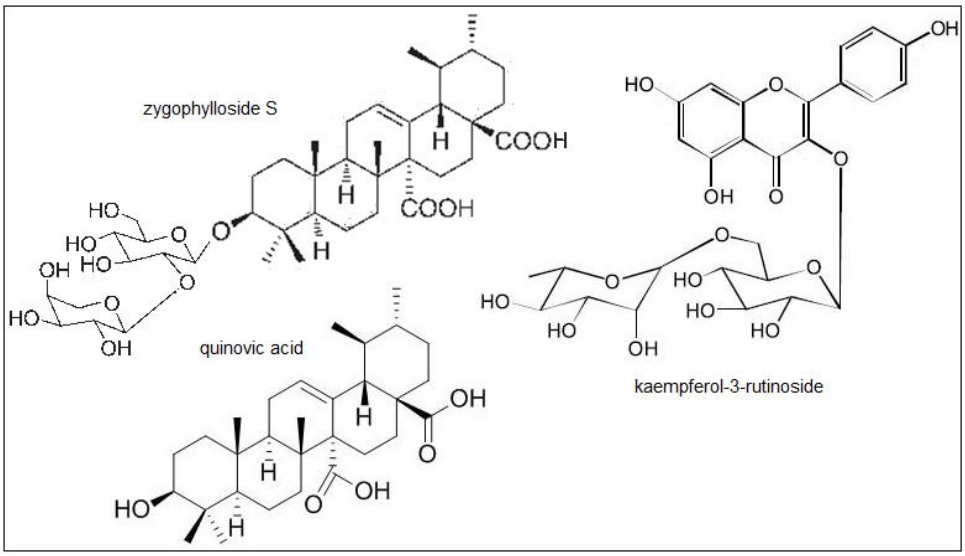


**Figure 4.** Structure of some secondary metabolites identified in *zygophyllum coccineum*.

**Figure 5.** *Zygophyllum simplex* (63).

*Zygophyllum* species are glabrous or nearly glabrous annual plants with branches often fleshy and opposite leaves, membranous or herbaceous petiole, paired or solitary axillary flowers, sepals caducous (4 or 5), orangish-red, white, or yellow petals, sometimes with pale or orange claw along the margin, rarely apetalous. Stamens are frequently twice as many as the petals, inserted at the base of the disc. The Disc is fleshy, habitually uniquely lobed, the fruit is a 4-5-angled loculicidal capsule or an indehiscent capsule with 3-4 longitudinal ridges or wings, or separating into 2-4 dorsally winged mericarps, seeds 1-6 in each loculus, with endosperm (13-14).

It has been indicated that several species of the genus *Zygophyllum* could be used to treat a variety of diseases. They are also used in traditional medicine in certain regions of the world. *Zygophyllum* species are used as anthelmintic agents and for controlling diabetes mellitus. Many in vitro and in vivo studies have confirmed their biological activities (2,15-17).

**Biological Properties**

***Zygophyllum album L.***

**Description*:*** *Zygophyllum album* (figure 1) is a perennial low shrub (20 to 30 cm in height) with many-branched stems. It has opposite succulent blue-green leaves with petioles. Its flowers are white, and flowering happens in March. The fruit has 5 dilated lobes welded to their base and then widening the peak (5,9,18-20).

*Zygophyllum album* is found in the whole North

**Figure 6.** *Zygophyllum fabago* (75).

African Sahara, Arabia and tropical east Africa. It is abundant in southern Algeria where it is commonly known as "Agaya" (18,20-21).

**Therapeutic and Biological Activities:** *Zygophyllum album* is used as a diuretic, local anesthetic, antihistaminic, antidiabetic, anti-spasmolytic, antihyperlipidemic, antidiarrheal, anti-inflammatory**,** carminative, antiseptic and stimulant agent for the treatment of skin diseases, diarrhea, and typhoid (2 ,21-25).

