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REVIEW ARTICLE

XANTHORRHOEACEAE PLANTS OF ISRAEL AND PALESTINE. UNIQUE MEDICINAL ACTIVITIES AND CHEMISTRY

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ABSTRACT

Xanthorrhoeaceae plants family is one of the smallest in the region of Israel and Palestine, where it is represented by seven species. Some of these species where notable in terms of medicinal activities and unique natural products, that have interesting structures and subunits. Interestingly, no review articles were published about the medicinal, chemical properties or even the ethnobotanical and ethnomedicinal uses of this family.In this review article, we will present the debated taxonomy of these plants, their reported medicinal activities, as well as the results of their chemical compositions investigations. Information will be presented in reader-friendly tables and figures. Special attention will be drawn to the toxicity of some species and in contrast, to their traditional use as food. In addition, a discussion of some of the topics related to medicinal activities and chemical aspects will be presented. Finally, conclusions will be presented, and future visions and recommendations will be introduced.

INTRODUCTION

Xanthorrhoeaceae plants family is one of the most taxonomically debated in the entire plant kingdom. This is so clear when searching for the classification of the species listed below. In our region, this family is represented by seven species, included in three genera:*Asphodeline brevicaulis*, *Asphodeline lutea*, *Asphodelus fistulosus*, *Asphodelus ramosus*, *Asphodelus refractus*, *Asphodelus tenuifolius*, *Eremurus libanoticus*.[1] But this statement is not accepted even by scholars of same region. For example, the most reliable botanical website in Israel in addition to reference 1, is "Flora of Israel Online" that was established by Prof. A. Danin, and it classifies these plant in the Liliaceae plant family.[2]In addition to this, "Flora of Israel Online" includes 9 species within the three genera of *Asphodeline*, *Asphodelus*, *Eremurus*. M. W. Chase and his colleagues do not consider these three genera part of the *Xanthorrhoeaceae*plants family.[3]But as far as this review article is concerned, we tend to agree with reference 1 and the classification presented by O. M. Grace and her colleagues.[4] To conclude this discussion we will indicate that the debate does not end with family, subfamily or genus taxonomy, but extends to species classification.[5]

In some parts of the world, plants of this family are growing out of their natural original habitat, which is the Asia, North Africa, and Southern Europe. In South Africa, *Asphodelus fistulosus* is considered alien species,[6]and in Mexico it is referred to as "highly problematic".[7]

Even though species of the *Xanthorrhoeaceae*plants family have extensive traditional uses in many societies (next section), it seems that ancient civilizations made very limited use of these plants. *Asphodeline lutea* was known to the Roman culture and it appeared in its drawings.[8]It was also consumed as a food in the same culture,[9] in the same manner that many other cultures still do.

As we mentioned above, no review articles were published about the *Xanthorrhoeaceae*plants family. In our literature search we could find only two. A short but excellent review article was published by I. Lazarova and R. Gevrenova.[10]It extensively presents the chemical composition of the plant, with many structural formulas. It also introduces a broad scan of the plant's ethnopharmacology. The only weakness of this article is that it brings very brief section of the medicinal properties of the plant as reported by modern research. Another excellent and comprehensive review article was published by M. Malmir and her colleagues.[11]It presents a comprehensive review of the botany, phytochemistry (no structures), ethnomedicine and modern research findings. The only weakness of this article is the presented classifications of the species, but authors are aware of this fact and indicate it.

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Figure 1 *Asphodeline lutea* and *Asphodelus ramosus*

Ethnobotanical uses of Xanthorrhoeaceae family

Contrary to the very little use of*Xanthorrhoeaceae*plants in remote history, modern traditional societies of Western Asia and the Mediterranean basin, have used and still using these plants for various purposes.

Summary of the published literature about the traditional uses of these plants is presented in Table 1.

were extensively studied and published, others were very limitedly investigated. Another worth mentioning aspect of our literature search about these plants was the fact that *Asphodelus rasmosus* was published with three botanical synonyms: *Asphodelus rasmosus*, *A. aestivus* and *A. microcarpus*. Other species are referred to with one scientific name for each, but as for most plant species of our region, with many common names.

Asphodeline brevicaulis

This species was very limitedly studied, and we found only two publications relevant to this review article.A comprehensive work was published about the methanolic extract of roots. It was tested for total phenolic content (TPC) and free anthraquinones, that were determined by HPLC. The antioxidant capacity was determined by DPPH, phosphomolybdenum and ferrous ion chelating. Enzyme inhibition activity is reported for AChE, BChE, α-amylase, α-glucosidase and tyrosinase.[63] Acetone and methanolic roots extracts inhibited hyaluronidase, and collagenase and elastase. Acetone extract was more active.[64]

