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A Comprehensive Review on Genus *Zygophyllum*

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ABSTRACT

Objectives: This study aimed to make a broad review of the chemical constituents and biological activities of genus *Zygophyllum*. **Methods:** This review covers the peer reviewed articles between 1977 and August, 2018, retrieved from PubMed, Science Direct, Sci-Hub, Springer and Wikipedia. **Results:** In traditional medicine, plants of genus *Zygophyllum* have been employed and utilized as anti-rheumatic, anti-gout, antidiabetic, anti-hyperlipidemic, antimicrobial, anti-oxidant, antihypertensive, antiseptic, anti-eczema and antidiarrheal. *Zygophyllum* species have been phytochemically studied leading to the identification of various classes of compounds including triterpenes, flavonoids, saponins, sterols, simple phenolic compounds, and esters. Biological studies on *Zygophyllum* species have also indicated various bioactive potentials including antioxidant, antidiabetic, antimicrobial antitumor and anti-inflammatory effects. The reported medicinal *Zygophyllum* species were selected and summarized on basis of their; geographical distribution, traditional uses, chemical constituents and biological activities. **Conclusion:** It would therefore be important to extensively investigate their phytochemicals and pharmacologically determine their activities for future drug discovery and development.

Keywords: Biological activities; Chemical constituents; Geographical distribution; Traditional uses; *Zygophyllum*

INTRODUCTION

Zygophyllaceae (Caltrop family) is a family of approximately 25 genera and 240 species adapted to semi desert and Mediterranean climates¹. Species belonging to genus *Zygophyllum* represent a group of succulent plants that are drought resistant and/or salt tolerant, living under severe, dry climatic conditions². Moreover, it is recorded by many authors as one of the important components of the desert vegetation³. The abundance of species related to this genus could be attributed to their high tolerance to environmental stresses as well as to their unpalatability⁴. The growth and distribution of *Zygophyllum* species are attributed to their dependence on the chemical nature of the soil of their habitats⁵. The genus *Zygophyllum* consist of 100 species, distributed in desert and steppe habitats from the Mediterranean to central Asia, South Africa

and Australia⁴. Most of plants of genus *Zygophyllum* are small perennial herbs with fleshy leaves and flowers, as in cases of *Z. simplex*, *Z. cocconem*, *Z. album*, *Z. fabago* and *Z. dumosum*⁶. Nine species are widespread in the deserts and salt marshes in Egypt and Sinai Peninsula⁵. They have been utilized in traditional medicine for various ailments, such as treatment of rheumatism, gout, diabetes, asthma, hypertension, dysmenorrhea, as well as fungal infection⁷⁻¹¹. Biological studies on *Zygophyllum* species have indicated significant antioxidant, antidiabetic, antitumor, antimicrobial and anti-inflammatory activities¹²⁻¹⁷. Such activities were contributed to their phytochemical constituents. Various classes of compounds including triterpenes, flavonoids, saponins, sterols, phenolic, essential oils and esters have been isolated from different *Zygophyllum* species¹⁸⁻²³.

Table 1. Reported *Zygophyllum* species, their distribution and traditional uses

<i>Zygophyllum</i> species	Distribution	Traditional use
<i>Z. aegyptium</i> ^{18,24}	Egypt, Tunisia, Cyprus	Rheumatism, gout, asthma and hypertension
<i>Z. album</i> ⁸	Egypt, Algeria, Tunisia	Diabetes, dermatitis, spasms and dysmenorrheal
<i>Z. atriplicoides</i> (Synonym: <i>Z. eurypterum</i>) ²⁵	Pakistan	Alzheimer's disease and brain diseases with deficiency in cholinergic function
<i>Z. coccenium</i> ^{9,26}	Egypt, Kuwait, Saudi Arabia	Gout, Rheumatic pain and hypertension
<i>Z. cornutum</i> ¹⁰	Algeria	Diabetes, hypertension and dermatitis
<i>Z. decumbens</i> ²⁷	Egypt, Syria, Sudan	Hypotension, fever and GIT spasm
<i>Z. dumosum</i> ^{23,28,29}	Egypt	Rheumatism, gout, asthma and hypertension
<i>Z. fabago</i> ¹⁹	China, Spain, Turkey, Iran, Kazakhstan and Iraq	Fungal infections, Parasitic worms, constipation, product cough, inflammation, and asthma
<i>Z. gaetulum</i> ¹¹	Morocco	GIT spasms, hyperglycemia accompanying diabetes and eczema
<i>Z. geslini</i> ¹²	Algeria	Hyperglycemia accompanying diabetes
<i>Z. hamiense</i> ³⁰	Deserts of Asia and Africa	As hepato-protective
<i>Z. macropodium</i> ³¹	China	Pain and inflammation
<i>Z. melongena</i> ²⁰	Mongolia	Snake poisoning (as it inhibits of the snake venom phosphodiesterase)
<i>Z. qatarense</i> ¹³	Iran	Fungal infections
<i>Z. simplex</i> ³²	Egypt, Saudi Arabia, India and Pakistan	Glaucoma, inflammation, fungal infections and hyperglycemia accompanying diabetes

MATERIALS AND METHODS

This review covers the peer reviewed articles between 1977 and August, 2018, retrieved from PubMed, Science Direct, Sci-Hub, Springer and Wikipedia.

RESULTS AND DISCUSSION

Distribution and traditional use

Data reported on *Zygophyllum* species used mostly in folk medicine is summarized in **Table 1** according to their geographical distribution and traditional uses.

Phytochemical constituents:

It was reported that the plants belonging to genus *Zygophyllum* are rich in essential oil, sterols, triterpenes, phenolic compounds, flavonoids and saponins. The previously isolated compounds from reported *Zygophyllum* species are labeled together with their chemical classes in **Table 2** and their chemical structures are shown below.

Biological studies

Reported biological activities of various *Zygophyllum* species included antioxidants,

antidiabetic, antimicrobial, antitumor and other effects are illustrated in **Table 3**.

Antioxidant activity

One of the most remarkable effects of the members of *Zygophyllum* genus is their antioxidant activity (**Table 3**). Such activity is attributed to the presence of the phenolic compounds as reported in cases of *Z. cornutum*¹⁰, *Z. album*^{6,8,38}, *Z. coccenium*⁷, *Z. hamiense*²⁸, *Z. simplex*^{16,64} and *Z. fabago*⁴⁶. The most active extracts with the highest antioxidant activity; were those of the alcohol (methanol and ethanol) ones followed by dichloromethane extracts while the hexane extracts were poorly active⁶. Consequently, *Zygophyllum* genus represents an important economical source of antioxidant agents.