It has been indicated that this plant could be toxic to the sheep causing high mortality. The toxicity/mortality of the crude plant was observed at 7.5-8.4g.kg$^{-1}$b.w. The oral LD50 and the intraperitoneal LD50 of the alcoholic extract for rats were 5.9g.kg$^{-1}$bw and 2.6g.kg$^{-1}$bw, respectively (26-27).

Several scientific research have revealed interesting activities, such as insecticidal activity against the mite of date palm *Oligonychus afrasiaticus*. Aqueous extracts from this plant caused a mortality rate of 76% in vivo antibacterial activity against *Bacillus*. The extract stops bacillosis after 8 to 10 days of treatment for male rats with non-toxic dose. The herbicidal activity against *Echinochloa crus-galli* was observed. The extract (75 g/L) was a potent inhibitor of seed germination (81.59% inhibition), root growth (98.87% inhibition), and shoot growth (84.61% inhibition) after

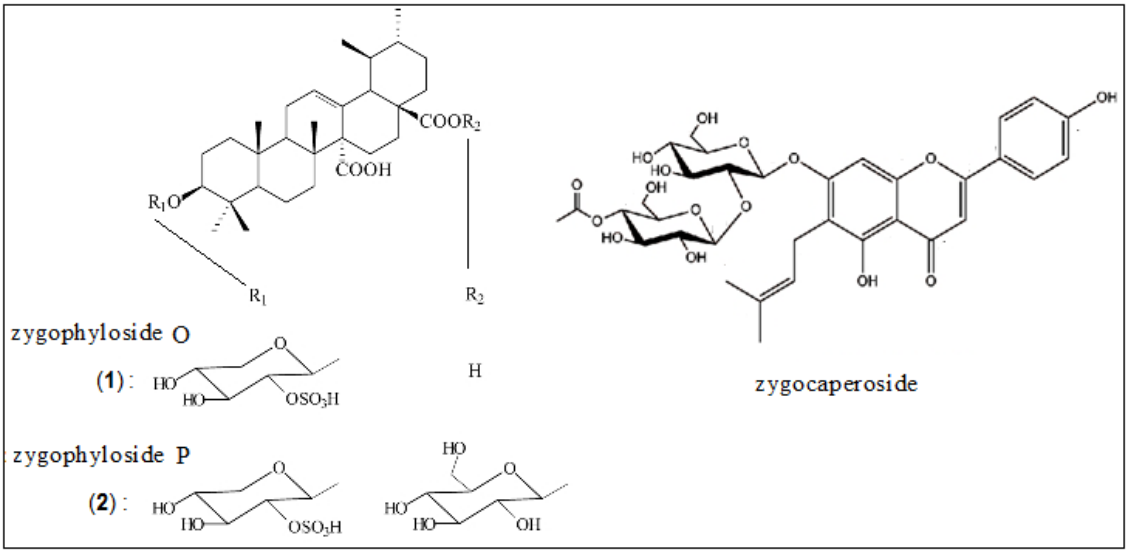


**Figure 7.** Chemical Structures of Zygophylosides O (1), P (2) and Zygocarperoside.

4 days of treatment (9,24-25).

The aqueous extract of *Zygophyllum album* exhibited in vivo antihyperglycemic, antihyperlipidemic and antioxidant activities. Consumption of the aqueous extract plant (100 and 300 mg/kg bw) for 15 days led to a noticeable decrease in hepatic glucokinase (GK), glycogen in STZ diabetic mice. Moreover, a remarkable increase in hepatic phosphofructokinase (PFK), and glucose-6 phosphate dehydrogenase (G6PDH) was observed in STZ diabetic mice. Furthermore, ethanolic extracts of *Zygophyllum album* exhibited in vitro inhibitory activity on pancreatic lipase with IC50 of 91.07 µg/ml and demonstrated a strong antihyperlipidemic effect (28-29).