Table 1 Ethnomedicinal and ethnobotanical uses of *Xanthorrhoeaceae* plants

Region	***Species*, uses, methods, references**
Algeria	*Asphodelus refractus* is used to treat indigestion, constipation, wound of stomach andskin diseases.It is also strengthening and stimulant.[12]*Asphodelus ramosus* oil prepared from tubers is used treat weakness as antiseptic.[13]To increase lactation in sheep.[14]Bulbs are powdered to treat hemorrhoids and acne.[15]
Armenia	*Eremurus spectabilis*young leaves are eaten as salads, fried, lacto-fermented. Roots infusion is used to treat digestive disorders.Powder from rhizomes used against skinabscesses and cysts.[16]
Bangladesh	*Asphodelus tenuifolius*whole plant extract treats bleeding from nostril (Epistaxis), ear (Otorregis) and applied into the anus forintestinal worm.[17]
Bosnia	*Asphodeline lutea* bulbs are ground to be consumed as mush or bread. *Asphodelus microcarpus* same use.[18]
Ethiopia	*Asphodelus fistulosus*is eaten by baboons.[19]
India	*Asphodelus tenuifolius* leaves are soaked in coconut oil and wrapped around suppurating tumor.[20]Bulb powder is used as toothpaste.[21]
Iran	*Eremurus spectabilis*seed cataplasm is applied forback pain.[22] Whole plant is used to treatdermal infection, sticking and hyperlipidemia.[23]
Iraq	*Eremurus spectabilis* leaves decoction is used to treatarthritis, intestinal worms and as a sedative.[24]
Italy	*Asphodelus microcarpus* tubers are used to feed animals. It is also a symbol of agricultural ferility.[25] Cooked and consumed in several ways.[27,31-33] *Asphodeline lutea*cooked and consumed in several ways.[26-28,30-35]Decoction of aerial parts is diuretic and treats skin pains.[29]
Jordan	*Asphodelus microcarpus* medicinal uses (no details).[36]*Asphodeline lutea* medicinal uses (no details).[36]*Asphodelus fistulosus*leaves are soaked in water and the liquid is used to prepare a cream with antispasmodic and analgesic.[37]
Libya	*Asphodelus refractus*leaves decoction isdiuretic. Whole plant is usedas a tonic and stomachic, against headache, liver affectionsrheumatisms, and for treatment of syphilis.[38]*Asphodelus microcarpus* roots juice is used to treatarthritis, rheumatism and for ovulation.[39]
Middle East	*Asphodelus ramosus* whole plant is boiled in water to prepare a decoction, which is antispasmodic and treats paralysis.[40]
Mexico	*Asphodelus fistulosus* is used for decoration.[41]
Morocco	*Asphodelus ramosus*is used to treat obesity, skin disease, and colds and rheumatism.[42]Roots and seeds are mixed with oil and applied externally to treat skin diseases and friction.[43] Tuber is used to treat diabetes.[44]*Asphodelus tenuifolius* decoction of roots and fruits treats digestive and circulatory disorders.[43]Leaves are used to treat diabetes.[44]
Oman	*Asphodelus tenuifolius* decoction of whole plant or leaves is used to treat heartburn, kidney stones and as laxative.[45]
Pakistan	*Asphodelus tenuifolius*leaf decoction is given in kidney stone.Leaf paste isapplied on swellings. Seeds are diuretic, used externally to ulcers and inflamed parts, hypotensive. It also treats piles. Fresh leaves are used a condiment. Stem and leaves powder topically used for epilepsy, and orally as expectorant, against insect bites, and diarrhea and cough. Leaves eaten as anti-obesity food. It is also used against arthritis, vomiting and constipation.[46-55]
Saudi Arabia	*Asphodelus fistulosus* whole plant or seeds are prepared as decoction, and ointment or poultice. It is diuretic, and antiulcer and anti-inflammatory.[56] Aerial parts are stimulant, laxative,anthelmintic and to treatstomachache.[57]*Asphodelus tenuifolius* seeds decoction is used against cold, hemorrhoids and rheumatic pain.[57]
Turkey	*Asphodelus fistulosus*is consumed as food in several ways. Aerial parts decoction is externally applied fot treating skin disorders.[58,60]*Asphodelus ramosus* roots are eaten or prepared as decoction, and they are used to treat stomach ailments, eczema, wounds and hemorrhoids.[59,60] *Eremurusspectabilis* aerial parts are eaten or cooked to assist digestive system.[61]
UAE	*Asphodelus tenuifolius*seeds or whole plant are used as laxative, diuretic, burn relief and toothache.[62]

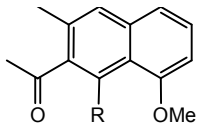
Biological, chemical, and other properties of Xanthorrhoeaceae plants

As for most plant families of our region, *Xanthorrhoeaceae* plants were studied with very different intensities: while some

Asphodeline lutea (Table 2)