Antidiabetic activity

The antidiabetic activity of members of the *Zygophyllum* genus have been reported in several studies (**Table 3**). The aqueous and butanol extract of *Z. gaetulum* in alloxan-induced diabetic rats ($n=6$) caused a continuous marked reduction of blood glucose levels particularly 6–9 hr {hours} after treatment. Significant difference was observed; ($P<0.001$) (52.82 ± 6.54 ; 69.80 ± 3.86 , respectively). The blood glucose level fell rapidly from 333 ± 47 mg/dl at fasting to 205 ± 34

Table 2. Reported *Zygophyllum* species; isolated compounds and chemical classes

<i>Zygophyllum</i> species	Identified compounds	Compound no.	Chemical classes
<i>Z. album</i> ^{6,14,23,33-39}	Isorhamnetin	1	Flavonoids
	Isorhamnetin-3- <i>O</i> - β - <i>D</i> -glucoside	2	Flavonoids
	Isorhamnetin-3- <i>O</i> - β galactopyranoside	3	Flavonoids
	Isorhamnetin-3- <i>O</i> - β -rutinoside	4	Flavonoids
	Quercetin-3- <i>O</i> - β -glucopyranoside (Isoquercitin)	11	Flavonoids
	Kaempferol	12	Flavonoids
	Gentisic acid	17	Hydroquinone carboxylic acid
	β -sitosterol	18	Sterols
	Stigmasterol	20	Sterols
	Ursolic acid	21	Triterpenoid
	Oleanolic acid	22	Triterpenoid
	quinovic acid 3- α - <i>L</i> -rhamnoside	34	Triterpenoid
	Malvidin 3-rhamnoside	60	Anthocyanins
	Linalool	61	Terpene alcohol
	Tricosane	63	Acyclic hydrocarbons
	Camphor	64	Bicyclic monoterpene ketone
	α -Terpineol	65	Monoterpene alcohol
	Carvone	66	Monoterpene
	Harmine (β -carboline alkaloid)	67	Alkaloids
	β -amyrin	68	Triterpenoid
<i>Z. aegyptium</i> ^{18,24}	Isorhamnetin-3- <i>O</i> - β -rutinoside	4	Flavonoids
	Quinovic acid-3- <i>O</i> - β - <i>D</i> -glucopyranoside	32	Triterpenoid
	Quinovic acid-3- <i>O</i> - β - <i>D</i> -2- <i>O</i> -sulphonylquinovopyranoside	33	Triterpenoid
	Quinovic acid-3- <i>O</i> - β - <i>D</i> -glucopyranosyl-(28 \rightarrow 1)- β - <i>D</i> -glucopyranosyl ester	36	Triterpenoid
	Quinovic acid-3- <i>O</i> - β - <i>D</i> -quinovopyranosyl-(28 \rightarrow 1)- β - <i>D</i> -glucopyranosyl ester	38	Triterpenoid
	Quinovic acid-3-[β - <i>D</i> -xylopyranosyl (1 \rightarrow 2) quinovopyranosyl]-(28 \rightarrow 1)- β - <i>D</i> -glucopyranosyl ester	52	Triterpenoid
	(7 <i>R</i> ,8 <i>S</i> ,8' <i>S</i>)-4, 9, 4'-trihydroxy-3, 3'-dimethoxy-4'-sulfonyl-7, 9'-epoxyignan	57	Lignans
	Quinovic acid-3- <i>O</i> - β - <i>D</i> -quinovopyranoside	69	Triterpenoid
	Quinovic acid-3- <i>O</i> - β - <i>D</i> -quinovopyranosyl-(27 \rightarrow 1)- β - <i>D</i> -glucopyranosyl ester	70	Triterpenoid
	<i>Z. atriplicoides</i> (Synonym: <i>Z. eurypterum</i>) ^{25,40}	β -Sitosterol-3- <i>O</i> - β - <i>D</i> -glucopyranoside	19
Atricarpan A		24	Isoflavonoids
Atricarpan B		25	Isoflavonoids
Atricarpan C		26	Isoflavonoids
Atricarpan D		27	Isoflavonoids
Atriplicosaponin B		37	Triterpenoid saponins
<i>Z. atriplicoides</i> ^{25,40}	Atriplicosaponin A	56	Triterpenoid saponins
<i>Z. coccienium</i> ^{6,23,36,41,42}	Isorhamnetin-3- <i>O</i> - β -rutinoside	4	Flavonoids
	5,6,7,8,4' penta hydroxy flavone 7 - β - <i>D</i> glucoside	15	Flavonoids
	β -sitosterol	18	Sterols
	β -Sitosterol-3- <i>O</i> - β - <i>D</i> -glucopyranoside	19	Sterols
	Stigmasterol	20	Sterols
	Ursolic acid	21	Triterpenoid
	Oleanolic acid	22	Triterpenoid
	Zygophylloside S	31	Triterpenoid saponins
	3- <i>O</i> -[β - <i>D</i> -glucopyranosyl]-quinovic acid	32	Triterpenoid
	3- <i>O</i> -[β - <i>D</i> -(2- <i>O</i> -sulphonyl)-quinovopyranosyl] quinovic acid	33	Triterpenoid
	3- <i>O</i> -[β - <i>D</i> -glucopyranosyl] quinovic acid-28- <i>O</i> - β - <i>D</i> -glucopyranosyl ester	36	Triterpenoid