In addition, various extracts showed a remarkable degree of ferric reducing power activity (7.689 ± 0.562 to 30.177 ± 2.397 mM), more efficient inhibition of radical DPPH (IC50 was ranged from 22.127 ± 0.837 to 84.104 ± 3.989 µg/ml), a powerful anti-acetylcholinesterase activity with IC50 values of 40-58 µg/ml and the highest β-carotene bleaching capacity. These biological activities depend on the bioactive compounds in each extract type (30-31).

**Phytochemicals*:*** *Zygophyllum album* contained high contents of saponins (18.47 mg/g dry weight), phenolics (12.94 mg/g– 403.46mg/g) and flavonoids (47.16mg/g) (9, 28). Chemical constituents of *Zygophyllum album* are carbohydrates, proteins/amino acids, tannins, lactones, kaempferol, isorhamnetin, Isorhamnetin-3-O-galactopyranoside, Isorhamnetin-3-O-glucopyranoside, isorhamnetin-3-O-rutinoside, isorhamnetin-3-O-robinobioside, quercetin-3-O-glucoside, alkaloids, such as β-carboline (harmine), n-alkanes (C12-C32), β-amyrin, stigmasterol, β-sitosterol, fatty acids (Table 1), from which the main fatty acids were decanoic acid 33.46% and palmitic acid 31.18% (26-27,32-33).

***Zygophyllum gaetulum Emb. and Maire***

**Description*:*** *Zygophyllum gaetulum* (figure 2) is a plant with branching small sheets constituted of two fleshy leaflets that could be used as a water reserve.

**Therapeutic and Biological Activities*:*** *Zygophyllum gaetulum* is extensively used in traditional medicine for its antidiarrheal, anti-eczema, anti-inflammatory, antidiabetic, and antispasmodic properties. It is also used against stomach and liver diseases. Several scientific works have highlighted its hypoglycemia activity (2,16,34-36).

Berzou *et al*. (37-38) indicated that *Zygophyllum gaetulum* aqueous extract attenuates hypercholesterolemia, oxidative stress in plasma and tissues, and increase plasma paraoxonase 1 (PON 1) activity of hypercholesterolemic rats. *Zygophyllum gaetulum* could have a protective effect against oxidative stress in rats fed with a high-cholesterol diet. A noticeable glutathione reductase (GR) activity was observed in the heart (+14%), brain (+47%), and aorta (+23%). Decreased GSH levels were raised by 78, 35, and 65% in the liver, heart, and aorta respectively. Superoxide dismutase activity was 4- and 1.2-fold higher in the liver and aorta respectively. A high level of catalase (CAT) activity was seen in the liver (+14%), heart (+27%), and aorta (+17%), while glutathione peroxidase (GSH-Px) activity was 2.3 and 1.6 fold higher in the liver and aorta respectively.

**Figure 8.** *Zygophyllum cornutum* (86).

**Figure 9.** *Zygophyllum geslini* (88).

Plasma total cholesterol and low-density lipoprotein cholesterol concentrations were 1.5- and 2.4-fold lower respectively, whereas there were higher levels of high-density lipoprotein cholesterol (+50%). Moreover, extracts from *Zygophyllum gaetulum* showed, in vivo, antipyretic activity (in rats) comparable to acetylsalicylic acid, and exhibited anti-inflammatory activity in mice (39-40).

Skim *et al*. (41) observed that the LD50 infusions was higher than 10g/kg body weight and suggested after oral administration of the plant. This plant has no toxicological effect in rats. However, El Youbi *et al*. (36) who investigated the acute toxicity of aqueous extract in mice by intraperitoneal route indicated that the determination of a lethal dose 50 is equal to 1.2 g/kg of body weight. The results of their study showed the stimulation of proliferative activity on T lymphocytes.

**Phytochemicals*:*** The phytochemical analysis revealed that *Zygophyllum gaetulum* contains saponins such as bisdesmosidic triterpene saponins, i.e. zygophyllosides I, zygophyllosides L, zygophylosides M, and quinovic acid glycosides (42).