Table 2 Biological, medicinal, and other properties of *Asphodeline lutea*

Activity/Property	Major Findings/Reference
Antibacterial, antifungal	Aqueous, methanolic and ethanolic extracts of bulbs and aerial parts were prepared, with assistance of 40 kHz ultrasonic. These extracts were active against methicillin resistant *S.aureus*.[65]Roots were extracted with methanol and extract was active against several bacteria species.[66] Aerial parts were extracted with 80% aqueous methanol, and extract was active against 4 bacteria species.[67]Aerial parts were extracted with water and extract was active against three fungi species.[75]
Anticancer and related activities	Roots were extracted with methanol and extract had antimutagenic activity.[66] Aerial parts were extracted with 80% aqueous methanol, and extract was active against several cancer cell lines.[67]Ultrasound assisted ethanolic extraction was performed for dried roots of plant sample, harvested in different locations of Bulgaria and Turkey. This extract was active against two cancer cell lines.[68]
Antioxidant	Aerial parts were extracted with 80% aqueous methanol, and the antioxidant capacity of this extract was determined with DPPH assay.[67] Roots were extracted with methanol and chloroform, separately. Methanolic extract was fractionized with several solvents, and both extracts and fractions were analyzed for general chemical composition and their antioxidant capacities were determined. Plants were of Bulgarian, Turkish and/or Syrian origin.[69,70,71]An extensive work that separately extracted all parts of the plant with methanol, and the antioxidant capacities of these extracts was determined with six different methods. Plants were harvested in various localities in Italy.[72]Roots were extracted with 70% aqueous ethanol and extract had antioxidant (*in vitro*, *in vivo*) activity.[73] In a follow-up study, the same research group compared the previous results with the activity of known compounds that were isolated from the same extract.[74]Plant edible parts were cooked and its antioxidant capacity (ABTS assay) as well as its general chemical composition were determined.[77]
Hepatoprotection	Roots were extracted with 70% aqueous ethanol and extract had antioxidant (*in vitro*, *in vivo*) activity against CCl_4-induced hepatotoxicity.[73] In a follow-up study, the same research group compared the previous results with the activity of known compounds that were isolated from the same extract.[74]
Enzyme inhibition	Ultrasound assisted ethanolic extraction was performed for dried roots of plant sample, harvested in different locations of Bulgaria and Turkey. This extract had anti-cholinesterase, anti-tyrosinase, anti-amylase and anti-glycosidase inhibition activity .[68]An extensive work that separately extracted all parts of the plant with methanol, and the enzyme (AChE, BChE, tyrosinase, α-amylase, α-glucosidase) inhibition capacities were determined..[72]
Nutrition	Nutritional protein quality was tested and reported.[76]
Chemical composition	General composition was determined and anthraquinone quantification were performed to ultrasound assisted ethanolic extract of dried roots of plant sample, harvested in different locations of Bulgaria and Turkey.[68]All parts of the plant were separately extracted with methanol, and the general chemical composition of the extracts was analyzed. Plants were harvested in various localities in Italy.[72] Roots methanolic extract was analyzed, and three new compounds were isolated and characterized (**Figure 2**).[78]



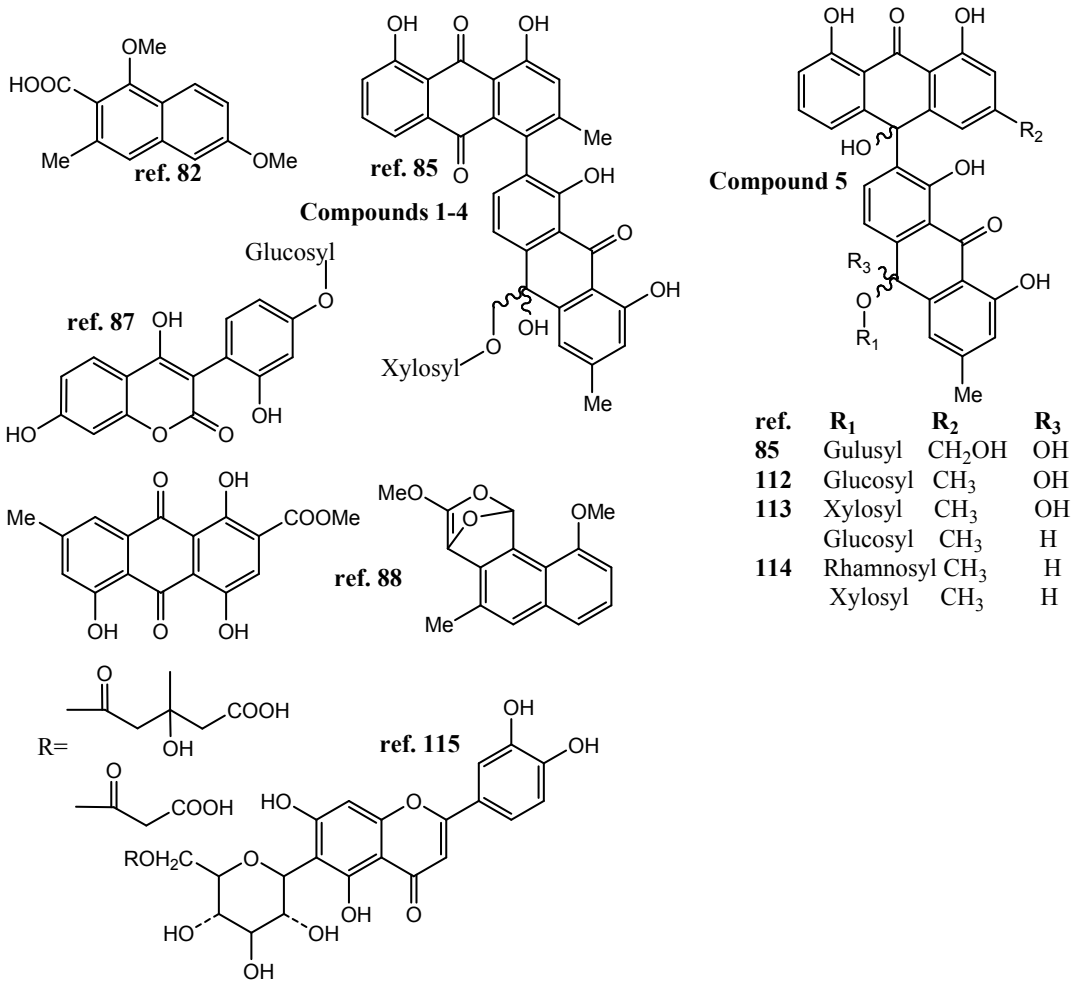
R= OMe, OH, H

Figure 2 Active natural products isolated from *Asphodeline lutea*

Asphodelus ramosus (syn. aestivus syn. microcarpus) (Table 3)