	3- <i>O</i> -[β - <i>D</i> -quinovopyranosyl] quinovic acid-28- <i>O</i> - β - <i>D</i> -glucopyranosyl ester	38	Triterpenoid
	3- <i>O</i> -[α - <i>L</i> -arabinopyranosyl-(1 \rightarrow 2)- β - <i>D</i> -quinovopyranosyl] quinovic acid	39	Triterpenoid
	3- <i>O</i> -[α - <i>L</i> -arabinopyranosyl-(1 \rightarrow 2)- β - <i>D</i> -quinovopyranosyl] quinovic acid-28- <i>O</i> - β - <i>D</i> -glucopyranosyl ester	40	Triterpenoid
<i>Z. cornutum</i> ^{6,43}	2-(3, 4-Dihydroxyphenyl)-3, 5, 7-trihydroxy-6-methoxy-4-benzopyrone (Patuletin)	59	Flavonoids
	Isorhamnetin-3- <i>O</i> - β -rutinoside	4	Flavonoids
	β -sitosterol	18	Sterols
<i>Z. decumbens</i> ^{6,27}	Isorhamnetin-3- <i>O</i> - β -D-glucoside	2	Flavonoids
	Isorhamnetin-3- <i>O</i> - β -rutinoside	4	Flavonoids
<i>Z. dumosum</i> ^{6,23,28,36}	Isorhamnetin 3-(4"-sulfatorutinoside)	5	Flavonoids
	Isorhamnetin 3-[6"-(2 <i>E</i>) butenoyl]-glucoside]	6	Flavonoids
	Isorhamnetin-3- <i>O</i> - β -glucopyranoside-7- <i>O</i> - α -rhamnopyranoside	7	Flavonoids
	Quercetin	8	Flavonoids
	Rutin	9	Flavonoids
	Quercetin-3,7-di- <i>O</i> - β -glucopyranoside	10	Flavonoids
	Quercetin-3- <i>O</i> - β -glucopyranoside (Isoquercetin)	11	Flavonoids
	Kaempferol	12	Flavonoids
	kaempferol-3- <i>O</i> - β -rutinoside (Nicotiflorin)	13	Flavonoids
	Ursolic acid	21	Triterpenoid
	Oleanolic acid	22	Triterpenoid
	3- <i>O</i> -[β - <i>D</i> -glucopyranosyl]-quinovic acid	32	Triterpenoid
	3- <i>O</i> -[β - <i>D</i> -2- <i>O</i> -sulphonyl quinovopyranosyl]-quinovic acid-27- <i>O</i> -[β - <i>D</i> -glucopyranosyl] ester	35	Triterpenoid
<i>Z. eichwaldii</i> ⁴⁴	Pomolic acid 3- <i>O</i> - α - <i>L</i> -arabinoside	28	Triterpenoid saponins
	28- <i>O</i> - β - <i>D</i> -glucopyranosyl ester of pomolic acid 3- <i>O</i> - β - <i>D</i> -2- <i>O</i> -sulfonyl-galactopyranoside.	29	Triterpenoid saponins
	28- <i>O</i> - β - <i>D</i> -glucopyranosyl ester of pomolic acid-3- <i>O</i> - α - <i>L</i> -arabinoside	30	Triterpenoid saponins
<i>Z. fabago</i> ^{19,21,45-48}	Isorhamnetin	1	Flavonoids
	β -sitosterol	18	Sterols
	β -Sitosterol-3- <i>O</i> - β - <i>D</i> -glucopyranoside	19	Sterols
	3- <i>O</i> -[β - <i>D</i> -glucopyranosyl] quinovic acid-28- <i>O</i> - β - <i>D</i> -glucopyranosyl ester	36	Triterpenoid
	3- <i>O</i> -[β - <i>D</i> -quinovopyranosyl] quinovic acid-28- <i>O</i> - β - <i>D</i> -glucopyranosyl ester	38	Triterpenoid
	Zygophyloside E	44	Triterpenoid saponins
	Zygophylosides O	48	Triterpenoid saponins
	Zygophylosides P	49	Triterpenoid saponins
	3 β ,4 α -3,23,30-trihydroxyurs-20-en-28-al 3,23-di(sulfate) sodium salt	53	Triterpenoid
	3 β ,4 α -3,23,28-trihydroxyurs-20-en-30-yl β - <i>D</i> -glucopyranoside 3,23-di(sulfate) sodium salt	54	Triterpenoid
	Zyofaboside A	55	Triterpenoid saponins
	Eicosane	62	Alkane
	1-hydroxyhinesol	72	Sesquiterpenoid
	Hinesol	71	Sesquiterpenoid
	Atractylenolactam	73	Sesquiterpenoid
	β -eudesmol	74	Sesquiterpenoid
	5- α -hydroperoxy- β -eudesmol	75	Sesquiterpenoid
	11-hydroxy-valenc-1(10)-en-2-one	76	Ketone
	Pubinernoid A	77	Sesquiterpenoid

	(6S,7E)-6-hydroxy-4,7-megastigmadien-3,9-dione	78	Sesquiterpenoid
	(3S,5R, 6S, 7E)-3, 5, 6-trihydroxy-7-megastigmen-9-one	79	Sesquiterpenoid
	(6R,7E,9R)-9-hydroxy-4,7-megastigmadien-3-one	80	Sesquiterpenoid
	Blumenol A	81	Carotenoids
	(S)-3-hydroxy-beta-ionone	82	Ketone
	3-hydroxy-5- α -6- α -epoxy-beta-ionone	83	Ketone
	Z-lanceol acetate	84	Sesquiterpene
	(E, Z)-geranyl linalool	85	Terpene alcohol
	β -bisabolenol	86	Sesquiterpene
	Menthol	87	Alcohols
	Geranyl valerate	88	Esters
	(E)- β -damascenone	89	Cyclic monoterpene ketone
	α -inone	91	Ketones
	butylated hydroxyl toluene	92	Phenols
	(E)-2-hexen-1-ol	93	Alcohols
	Phytol	94	Acyclic diterpene
	Octadecane	95	Alkane
	σ -deca lactone	105	Ketones
	Zygocaperoside	58	Triterpenoid saponins
<i>Z. gaetulum</i> ^{49,50}	3-O-[β -D-glucopyranosyl] quinovic acid-28-O- β -D-glucopyranosyl ester	36	Triterpenoid
	Zygophyloside G	43	Triterpenoid saponins
	Zygophyloside E	44	Triterpenoid saponins
	Zygophyloside I	45	Triterpenoid saponins
	Zygophyloside L	46	Triterpenoid saponins
	Zygophyloside M	47	Triterpenoid saponins
	Linalool	61	Terpene alcohol
	Eicosane	62	Alkane
	Camphor	64	Bicyclic monoterpene ketone
	α -Terpineol	65	Monoterpene Alcohol
	3 β -O- α -L rhamnopyranosyl (1 \rightarrow 2) - α -L-arabinopyranosyl - (1 \rightarrow 2) - β -D-glucopyranosyl urs - 20(21)-en-28-oic acid 28-O-[β -D-glucopyranosyl] ester	96	Triterpenoid
	3 β -O- β -D-quinovopyranosyl - 27 - nor - olean - 12- en - 28 - oic acid 28 - O- β - D-glucopyranosyl ester		Triterpenoid
	3 β -O- α -L rhamnopyranosyl (1 \rightarrow 2) - α -L-arabinopyranosyl - (1 \rightarrow 2) - β -D- glucopyranosylurs - 20(21)-en-28-oic acid 28-O-[β -D-2-O-sulphonylglucopyranosyl] ester	97	Triterpenoid
<i>Z. geslini</i> ⁵¹	3-O-[α -L-arabinopyranosyl-(1 \rightarrow 2)- β -D-glucopyranosyl] quinovic acid 28-(β -D-glucopyranosyl) ester	41	Triterpenoid
	3-O-[β -D-(2-O-sulphonyl) glucopyranosyl] quinovic acid	42	Triterpenoid
	(3 β)-3-[[6-deoxy- α -L-mannopyranosyl-(1 \rightarrow 2)- α -L-arabinopyranosyl (1 \rightarrow 2)- β -D-glucopyranosyl] oxy} urs-20-en-28-oic acid 28-(2-O-sulfo- β -D-glucopyranosyl) ester	50	Triterpenoid
	3 β -3-[(2-O-sulfo- β -D-glucopyranosyl) oxy]-urs-20-en-28-oic acid 28-(2-O-sulfo- β -D-glucopyranosyl) ester.	51	Triterpenoid
<i>Z. melongena</i> ^{6,20}	kaempferol 3-O- β -D-glucoside	14	Flavonoids
	D-pinitol	23	Cyclic polyol
	3-O-[β -D-glucopyranosyl]-quinovic acid	32	Triterpenoid
	3-O-[β -D-glucopyranosyl] quinovic acid-28-O- β -D-glucopyranosyl ester	36	Triterpenoid
<i>Z. propinquum</i> ⁵²	3-O-[β -D-2-O-sulphonyl-quinovopyranosyl]-quinovic acid.	33	Triterpenoid
	3-O-[β -D-2-O-sulphonyl-quinovopyranosyl]-quinovic acid-27-O-O-[β -D-glucopyranosyl] ester	35	Triterpenoid