***Zygophyllum coccineum L.***

**Description*:*** *Zygophyllum coccineum* (figure 3) is a small perennial herb characterized by numerous stems and erect, young, green branches with fleshy leaves and moderately whitish flowers of saline and sandy habitats at the vicinity of the sea. Its flowering time is starting from October to November). It is a plant abundantly found in the Eastern (Arabian) Desert and represents the most widespread *Zygophyllum* species in Egypt and Saudi Arabia, where it is found in distinct habitats and wide soil range. It is also found in the Sindh and Baluchistan provinces of Pakistan (10,43-47).

**Therapeutic and Biological Activities:** Traditional medicinal endorses the use of *Zygophyllum coccineum* in the treatment of rheumatism, gout, cough, asthma, hypertension, flatulent colic and diuresis. The juice from fresh leaves and stems has been utilized as an abrasive cleanser. Furthermore, it has been used in the treatment of skin diseases. It has also been used as both an anthelminthic and antidiabetic agent, and an antipyretic and local anesthetic (2,15,46, 48-51).

In vivo studies, monitored on extracts of *Zygophyllum coccineum* exhibited remarkable antihypertensive characteristics in normotensive as well as spontaneously hypertensive rats. The impacts of the aqueous extract of *Zygophyllum coccineum* on rat blood pressure (BP) and on the mesenteric vascular bed were examined in rat model animal. The extract dose-dependently decreased BP and heart rate in normotensive and spontaneously hypertensive rats (SHRs). Moreover, it was able to decrease BP in pithed SHRs. The extract did not have any impact on the basal perfusion pressure of the mesenteric vascular bed. Following the increase in the perfusion pressure with noradrenaline or potassium chloride, the extract dose-dependently reduced perfusion pressure. Nonetheless, in preparations in which the perfusion pressure increased with KCl, the depressor reaction to lower doses of the extract was not observed; while

higher doses resulted in responses that were reduced in magnitude in comparison with identical responses in preparations in which the perfusion pressure increased with noradrenaline. According to these authors, extracts of *Z. coccineum* could exhibit remarkable antihypertensive activity that may involve some membrane hyperpolarization (2,52).

High antioxidant activity (90.76%) was observed by DPPH radical assay at 1mg/mL of aqueous methanol extract (51). *Zygophillum coccinium* has also antimicrobial, larvicidal and cytotoxic properties. 32-77% fungal growth inhibition at a concentration of 30µM was effective against *Phomopsis viticola* and exhibited a moderate activity against *Candida albicans* ATCC 10231, while potent antimicrobial and antifungal activities were shown against *Pseudomonas aeruginosa* and *Fusarium moniliforme*. Moreover, *Zygophillum coccineum* (ethyl acetate extract) had a significant insecticidal and toxic impact against larvae of *Culex pipiens* L. with 100% mortality after 24 h of treatment (53-55).

With regard to the plant toxicity, Al-Salihi and Al-Rammahi (47) reported that acute poisoning diarrhea in a herd of camels due to Z*ygophyllum coccineum* is related to a high concentration of saponins. The prominent clinical signs were severe diarrhea, polyuria, and photosensitization.

**Phytochemicals:** Phytochemical compounds (figure 4) isolated from *Zygophyllum coccineum* are ursane-type triterpene saponins flavonoid glycoside, and sterol glycoside. *Zygophyllum coccineum* contains zygophylloside S, kaempferol- 3- rutinoside, Quinovic acid (leaves: 0.36%; fruits: 0.31%; stems: 0.47%), and Zygophyllin (leaves: 28%; fruits 0.26%; stems: 0.18%). The phytochemicals identified in leaf extracts, obtained by acetone solvent, are 1-Hexyl-2-nitrocyclexane; 2-Octadecyl-propane-1,3-diol; Octadecanal; Cyclohexane,1-(1,5- dimethylhexyl)-4-(4-methylpentyl) ; 2-Octadecyl-propane-1,3-diol and 2(3h)-Furanone,3-(15-hexadecynylidene) (51,53-54,56).