Table 3 Biological, medicinal, and other properties of *Asphodelus ramosus*

Activity/Property	Major Findings/Reference
Allelopathy	Tubers were dried and ground, and the resulting powder had allelopathic activity against *Chenopodium album*, a major weed of Wheat *Triticum aestivum* crops.[79]
Analgesic	Leaves methanolic extract had analgesic activity in rats, tested by two methods.[80]
Antiallergy	Seed extracts(methanol, chloroform, ethyl acetate and *n*-butanol) were preparedin the form of Vaseline ointment. They had activity against dinitrochlorobenzene-induced eczema in mice. General composition was determined.[94]
Antibacterial, antifungal, antiviral	Aqueous, methanolic and ethanolic extracts of bulbs and aerial parts were prepared, with assistance of 40 kHz ultrasonic. These extracts were active against methicillin resistant *S.aureus*.[65] Aerial parts were extracted with water and extract was active against three fungi species.[75] Leaves and flowers were extracted with methanol and both extracts had anti-acne activity.[81]Tubers were extracted with ethanol and extract was analyzed for pure compounds. These showed antibacterial and antifungal activities.[82]Ethanolic extract (plant part/s not indicated) had activity against 8 bacteria species.[83]Leaves methanolic extract had activity against 2 bacteria species and HAV-10 virus.[84]Tubers ethanolic extract analysis afforded new compounds (**Figure 3**), where two of them had activity againstmethicillin resistant *S. aureus*.[85,88]Seeds essential oil was analyzed for fatty acids composition and it had activity against several bacteria species.[86]Bulbs and roots were extracted with acetone, and extract had activity against five bacteria species. A new compound was isolated and characterized (**Figure 3**).[87]Leaves ethanolic extract was active against 13 bacteria species.[89]Leaves aqueous and ethanolic extracts were active against *A. niger*.[90] Whole plant ethanolic and aqueous extract had very weak activity against HIV-virus.[91]Roots methanolic extract had activity against 3 viruses.[92]
Anticancer and related activities	Tubers were extracted with ethanol and extract was analyzed for pure compounds. These showed antiluekemia activity.[82] Leaves methanolic extract had activity againstlung carcinoma cell line(A-549).[84]Tubers were extracted with several solvents and methanolic extract had anticancer (MCF-7) activity.[93]
Antioxidant, anti-inflammatory	Roots were extracted with methanol and was analyzed for general chemical composition and its antioxidant capacity was determined.[71] Leaves ethanolic and aqueous extracts were prepared, and their antioxidant capacities were determined by several methods, including *in vitro*.[90]Tubers were extracted with several solvents and antioxidant capacity of methanolic extract was determined (DPPH).[93]Tubers were extracted with 80% aqueous ethanol, and extract had activity against carrageenan-induced paw edema in mice. Antioxidant capacity of this extract was determined with DPPH method. Extract was analyzed for general composition.[95]Different parts were separately extracted with methanol, and extract had activity against carrageenan-induced ear edema in mice. Antioxidant capacity of this extract was determined with several methods. Extract was analyzed for general composition.[96] Whole plant was extracted with water, and ethanol and chloroform. All extracts showed mild activity against arachidonic acid-induced ear edema in mice earor carrageenan-induced paw edema in rats.[97]Different parts were separately extracted with methanol and extract showed activity against carrageenan-induced paw edema in rats.[98]Leaves methanol and acetone extracts were separately prepared and their antioxidant capacities were determined with various methods. General chemical composition was also reported.[99]Whole plant was extracted with and this extract was fully analyzed for nutritional components. It was also tested for antioxidant (DPPH) activity.[100]Water, and ethanol and methanol were used to separately extract leaves, and tubers and flowers. All (9) extracts were tested for antioxidant activity (DPPH, ABTS).[101]Whole plant was extracted with four solvents, and each extract was analyzed for general chemical composition, and tested for antioxidant activity, using various methods.[102]
Enzyme inhibition or activity	Water, and ethanol and methanol were used to separately extract leaves, and tubers and flowers. All (9) extracts had tyrosinase inhibition activity.[101] Seasonal variations in nitrate reductase and nitrogen content was observed in different parts of the plant.[103]
Insecticidal, molluscicidal, antiparasitic	Tubers were extracted with ethanol and extract was analyzed for pure compounds. These showed antimalarial and antileishmanial activities.[82]Roots extract had activity (more than leaves) against *T. cinnabarinus*.[104,105]
Metal nanoparticle preparation	Aerial parts aqueous extract was used to reduce $AgNO_3$ in the preparation of silver nanoparticles (AgNP's) and studying their properties.[106]Aerial parts aqueous extract was used to reduce $FeCl_3$ in the preparation of iron nanoparticles (FeNP's) and studying their properties.[107]
Nutrition, toxicity	Different parts were separately extracted with methanol and extract showed mild toxicity in rats.[98]
Chemical composition	Tubers ethanolic extract was analyzed and a new compound (**Figure 3**) was isolated and characterized, along with nine other known compounds.[82]General chemical composition in various levels of details was reported by several groups, but these reports do not include isolation of new compounds: heavy metals,[108]*n*-alkanes,[109]phenolics with detailed NMR spectra,[110]and, phenolics, alkanes and fatty acids.[111]New compounds were isolated and characterized without testing their medicinal activities (Some of them are presented in **Figure 3**).[112-115]