<i>Z. simplex</i> ^{6,22,53,54}	Isorhamnetin	1	Flavonoids
	Isorhamnetin-3-O-β-D-glucoside	2	Flavonoids
	Isorhamnetin-3-O-β-rutinoside	4	Flavonoids
	Isorhamnetin 3-[6''-(2(E) butenoyl) glucoside]	6	Flavonoids
	Isoquercetin	11	Flavonoids
	kaempferol-3-O-β-rutinoside (Nicotiflorin)	13	Flavonoids
	Luteolin-7-O-β-D-glucoside	16	Flavonoids
	Genticic acid	17	Hydroquinone carboxylic acid
<i>Z. simplex</i> ^{6,22,53,54}	β-sitosterol	18	Sterols
	β-sitosterol-3-O-β-D-glucoside	19	Sterols
	Ursolic acid	21	Triterpenoid
	Oleanolic acid	22	Triterpenoid
	Quinovic acid 3-α-L-rhamnoside	34	Triterpenoid
	Stigmast-3,6-dione	90	Sterols
	Isorhamnetin-3, 7-diglucoside	98	Flavonoids
	Isorhamnetin-3-O-β-D-(6'-malonyl) glucoside	99	Flavonoids
	Quercetin-3-O-(6''-malonyl) glucoside	100	Flavonoids
	P-hydroxy acetophenone	101	Phenols
	Vanillic acid	102	Dihydroxy benzoic acid
	Ferulic acid	103	Hydroxyl cinnamic acid
	Androsin	104	Aromatic ketone

mg/dl at 3 hr and to 182±34 mg/dl at 6 hr^{11,61}. In another study, the ethanol extract of *Z. album* to diabetic mice significantly decreased the level of blood glucose and increased plasma insulin gain to near normal level by (p < 0.05, post hoc Dunnett's test)^{14,35,56}. The ethanol extract of *Z. album* with IC₅₀ {concentration of 50% inhibition} value (43.48 µg/ml) evidenced a better pancreatic α-amylase inhibition than that of the other fractions. Meanwhile, it was observed that the pancreatic α-amylase inhibitory activities increased in the order of hexane fraction, butanol fraction & ethanol extract¹⁴. The pancreatic and serum α-amylase activities of essential oil of *Z. album* in treated diabetic rats were noted to undertake considerable reductions of 43 and 38%, respectively³⁵. The IC₅₀ value of essential oil of *Z. album* against α-amylase was 43.17 µg/ml and that against pancreatic lipase was 85.95 µg/ml⁵⁶. Also, diabetic rats treated with methanol extract of *Z. cornutum*, a significant decrease of glycaemia was noted from the second week and the value recorded after six weeks was 145 ± 12.3 mg/dL. The hypoglycemic effect of methanol extract of *Z. cornutum* may be attributed to its saponins content⁵⁸.

Antimicrobial and antifungal activities

One of the most attracting activities of the extracts of genus *Zygophyllum* is the antimicrobial activity against gram positive, gram negative bacteria and several fungi (Table 3). A good example is the effectiveness of the aqueous methanol roots extracts of *Z. dumosum*, *Z. coccineum* and *Z. qatarense* on inhibition of the spore germination of *Verticillium albo-atrum* and *Fusarium oxysporum*^{13,15,29}.

The shoot extract using the same solvent showed variable toxicity among the extracted *Zygophyllum*^{13,15,29} such that the extracts of *Z. dumosum* were suppressive only to *Fusarium oxysporum*²⁹. On the other hand, the extract of *Z. coccineum* was inhibitory only to *Verticillium albo-atrum*¹⁵. In another study, the ethanol extract of *Z. coccineum* has antimicrobial activity against *Bacillus subtilis*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Candida albicans*, *Microsporum canis* and *Trichophyton mentagrophytes*⁵⁷. The antifungal activity of the isolated compounds of *Z. coccineum* was investigated against *Colletotrichum acutatum*, *Colletotrichum fragariae*, *Colletotrichum gloeosporioides*, *Botrytis cinerea*, *Phomopsis obscurans*, *Phomopsis viticola*, and *Fusarium oxysporum*. The observed results were recorded against *Phomopsis viticola* after 144 hr exposure⁵⁷. The methanol extract of *Z. simplex* showed marked antimicrobial activity against seven standard bacteria (*Proteus vulgaris*, *Escherichia coli*, *Bacillus cereus*, *Salmonella typhi*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa* and *Staphylococcus aureus*) and one standard fungus (*Candida albicans*)¹⁷. Also, the nanoparticles of the methanol extract of *Z. qatarense* leaf exhibited antifungal activity against *Aspergillus niger* and *Penicillium digitatum* was evaluated by standard disk diffusion, the results showed minimum inhibitory concentration {MIC} and minimum fungal concentration {MFC} against *Aspergillus niger* equal to 16 and 128 µg/ml respectively and against *Penicillium digitatum* equal to 32 and 64 µg/ml respectively¹³. Leaves', seeds' and roots' extract of *Z. fabago* were evaluated their antimicrobial activities against