Amin *et al*. (53) isolated nine ursane-type triterpene saponins. These compounds were examined for their antifungal activity against several significant plant pathogens as well as for their insecticidal effect against two important mosquito species. Among the isolated compounds, five of them indicated 32-77 % fungal growth hindrance at a concentration of 30µM against *Phomopsis viticola*. One of the compounds had 90 % and 80 % mosquitocidal activity at 3.1µg/0.5µL against *Aedes aegypti* and *Culex quinquefasciatus*, respectively.

The contents of metabolites in *Zygophyllum coccineum* were variable with the habitat of the plant. Tannins, alkaloids, glucosinolates, proline, and total ascorbate contents are higher in a desert habitat, while the contents of saponins and total glutathione were higher in coastal than in desert plants (57).

***Zygophyllum simplex L.***

**Description*:*** *Zygophyllum simplex* (figure 5) is an annual, perennial plant spreading with up to 40 cm long stems. This glabrous plant has simple leaves, and is sessile, cylindrical to obovate, fleshy up to 15 x 4 mm. It has stipules membranous, filiform, flowers axillary, solitary or in pairs, obovate sepals and yellow petals.

**Therapeutic and Biological Activities:** *Zygophyllum simplex* is used for the treatment of horny patches of skin. Infusion of the leaves acts as a skin cleanser. *Zygophyllum simplex* acts as an anthelmintic, analgesic, anti-inflammatory, hypoglycemic, hypolipidemic and laxative agent. The plant is efficient in the treatment of the cold, flu, and cough. Moreover, it has vermifuge properties and is used as eye drop and to cure heart diseases. Furthermore, the plant showed antibiotic activity and a noticeable reduction in total serum cholesterol, blood glucose and CK level (2,58-61).

**Phytochemicals:** The plant contains free ascorbic acid, sitosterol glucoside, phenolic acids and flavonoids such as kaempferol, kaempferol-3-O-rutinoside, quercetin, quercetin-3,7-di-O-b-glucopyranoside, isorhamnetin, isorhamnetin-3-O-β-D-rutinoside, isorhamnetin-3-O-beta-glucopyranoside, Isorhamnetin-3-O-beta-glucopyranoside-7-O-alpha-rhamnopyranoside, 6″-(2-*E*-butenoyl) isorhamnetin-3-O-glucoside, Gentisic acid, Gentisic acid 5-O-alpha-rhamnopyranoside, myricitrin, luteolin-7- O-β-D-glucoside and quinovic acid-3- and alpha-L-rhamnoside (33,59,61,63). The two flavonoids, myricitrin and luteolin-7- O-β-D-glucoside have indicated the highest level if antioxidant activity. They were shown to be the most efficient agents in decreasing NFκB p65, IL-6, IL-1β and TNF-α levels

**Figure 10.** *Zygophyllum hamiense* (4).

at the lowest concentration (1µM), in vivo (63).

***Zygophyllum fabago L.***

**Description:** *Zygophyllum fabago* (figure 6) is frequently known as Syrian bean-caper, oftentimes found within the arid regions of Southern Europe and within the arid zones of the Mediterranean coastal region, like Afghanistan, Pakistan, Iraq, Iran, Saudi Arabia, Turkey, Spain, France, Italy, and North Africa. It is also found in disturbed sites and waste areas (2,64-66).

This succulent, perennial and multi-branched shrub is characterized by its noticeable ability to adapt to severely polluted neutral mine tailings even when the soil has a high level of salinity. The metal uptake into shoots is moderately small. Hence, this herb may be regarded as a significant choice to re-vegetate neutral pH mine tailings (65-66).

**Therapeutic and Biological Activities:** *Zygophyllum fabago* is employed as an antitussive, expectorant, and anti-inflammatory agent and for relieving pains. Aerial parts at the flowering stages are used as antirheumatic, antihelmintic, cathartic, and antiasthmatic substances. The extract of the plant did not show any toxic sign or mortality at the dose of 5000mg/kg (2,67-70).