ref.	R_1	R_2	R_3
85	Gulusyl	CH_2OH	OH
112	Glucosyl	CH_3	OH
113	Xylosyl	CH_3	OH
	Glucosyl	CH_3	H
114	Rhamnosyl	CH_3	H
	Xylosyl	CH_3	H

Figure 3 Active natural products isolated from *Asphodelus ramosus*

Asphodelus fistulosus (Table 4)

Table 4 Biological, medicinal, and other properties of *Asphodelus fistulosus*

Activity/Property	Major Findings/Reference
Antibacterial, antifungal, antiviral and related activities	Seeds were extracted with 95% aqueous ethanol, and extract was fractionized with several solvents. Extract and fractions were active against 9 bacteria and fungi species.[116] Whole plant aqueous and methanolic extracts were active against 7 bacteria species.[117]
Antioxidant, anti-inflammatory and related activities	Seeds were extracted with 95% aqueous ethanol, and extract was fractionized with several solvents. Extract and fractions were tested for antioxidant capacities (DPPH, superoxide reduction).Total phenolic content was determined.[116]
Hypotensive, vasorelaxant	Whole plant was extracted with 30% aqueous ethanol, and the extract had vasorelaxant and hypotensive activities.[119]
Antidiarrheal, laxative, diuretic	Whole plant was extracted with 70% aqueous ethanol, and extract had antidiarrheal and laxative activities in mice. Mechanism of action was investigated. General chemical composition was determined.[118]Whole plant was extracted with 30% aqueous ethanol, and the extract had diuretic activity.[119]
Antiparasitic, insecticidal	Seeds were extracted with 95% aqueous ethanol, and extract was fractionized with several solvents. Extract and fractions were active against 4 parasitic species.[116] Whole plant was extracted with *n*-hexane, and acetone and methanol. All extracts had activity against *T. castaneum*.[120]
Nutrition	Various growth conditions increased the protein content of the edible parts.[121]
Chemical composition	General chemical composition was published, focusing on fatty acids and phytosterols.[122]Aerial parts extraction afforded known natural products with new asphodelin-10'-anthron (**Figure 4**).[123]

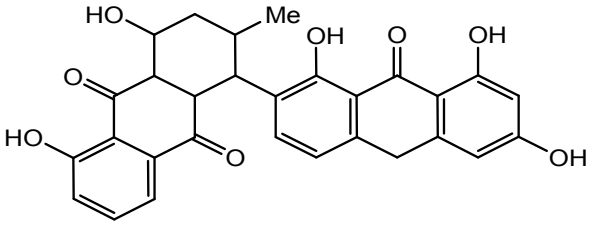


Figure 4 Active natural products isolated from *Asphodelus fistulosus*

Asphodelus refractus

Aerial parts were extracted with 70% aqueous methanol. The extract was tested for cytotoxicity (HCT-116 and HepG-2 human cancer cells), activity against several bacteria and fungi species (along with fractions with various solvents), total flavonoid content, total phenolic contend and antioxidant activity (DPPH). Several compounds were isolated and characterized, including a new natural product, refractlin (Figure 5).[124]

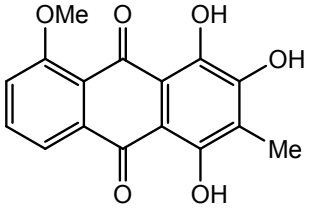


Figure 5 Active natural products isolated from *Asphodelus refractus*

Asphodelus tenuifolius (Table 5)