Table 3. Reported *Zygophyllum* species; their biological activities

<i>Zygophyllum</i> species	Biological activities
<i>Z. album</i>	Antioxidant ^{6,8,38} Anti-acetylcholinesterase ⁸ Antidiabetic ^{35,55,56} Antiinflammatory ¹⁴ Antihyperlipidemic ⁵⁶ Anti-hypertensive ¹⁴ Weight lowering ³⁷
<i>Z. coccenium</i>	Antioxidant ⁷ Anti-hypertensive ⁹ Antimicrobial and antifungal ^{15,57} Cytotoxic activity ¹⁵
<i>Z. cornutum</i>	Antioxidant ¹⁰ Antidiabetic ⁵⁸
<i>Z. dumosum</i>	Antimicrobial and antifungal ²⁹
<i>Z. fabago</i>	Antioxidant ⁴⁶ Antimicrobial and antifungal ⁵⁹ Urease inhibitor ⁶⁰
<i>Z. gaetulum</i>	Antidiabetic ^{11,61} Antispasmodic ⁶²
<i>Z. gaetulum</i>	Hepatoprotective ¹¹
<i>Z. geslini</i>	Antidiabetic ^{12,63}
<i>Z. hamiense</i>	Antioxidant ²⁸
<i>Z. macropodium</i>	Analgesic and anti-inflammatory ³¹
<i>Z. qatariense</i>	Antimicrobial & antifungal ¹³
<i>Z. simplex</i>	Antioxidant ^{16,64} Anti-inflammatory ^{64,65} Analgesic ⁶⁵ Antimicrobial and antifungal ¹⁷ Antihyperlipidemic ⁶⁶ Cytotoxic activity ⁶

Bacillus subtilis showing MIC equal to 10, 1, 20 mg/ml respectively, *Staphylococcus aureus* showing MIC equal to 20, 1, 30 mg/ml respectively, *Escherichia coli* showing MIC equal to 30, 10, 50 mg/ml respectively, *Pseudomonas aeruginosa* MIC were 50, 20, 30 mg/ml respectively and *Candida albicans*, which was the most resistant for all extracts⁵⁹. The ethyl acetate extract of *Z. coccenium* showed antibacterial activities against; *Pseudomonas aeruginosa* with inhibition zone 20 mm, *Fusarium moniliforme* with inhibition zone 22 mm, and *Klebsiella pneumonia* showed inhibition zone 22 mm⁵⁷.

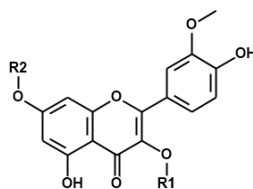
Cytotoxic activity

Recent study showed that the cytotoxic activity of dichloromethane fraction of *Z. simplex* showed powerful effect against cancer cell lines; Human lung carcinoma cells {A-549} and Human colon adenocarcinoma cells {DLD-1} with important IC₅₀ values of 37 and 48 µg/ml, respectively⁶. Also *Z. coccinium* extracts showed maximum cytotoxic activity

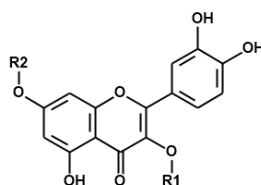
of the acetone extract against Human cervix epithelioid carcinoma {HeLa cell line}, whereas methanol extract showed maximum cytotoxic activity on breast cancer cell line {MCF-7 cell line} with cell line viability 13.36 and 35.19%.¹⁵

Other effects

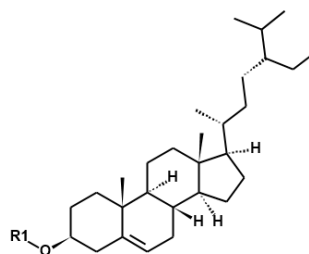
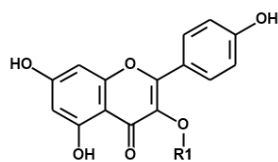
Other activities have also been reported on members of genus *Zygophyllum* **Table 3**. Anti-inflammatory activity best results were recorded for *Z. album* and measured by serum level of C-reactive protein and pancreatic tumor necrosis factor were decreased by 59 % and 64 %, respectively¹⁴. Also, the analgesic activity was reported for the ethanol extract of *Z. macropodium* (ZME) in acetic acid induced writhing method. The inhibition percentages of ZME 100, 300, and 600 mg/kg were 8.7%, 24.9%, 51.3%, respectively having significant inhibitory effect on increased vascular permeability induced by acetic acid in mice ($P < 0.05$ and $P < 0.001$, respectively) compared to normal control³¹.



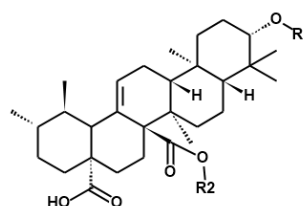
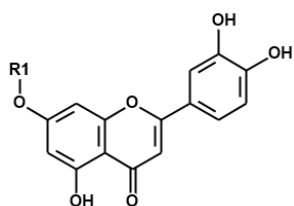
R ₁	R ₂	Compound no.
H	H	1
<i>O</i> -β-D-glucoside	H	2
<i>O</i> -β galactopyranoside	H	3
<i>O</i> -β -rutinoside	H	4
(4"-sulfatorutinoside)	H	5
6"--(2(<i>E</i>) butenoyl) glucoside]	H	6
<i>O</i> -β-glucopyranoside	<i>O</i> -α-rhamnopyranoside	7
<i>O</i> -β-D-glucoside	<i>O</i> -β-D-glucoside	98
<i>O</i> -β - D- (6'-malonyl)glucoside	H	99



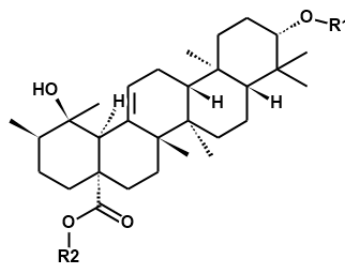
R ₁	R ₂	Compound no.
H	H	8
<i>O</i> -β -rutinoside	H	9
<i>O</i> -β-glucopyranoside	<i>O</i> -β-glucopyranoside	10
<i>O</i> -β-glucopyranoside	H	11
<i>O</i> -(6"-malonyl) glucoside	H	100



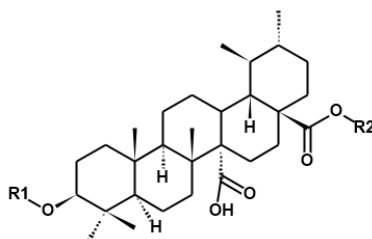
R ₁	Compound no.	R ₁	Compound no.
H	12	H	18
3- <i>O</i> -β-rutinoside	13	<i>O</i> -β-D-glucopyranoside	19
3- <i>O</i> -β-D-glucoside	14		



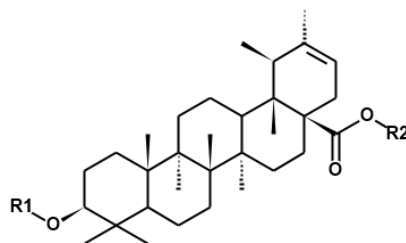
R ₁	Compound no.	R ₁	R ₂	Compound no.
<i>O</i> -β-D-glucoside	16	<i>O</i> -[β-D-2- <i>O</i> sulphonyl quinovopyranosyl	<i>O</i> -β-D-glucopyranosyl	35
		<i>O</i> -β-D-quinovopyranosyl	<i>O</i> -β-D-glucopyranosyl	70