*Zygophyllum fabago* extracts have allelopathic effects on *Cuscuta monogyna* Vahl (eastern dodder), a parasitic weed of woody species. The extracts showed higher inhibition impacts on seed germination (up to 90.6%) and on growth (66). The antifungal activities of aqueous extracts on two plant phytopathogenic fungal species (*Fusarium oxyosporum* f.sp. *melonis* and *Pythium aphanidermatum*) were investigated by Dana *et al*. (71). The plant extracts repressed the growth of *Fusarium oxyosporum* (42.9%) and *Pythium aphanidermatum* (85.3%) at a dose of 10%.

The plant has exhibited a really sturdy activity against the human pathogen yeast; *Candida albicans*. The toxicity of fractions, extracted by hexane, ethyl acetate, chloroform, methanol, butanol and water was specified by flow cytometry on $2.10^6$ CFU/ml of *Candida albicans* at diverse concentrations of extracts for a period of 1, 2, and 24 h at 25ºC. The 1h exposure showed that 1.0 g/ml hexane and ethyl acetate extracts of *Zygophyllum fabago* killed 98% and 90% of cells, respectively. Furthermore, plant extracts might also have antiviral photosensitizers, but the activities have been observed only at elevated concentrations (2,72-74).

**Phytochemicals:** *Zygophyllum fabago* contains ash (5.43%), moisture (8.26%), amino acids (0.95%), carbohydrates (0.90%), organic acids (7.96%), flavonoids (1.10%), saponins (10.31%), alkaloids (0.44%), and macro/micro-elements (75).

The amino acid and fatty acids profiles of *Zygophyllum fabago* were investigated. The most plentiful essential amino acid and non-essential amino acid were leucine (4.75µg/g) and glutamate (23.42µg/g). The amounts of MUFA (monounsaturated fatty acid) and PUFA (polyunsaturated fatty acid) were 78% and 13.1% of the total fatty acid content, respectively. The monounsaturated fatty acid; Oleic acid; was the main

**Table 2:** Contents of Simple Phenols and Flavonoids. Identified in zygophyllum *hamiense* (17).

| **Constituent** | **Amount (%)** |
|---|---|
| Pyrogallol | 1.94 |
| Gallic acid | 2.02 |
| Protocatechuic acid | 0.97 |
| Catechin | 1.81 |
| Chlorogenic acid | 2.31 |
| Catechol | 2.57 |
| Caffeic acid | 1.54 |
| Vanillic acid | 1.37 |
| Ferulic acid | 0.84 |
| Salicylic acid | 1.10 |
| Benzoic acid | 1.51 |
| Coumaric acid | 1.20 |
| Chrysin | 0.34 |
| Quercetin | 0.04 |
| Rosmarinic acid | 2.33 |
| Rutin | 10.71 |
| Quercitrin | 0.77 |
| Naringenin | 0.94 |

constituent in *Zygophyllum fabago* (77.1% of total fatty acids), followed by linoleic acid (12.8%). (76).

In the seed oil, the most important constituents were unsaturated fatty acids. The total unsaturated acid was 72.58%. The element with the highest content was linoleic acid (51.02%), followed by oleic acid (21.56%). The amount of palmitic acid (8.34%) was higher than stearic (4.88%), arachidic (1.41%), and behenic acid (1.05%) (69).

The aerial part of the plant contains triterpenoid saponins such as Zygofaboside C, a sulfated saponin with chemical name 3β,23,30-trihydroxyurs-20-en-28-al-23-sulfate 3-O-β-D-xylopyranoside (2,69,77).

The bark of *Zygophyllum fabago* L. contains the 27-nor-triterpenoid glycoside, 3-*O*-β-d-glucopyranosyl-pyrocincholate, 3-O-6-deoxy-β-d-glucopyranosyl-pyrocincholate, quinovic acid, 3-O-6-deoxy-β-d-glucopyranosyl-quinovic acid, 3-O-β-d-glucopyranosyl- quinovic acid, 3-O-6-deoxy-β-d-glucopyranosyl-cincholic acid, zygophylosides O and P (figure 7). Compounds such as 3-O-β-d-glucopyranosyl-pyrocincholate, 3-O-6-deoxy-β-d-glucopyranosyl-pyrocincholate, and quinovic acid have shown certain anti-tumor activities by MTT

assay, while Zygophyloside O exhibited weaker nitric oxide (NO) inhibitory activity (67,78).