Table 5 Biological, medicinal, and other properties of *Asphodelus tenuifolius*

Activity/Property	Major Findings/Reference
Allelopathy	Water extracts of roots, shoots and flowers had allelopathic effect on *Cicer arietinum* (Chickpea).[125]When grown with *Triticum aestivum* (Wheat), it showed allelopathic effect, but when grown with*Sorghumbicolor* Sorghum, the later had allelopathic effect on it.[126]Aqueous extracts of shoots and seeds showed allelopathic effect on *Zea mays* (Corn).[127]
Antibacterial, antifungal, antiviral and related activities	Different parts were separately extracted with several solvents with increasing polarity. All extracts had activity against some bacteria species.[128,129]Aerial parts were extracted with 95% aqueous ethanol, and extract had activity against *C. albicans* .[130]Aerial parts were extracted with *n*-butanol and fractionized by several solvents. Extract and fractions had activity against some bacteria and fungi species. Known phenolics were isolated and characterized in this study.[131] Whole plant 80% aqueous methanolic extract showed activity against several bacteria species. General chemical composition is presented.[132]Leaves were extracted with several solvents and extracts had activity against some fungi species.[133]Aerial parts aqueous extract had activity against *Fusarium graminearum* and *F.sporotrichioides*.[134]
Anticancer	Aerial parts were extracted with 80% aqueous ethanol, and two new compounds (**Figure 6**) were isolated and characterized. These compounds had activity against A375 human melanoma cells.[135]
Anti-inflammatory, Antioxidant and related activities	Aerial parts were separately extracted with *n*-hexane and ethanol, and both extracts showed activity in wide range on induced inflammation and arthritis in rats.[136]Different parts of the plant were extracted with ethyl acetate, using four different extraction methods. The extracts were analyzed for their general chemical compositions. Their antioxidant capacities were determined with five methods.[137]Bulbs and seeds were separately extracted with 50% aqueous ethanol. General chemical compositions of extracts were determined, as well as their antioxidant capacities (6 methods).[138]Dried leaves were analyzed for general chemical composition, and their antioxidant capacity was determined with three methods.[139]
Hypotensive	Whole plant was extracted with 70% aqueous methanol and extract was fractionized with several solvents. Both extract and its *n*-butanol fraction had hypotensive and vasorelaxant activities.[140]Whole plant was extracted with 30% aqueous ethanol and this extract had hypotensive effect in rats.[142] Seeds were extracted with 30% aqueous methanol, and this extract had hypotensive effect in rats. A mechanism of action is presented, and general chemical composition is provided.[143]
Antidiarrheal, laxative, diuretic	Whole plant was extracted with 30% aqueous ethanol and this extract had antidiarrheal and laxative effect in mice. Mechanism of action is proposed.[141]Whole plant was extracted with 30% aqueous ethanol and this extract had diuretic effect in rats.[142] Seeds were extracted with 30% aqueous methanol, and this extract had diuretic effect in rats. A mechanism of action is presented.[143]
Enzyme inhibition	Whole plant was extracted with methanol, and extract was fractionized with chloroform, ethyl acetated, *n*-butanol and water. The ethyl acetate fraction analysis afforded new compound, asphorodin (**Figure 6**), that inhibited lipoxygenase.[144]
Antiparasitic	Whole plant 80% aqueous methanolic extract showed antigiardial activity.[132]
Chemical composition	Whole plant was extracted with methanol and extract was fractionized with various solvents. Analysis of extract and fractions yielded known compounds that were isolated from this plant for the first time.[145]Analysis of roots ethanolic extract yielded known compounds that were isolated for the first time from this plant, in addition to two new compounds (**Figure 6**).[146]Methanolic whole plant extract was fractionized with ethyl acetate resulted in the isolation and characterization of three new compounds (**Figure 6**).[147]

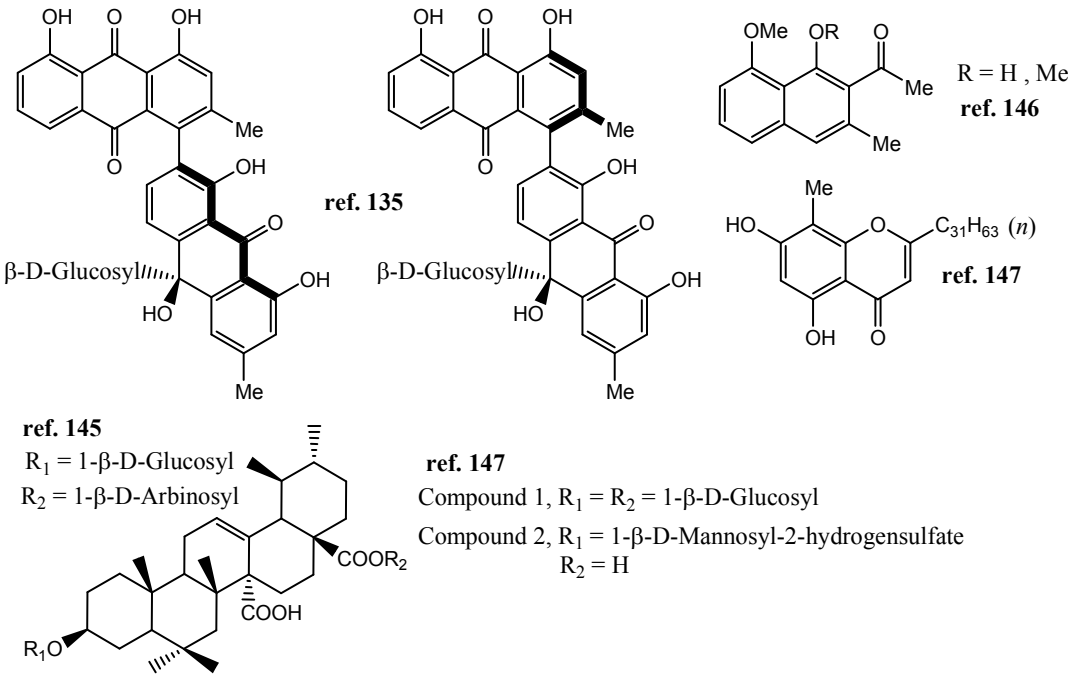


Figure 6 Active natural products isolated from *Asphodelus tenuifolius Eremurus spectabilis* (Table 6)