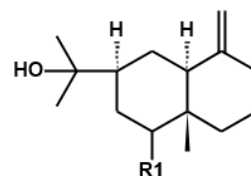
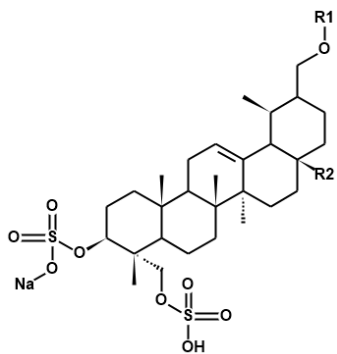
R ₁	R ₂	Compound no.
<i>O</i> - α - <i>L</i> -arabinoside	H	28
<i>O</i> - β - <i>D</i> -glucopyranosyl	β - <i>D</i> -2- <i>O</i> -sulfonyl-galactopyranoside	29
<i>O</i> - β - <i>D</i> -glucopyranosyl	<i>O</i> - α - <i>L</i> -arabinoside	30



R ₁	R ₂	Compound no.
α - <i>L</i> -arabinopyranosyl-(1 \rightarrow 2)- β - <i>D</i> -glucopyranosyl	H	31
β - <i>D</i> -glucose	H	32
β - <i>D</i> -(2- <i>O</i> -sulphonyl)-quinovo pyranosyl	H	33
α - <i>L</i> -rhamnoside	H	34
<i>O</i> - β - <i>D</i> -glucopyranosyl	<i>O</i> - β - <i>D</i> -glucopyranosyl	36
<i>O</i> - β - <i>D</i> -quinovo pyranosyl	<i>O</i> - β - <i>D</i> glucose	38
<i>O</i> - α - <i>L</i> -arabinopyranosyl-(1 \rightarrow 2)- β - <i>D</i> -quinovopyranosyl	H	39
<i>O</i> - α - <i>L</i> -arabinopyranosyl-(1 \rightarrow 2)- β - <i>D</i> -quinovo pyranosyl	<i>O</i> - β - <i>D</i> glucose	40
<i>O</i> - α - <i>L</i> -arabinopyranosyl-(1 \rightarrow 2)- β - <i>D</i> -glucopyranosyl	<i>O</i> - β - <i>D</i> glucose	41
<i>O</i> - β - <i>D</i> -2- <i>O</i> -sulphonyl glucopyranosyl	H	42
<i>O</i> - β - <i>D</i> -2- <i>O</i> -sulphonyl glucopyranosyl	<i>O</i> - β - <i>D</i> glucose	43
<i>O</i> - β - <i>D</i> -2- <i>O</i> -sulphonyl quinovo pyranosyl	<i>O</i> - β - <i>D</i> glucose	44
<i>O</i> - β - <i>D</i> -2- <i>O</i> -sulfo-xylopyranosyl	H	48
<i>O</i> - β - <i>D</i> -2- <i>O</i> -sulfo-xylopyranosyl	<i>O</i> - β - <i>D</i> glucose	49
<i>O</i> - β -[6-deoxy- α - <i>L</i> -mannopyranosyl-(1 \rightarrow 2)- α - <i>L</i> -arabinopyranosyl-(1 \rightarrow 2)- β - <i>D</i> -glucopyranurosonyl]	2- <i>O</i> -sulfo- β - <i>D</i> -glucopyranosyl	50
2- <i>O</i> -sulfo- β - <i>D</i> -glucopyranurosonyl	2- <i>O</i> -sulfo- β - <i>D</i> -glucopyranosyl	51
<i>O</i> - β - <i>D</i> -xylopyranosyl (1 \rightarrow 2) quinovo pyranosyl	<i>O</i> - β - <i>D</i> glucose	52
<i>O</i> - β - <i>D</i> -quinovo pyranosyl	H	69

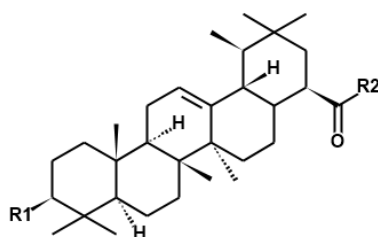


R ₁	R ₂	Compound no.
<i>O</i> - α - <i>L</i> -rhamnopyranosyl-(1 \rightarrow 2)- α - <i>L</i> -arabinopyranosyl-(1 \rightarrow 2)- β - <i>D</i> -glucopyranosyl	<i>O</i> - β - <i>D</i> (2- <i>O</i> -sulphonyl) glucopyranosyl	45
<i>O</i> - α - <i>L</i> -rhamnopyranosyl-(1 \rightarrow 2)- α - <i>L</i> -arabinopyranosyl-(1 \rightarrow 2)- β - <i>D</i> -glucopyranosyl	<i>O</i> - β - <i>D</i> glucose	46

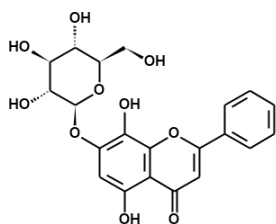


R ₁	R ₂	Compound no.
H	CHO	53
<i>O</i> -β- <i>D</i> glucose	CH ₂ OH	54

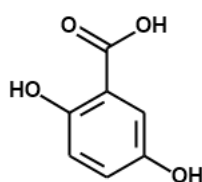
R ₁	Compound no.
H	74
<i>α</i> -hydroperoxy	75



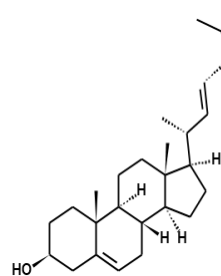
R ₁	R ₂	Compound no.
β- <i>O</i> - <i>α</i> - <i>L</i> rhamnopyranosyl (1→2) - <i>α</i> - <i>L</i> -arabinopyranosyl - (1→2) - β- <i>D</i> -glucopyranosyl	<i>O</i> -β- <i>D</i> -glucopyranosyl	96
β- <i>O</i> - <i>α</i> - <i>L</i> rhamnopyranosyl (1→2) - <i>α</i> - <i>L</i> -arabinopyranosyl - (1→2) - β- <i>D</i> -glucopyranosyl	<i>O</i> -β- <i>D</i> -2- <i>O</i> -sulphonylglucopyranosyl	97