Phytochemical active compounds identified in the plant roots are zygocaperoside (figure 7) and Isorhamnetin -3-O glucoside (79).

***Zygophyllum cornutum Coss.***

**Description:** *Zygophyllum cornutum* Coss. (figure 8) is a xerophyte herb known for its dilated fruits on top in a free portion of carpels recurved into hooks as long as the welded portion**.** It is an endemic plant distributed in the Northern Sahara of Algeria.

**Therapeutic and Biological Activities:** It is used in traditional medicine in the treatment of diabetes, hypertension, dermatitis, rheumatism, gout and asthma. This species has shown hypocholesterolemic, hypolipidemic and antioxidants activities (2,80-82).

It was shown via free radical DPPH assay that crude extract of *Zygophyllum cornutum* and its fractions could have significant antioxidant activities. EC50 (µg/ml) enregistred are (67.059 ± 4.727); (38.478 ± 2.085); (47.767 ± 1.571); (42.159 ± 3.029); (24.935 ± 1.983) for crude extract and fractions (chloroform, ethyl acetate, butanol and water) respectively (81). Boumaza (83) has also shown a significant scavenger effect and high antioxidant activity. The results registered by this author revealed increased blood glucose, urea, uric acid, creatinine, low density lipoprotein-cholesterol ($LDL_C$), cholesterol and triglycerides with decreased level of high-density lipoprotein-cholesterol ($HDL_C$) and total proteins in diabetic rats. Moreover, TBARS (Thiobarbituric acid reactive substance) in the different organs' tissues were markedly increased while GSH (glutathione ) and CAT (Catalase) were significantly modified compared to control normal rats. Oral administration of ZCME (*Zygophyllum cornutum* methanolic extract) in a dose of 700mg/kg.bwt improved serum glucose, lipid profile and renal function tests. TBARS were significantly reduced in all organs' tissues, while CAT and GSH were markedly restored.

**Phytochemicals:** Phytochemical compounds of *Zygophyllum cornutum* are β-sitosterol, polyphenols, flavonoids such as isorhamnetin-3-rutinoside (narcissin), coumarins, alkaloids, tannins and ursane-type saponins: 3-O-(β-D-quinovopyranosyl) quinovic acid, 3-O-(2-O-sulfo-β-D-glucopyranosyl) quinovic acid, 3-O-(β-D-quinovopyranosyl) quinovic acid-28-(O-β-D-glucopyranosyl) ester and its sulfated derivative: zygophyloside E, zygophyloside G, zygophyloside H (83-85).

***Zygophyllum geslinii Coss.***

Description: *Zygophyllum geslini* Coss. (figure 9) is a species endemic to Algerian central Sahara.

Therapeutic and Biological Activities: It is used in traditional medicine as a complement in the treatment of diabetes.

The aqueous and methanol extracts from *Zygophyllum geslini* were able to hinder the activity of α-amylase in proportion to the concentration of the extracts. Extracts from *Zygophyllum geslini* are equipped with an important antioxidant potential. Activities of 88.22% and 75.89% are noted for a concentration of 2mg/ml with methanolic and aqueous extracts.

**Phytochemicals:** This medicinal plant contains flavonoids, saponins, tannins and alkaloids, glycosides zygophylosides E, G, and H, and 3-O-(β-D-quinovopyranosyl) and quinovic acid 28-(O-β-D-glucopyranosyl) ester. Total polyphenols and flavonoids values are 7.5mg EGA/g and 2.41mgCEQ/g for the methanolic extract and 6.3mg EGA/g and 2.32 mgCEQ/g for the aqueous extract (87-89).