Table 6 Biological, medicinal, and other properties of *Eremurus spectabilis*

Activity/Property	Major Findings/Reference
Antibacterial	Leaves (fresh) ethanolic extract had strong activity against *S. aureus*.[148]Leaves and roots were separately extracted with acetone, and ethanol and water. The antibacterial activity was observed against 5 bacteria species.[149]Leaves were separately extracted with chloroform, ethyl acetate, and toluene and water. Extracts had activity against *C. albicans*.[150]Leaves were extracted with 80% aqueous methanol and extract had activity against four bacteria species.[151]Roots were extracted with methanol and extract had activity against 4 bacteria species.[152] Whole plant was separately extracted with ethanol, methanol and water. All extracts had activity against several bacteria species, out of 12 tested.[156]
Anticancer	Leaves and roots were separately extracted with acetone, and ethanol and water. The anticancer activity was observed against FC-3 prostate cancer cell lines.[149]Leaves were extracted with water and 82% *n*-hexane in ethanol. Both extracts had activity against RD cancer cell lines. General chemical composition is presented.[153]Leaves methanolic extract had activity against SH-SY5Y neuroblastoma cancercells. Authors refer this activity to high concentrations of orientin and isoorientin.[154]
Anti-inflammatory, antioxidant	Leaves and roots were separately extracted with acetone, and ethanol and water. The antioxidant activity was tested using DPPH and hydroxyl radical scavenging methods. General chemical composition was determined.[149]Leaves were separately extracted with chloroform, ethyl acetate, and toluene and water. Extracts were tested for antioxidant activity (DPPH). General chemical composition is presented.[150] Leaves were extracted with 80% aqueous methanol and antioxidant capacity (DPPH, ferric chelation) was determined. General chemical composition is presented.[151]Roots were extracted with ethanol. Extract antioxidant activity was determined with DPPH method, and anti-inflammatory activity was performed through TNF-α test.[155]Whole plant was separately extracted with ethanol, and methanol and water. All extracts were tested for antioxidant capacity (DPPH). General composition of volatile compounds is presented.[156] Aerial parts were extracted with acetone-water-acetic acid (70:29.5:0.5, v/v/v). The antioxidant capacity (DPPH) and the general chemical composition of this extract were determined.[157]Leaves were extracted with 80% aqueous methanol. Extract antioxidant capacity (DPPH, phosphomolybdate method) was determined, and its general chemical composition was analyzed.[158]
Gastroprotective	Leaves methanolic extract was prepared, fractionized with several solvents, and analyzed for general chemical composition. Extract and its component isoorientin, had activity against indomethacin-induced gastric ulcer in rats.[159]
Enzyme inhibition	Leaves were extracted with methanol and fractionized with several solvents. The *n*-hexane fraction had iNOS inhibition activity. Extract was analyzed affording five known compounds(methyl linolenate, chrysophanol, *β*-sitosterol, isoorientin and inosine) that were isolated for the first time from this plant.[160]
Nanoparticles	ZnO nanoparticles prepared and combined with leaves ethanolic extract, showed antibacterial activity against three bacteria species.[161]
Chemical composition	Seeds essential oil was prepared and analyzed with GC-MS. New compounds are not reported.[152]A new water-soluble polysaccharide was isolated and characterized from roots aqueous extract (**Figure 7**).[162]

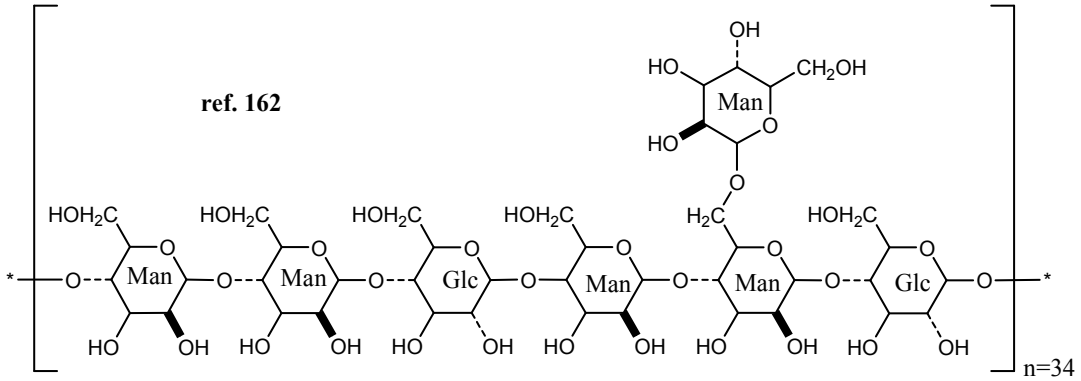


Figure 7 Active natural products isolated from *Eremurus spectabilis*

DISCUSSION

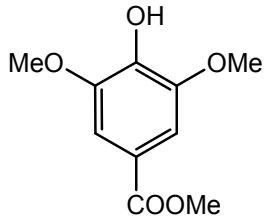
In the Introductin we indicated that we found only two review articles about the *Xanthorrhoeaceae*plants family.[10,11] In addition to these, an excellent review article was published about the *Asphodelus* genus, that includes four out of seven plant species of this family, that grow in our region.[163]The main strength of this article is the table presented on page 6 there, where a summary of 11 important, published studies appear there.