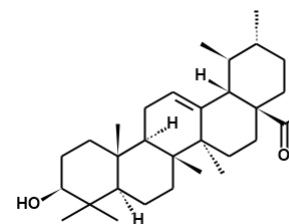
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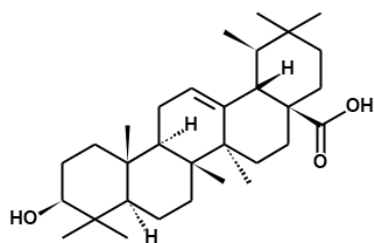
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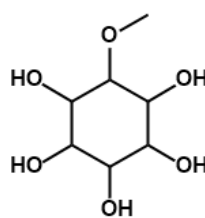
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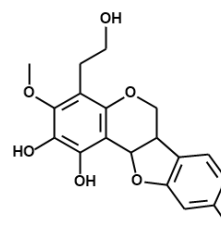
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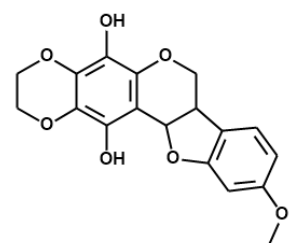
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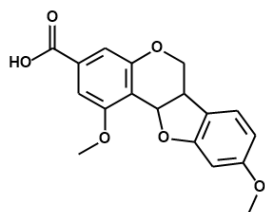
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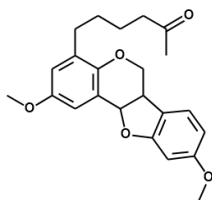
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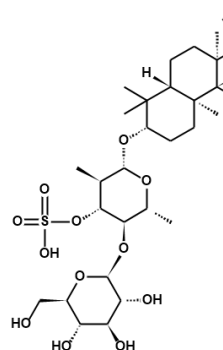
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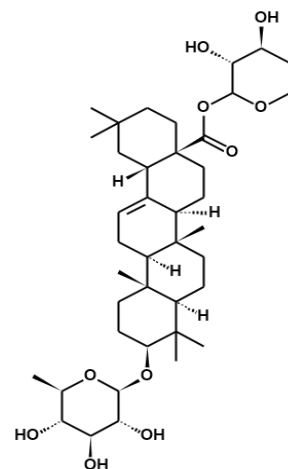
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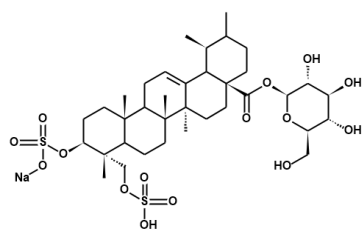
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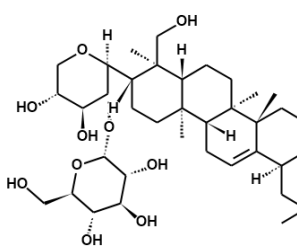
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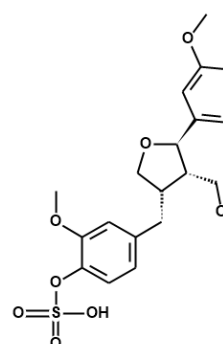
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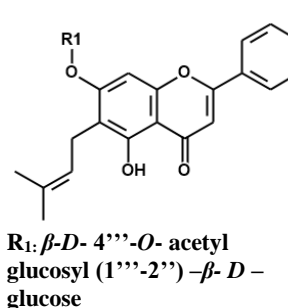
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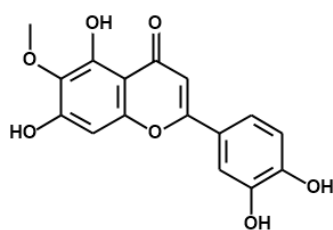
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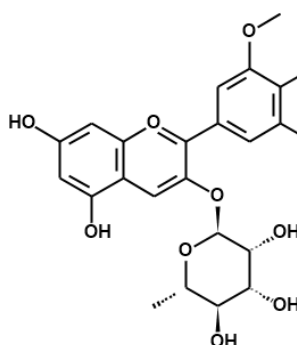
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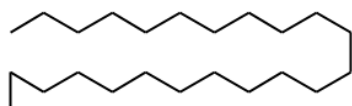
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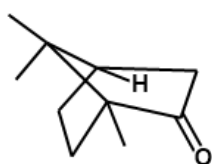
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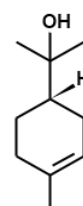
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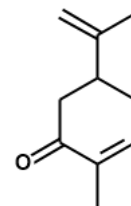
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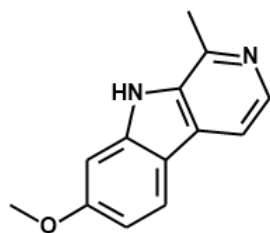
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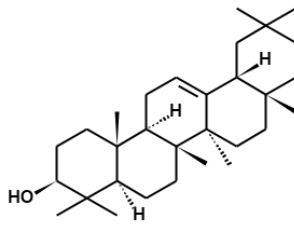
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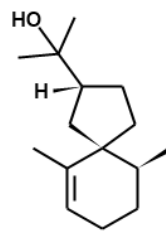
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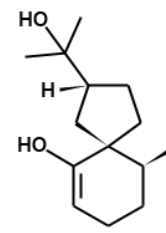
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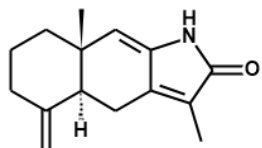
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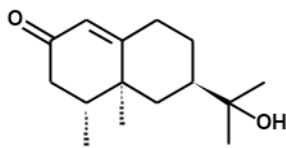
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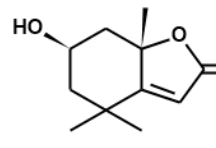
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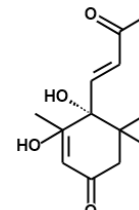
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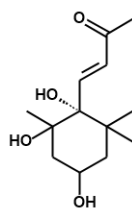
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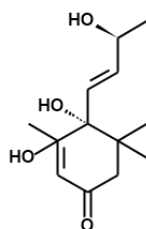
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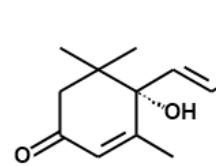
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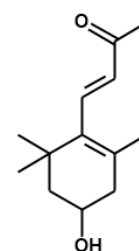
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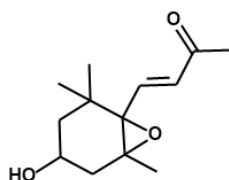
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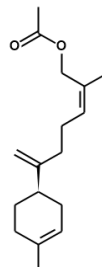
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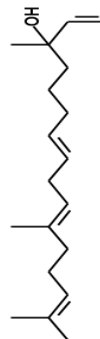
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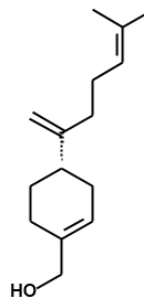
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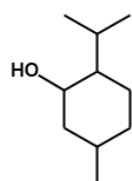
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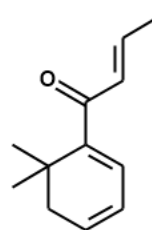
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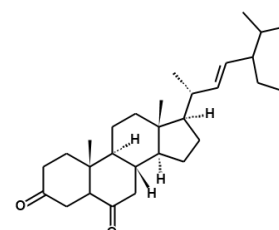
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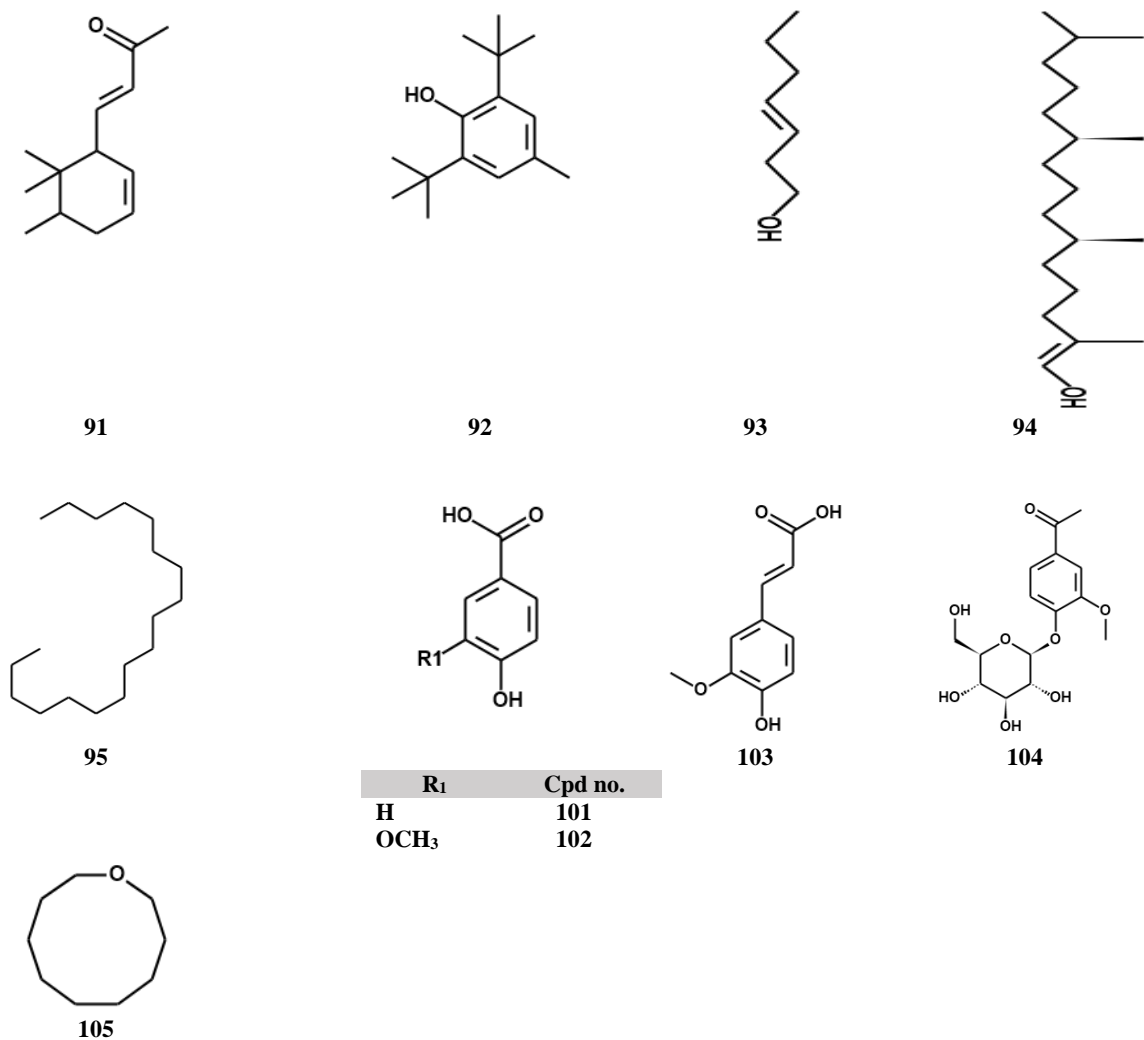