***Zygophyllum hamiense Schweinf.***

**Description:** *Zygophyllum hamiense* (figure 10) is a perennial shrubs, with green, reddish or yellowish green colors. Its height and width reach up to 80cm and 90cm respectively. Its stems are pubescent with unicellular simple trichomes. Leaves of this plant are mostly 1-foliolate, sometimes 2-foliolate in upper branches, terete, globular or cylindrical or clavate, 4-9 mm long, 3-6 mm wide, fleshy, pubescent or glabrous, petiole equal or longer than leaflets up to 9 mm long, stipules triangular, herbaceous, 1 × 1.5 mm, pubescent. Flowers are bisexual, solitary at each node, white, 4-6 × 3-5 mm, and pedicle is 3-5 mm long. This plant is found largely along the Persian Gulf region and grows on salt accumulated lands.

**Therapeutic and Biological Activities:** The plant is commonly used as firewood but its sprouts are used to feed camel. It has been indicated that the extract of this plant is a potent DPPH free radical scavenger. Moreover, the acute toxicity determination of the

LD50 revealed that *Zygophyllum hamiense* extracts was found to be safe up to dose 5 g/kg. The maximum flavonoid content (1.48 %) was extracted with acetone, meanwhile ethyl acetate and ethanol was highly beneficial for solubilization of total phenol (4 and 3.61 mg GAE/g dry plant wt., respectively) (4,17).

**Phytochemicals:** Zygophyllum hamiense contains polyphenols and flavonoids. Total of 18 phenolic components were identified in Zygophyllum hamiense (Table 2), where rutin is the major phenolic constituent (17).

***Zygophyllum eurypterum Boiss. & Buhse***

**Description:** *Zygophyllum eurypterum* is an erect shrub. It is 1m to 1.2m tall. Stem and branches are whitish grey. Leaves are 1.5-3 cm long. Flowers are creamy white. Seeds are brown and 6-7 mm long. It is widely distributed in Iran, Afghanistan, Russia and Pakistan (80-91).

**Therapeutic and Biological Activities*:*** It has been shown that antimicrobial activities are efficient against *Steptococcus*, *Staphylococcus aureus*, *Escherichia coli*, *Aspergillus niger* and *Candida albicans*. Moreover, antioxidant activities examined in the stem and leaves and evaluated by DPPH radical scavenging activity revealed the respective IC50 values of 80.41% and 424.4% for n-hexane fraction and methanolic extracts. The IC50 values are 15.37% and 84.61% for the stem and leaves respectively. On the other hand, the respective % inhibitions in linoleic acid system for the stem and leaves vary from 26.7% (n-hexane) to 96% (methanol) and from 44.7% (n-hexane) to 87.5% (n-butanol) (91).

**Phytochemicals*:*** *Zygophyllum eurypterum* contains stigmasterol, β- sitosterol, β-sitosterol glucoside, oleanolic acid, harmine, 7,3',4'- trimethoxyflavone, 5-methylflavanone, atriplicoide A, atriplicoide B and four pterocarpans, atricarpan A atricarpan B, atricarpan C and atricarpan D. It was shown that atricarpan D could inhibit AChE with an IC50=20.5µM.

Total phenolic contents observed in the leaves of this plant ranged from 5.52 mg/100 g (n-hexane) to 98.25 mg/100 g (methanol). Similarly, the range of total flavonoids contents varied from 1.46 mg/100 g (n-hexane) to 24.41 mg/100 g (methanol) in the stem and 0.70 mg/100 g (n-hexane) to 4.46 mg/100g (methanol) for leaves (92-94).

## Conclusion

Zygophyllum species are potential sources of highly interesting active compounds used in the treatment of many diseases. These species could be used as raw materials of primary significance for pharmaceutical industries and drug preparation as well as design. They are particularly used as dietary supplements for the management of diabetes.

## Acknowledgements

I would like to thank all the researchers whose works have contributed in various ways to this review study.

## Conflict of Interest

The authors declare that they have no conflict of interest.

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