In our literature scan, we found out that very limited research was published about *Asphodeline brevicaulis* and its chemical composition is completely unknown. The publications about *Asphodelus refractus* are even less than that. But even some species that can be considered as reasonably investigated, such as *Asphodeline lutea*, *Asphodelus fistulosus* and *Eremurus spectabilis*, we discovered that their chemical compositions are almost unknown, and very few new compounds were isolated from each one of them.

Contrary to that, *Asphodelus ramosus* (syn. *aestivus* syn. *microcarpus*) (Table 3) and *Asphodelus tenuifolius* (Table 5), were extensively studied, and many new active natural products were isolated from each one of them.

This can possibly be referred to two major reasons in the case of *A. ramosus*, that are strongly interrelated. First, it is one of the most widespread plants of this family, not only in the reviewed area, but globally. Second, it was found that this species is highly adaptable to different growth conditions, especially in the Mediterranean basin harsh climate.[164]This ability of *A. ramosus* to grow under stress condition, obviously affects its medicinal properties. In case of drought, it was reported that its chemical composition was altered, and also the derived medicinal properties such as antioxidation.[165]It was also reported that this stress can emerge from seasonal changes, and in such case as well, changes of contents and activities were observed, as it was found for three proteolyticenzymes, endopeptidase, leucine aminopeptidase, and carboxypeptidase.[166]

In traditional medicines and societies, *A. ramosus* has different uses, including nutrition, and as we have presented above, modern science approved these traditional uses. In this sense, one of the interesting reports was published about methyl syringate (Figure 8) asa Chemical marker of mono-floral honey in Italy.[167]

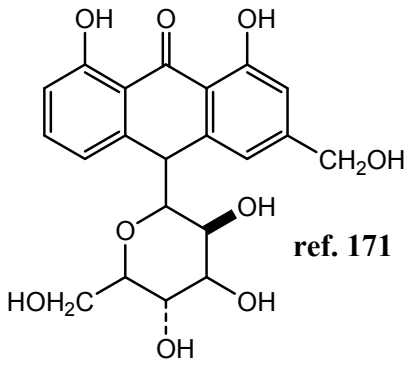


ref. 167

Figure 8 Methyl syringate found in*A. ramosus* and its mono-floral honey

But contrary to that, the fact that herbivores do not consume this plant is rather interesting. Moreover, reports indicated that it is even toxic to some livestock animals in the reviewed region. Strangely enough, a report of severe poisoning of sheep that consumed the tips of the plants leaves, occurred in Turkey.[168] Authors suspected that anthraquinone glycosides are responsible for this toxicity.The consumption of the plants by sheep in Turkey,is contradicting other report that was published in the same year from Greece, of the ability of this plant to "avoid grazing".[169]This study showed also that under stress of the Mediterranean basin conditions, the plant increases its ability as antifeedant.Ten years later, another study from Turkey confirmed the facts that sheep do not normally consume the plant, and in order to test its effect on the animals, a special experimental design was needed.[170] Seeds powder was mixed in small concentration with animals food, resulting in severe neurotoxicity after six months.[170]

To conclude the discussion about *A. ramosus*, we present the successful synthesis of 1,8-Dihydroxy-10-glycopyranosyl-9(10*H*)-anthracenones and testing their ^{13}C-NMR.[171] These compounds are analogues to natural products present in this plant, and one of these analogues is shown in Figure 9.



ref. 171

Figure 9 Synthetic analogue of natural products present in *Asphodelus ramosus*

Asphodelus tenuifolius is a real challenge for agriculture since it is a harmful weed, especially in Chickpea (*Cicer arietinum*). For this reason, many attempts of combating it were reported, including integrated approaches of using a combination of synthetic herbicides.[172]Despite this, four endophytic actinomycetes isolated from leaves of this plant, showed strong antibacterial activity, especially against *C. albicans*.[173] In addition, their ethyl acetate extracts had high antioxidant (DPPH) capacity.

Eremurus spectabilis was sufficiently studied so far (Table 6), but its chemicalcomposition is hardly known, and the only reported new natural product that was isolated from this plant, is a water-soluble polysaccharide (ref. 162, Figure 7). But there was relatively good interest in another type biologically active poly-fructose saccharides,[174] fructans, present in this plant. No publication reported the accurate composition of such fructan, but other related properties were investigated: fractionation byethanol: Box-Behnken design and principal component analysis,[175]effect of extraction method on the properties and quantities,[176]effect of drying methods on the physiochemical properties,[177] and improvement of whey protein isolate film using fructans from this plant.[178]

In addition to these fructans, isoorientin isolated from this plant, drew major attention, particularly for its anticancer activity. The mechanism of action of this compound was published.[179]

CONCLUSIONS AND FUTURE VISION

1. Plants of the *Xanthorrhoeaceae* family in the reviewed region were insufficiently studied and published.
2. The properties and the chemical compositions of some species are almost unknown.
3. The plants of this family possess interesting natural products, especially quinones.
4. The biological activities of these natural products were limitedly studied.
5. Analogues of these natural products were very limitedly prepared.
6. An extensive research is needed to reveal the medicinal and chemical properties of these plants, as well as to discover the biological activities of the unique natural products that these plants contain.

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