Figure 1. Structures of isolated compounds from different *Zygophyllum* species

Hypoglycemic and hypolipidemic activities of the aqueous extract of *Z. gaetulum* showed hypoglycemic and hypolipidemic activities in Streptozotocin induced-diabetic rats^{11,61}, these effects may be due to the antioxidant potential of this plant. Moreover, *Z. gaetulum* aqueous extract prevented lipid peroxidation by enhancing PON1 {paraoxinase activity} and LCAT {Lecithin cholesterol acyltransferase} activities. In addition, it reduced oxidative stress in the liver and kidney by decreasing thiobarbituric acid reactive substances levels and increasing antioxidant enzyme activities¹¹. Oral administration of *Z. simplex* to hyperlipidemic rats were appreciably effective in decreasing the levels of serum total cholesterol, low-density lipoprotein cholesterol, triacylglycerol and tissue lipid accumulation while

increasing the levels of serum high-density lipoprotein cholesterol, adjusting the metabolic disturbance of lipoprotein and increasing the antioxidant enzyme activity and repressing the development of atherosclerosis⁶⁶.

CONCLUSION

In the review, chemical investigations and biological activity have been reported for only 16 out of 100 known *Zygophyllum* species. However, members of *Zygophyllum*, such as *Z. album* and *Z. simplex*, revealed significant biological activity, especially as anti-inflammatory and antioxidant. Investigation of the chemical constituents of plants of genus *Zygophyllum* showed diverse compounds, including triterpenes,

saponins, flavonoids, sterols and simple phenolic compounds. It should be emphasized that phenolic compounds from *Z. cornutum*, *Z. album*, *Z. cocconem*, *Z. hamiense*, *Z. simplex* and *Z. fabago* had particularly prominent anti-oxidant activity, in addition to some other biological properties. Also, the presence of essential oils and saponins in *Z. cornutum* contributed to its antidiabetic activity. Previous studies have provided a base for the medicinal use of *Zygophyllum* species. It is important to note that the safety and toxicity of *Zygophyllum* species have not been explored. Therefore, the toxicities of traditional remedies and isolated chemical compounds should be further assessed as well.

Conflict of Interest

The authors declare that they don't have any kind of conflict of interest.

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