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Review Article

Eryngium creticum – ethnopharmacology, phytochemistry and pharmacological activity. A review

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ABSTRACT

Eryngium creticum Lam. (*E. cyaneum* Sibth. & Sm., *E. syriacum* Lam.), Saniculoideae, Apiaceae is of great importance in the traditional Greco – Arab medicine. This study was carried out in order to contribute to the ethnopharmacological knowledge of this medicinal species. This review describes the botanical characterization and distribution, as well as critically assesses the phytochemical properties and biological activities of *E. creticum*, a species that has been used in traditional medicine for many decades. Possible trends and perspectives for future research of this plant are discussed, as well. *E. creticum* has been found to contain several chemical constituents, mostly sesquiterpenes, monoterpenes, aldehydes, coumarins, sitosterols and sugars. Eryngo with its bioactive compounds possesses a wild range of biological activities. It was reported that in traditional medicine *E. creticum* was applied mainly as the remedy for snake and scorpion bites. Some published studies have shown a broad spectrum of biological and pharmacological activities, including anti-snake and anti-scorpion venom, as well as antibacterial, antifungal and antileishmanial effects. Other have indicated antihyperglycemic, hypoglycemic and antioxidant activities of this species. The *in vitro* studies and *in vivo* models have provided a simple bioscientific explanation for its various ethnopharmacological uses.

Introduction

To promote traditional medicine and herbal therapeutics, there should be provided the knowledge of plant bioactive compounds playing an important role in human healthcare and the scientific confirmation of their traditional use. *Eryngium creticum* Lam., Apiaceae is an example of a species that has remained a wild edible plant and it is known mostly to gatherers. This article provides an overview of *E. creticum*, a traditional herbal remedy used mostly for snake and scorpion bites: the distribution pattern and botanical description of the species, the status of ethnopharmacology, phytochemistry and the laboratory data on the bioactivity. The current status of literature on eryngo has been reviewed.

In brief, this review presents the results of the investigations on *E. creticum* that have been conducted so far and points out the gaps in knowledge, which disclosure is necessary to understand the mechanism of action of the extracts used in a traditional medicine. Also it indicates the necessity to conduct in-depth examination of the correlation between the pharmacological effect and the presence of the bioactive compounds responsible for the action. The review summarizes the phytochemical analysis and biological studies that may be helpful for researches to undertake further studies supporting the existing knowledge necessary to understand the action and may contribute to the discovery of new uses of this interesting species.

Botanical characteristics and distribution

Genus *Eryngium* L. comprises about 250 species and is distributed throughout temperate regions of every continent. The *Eryngium* species grow in Eurasia, North Africa, North and South America, and Australia. It is the most species-rich genus of the Apiaceae (Wolff, 1913; Wörz, 1999, 2004, 2005, 2006; Calvino et al., 2008; Wörz and Diekmann, 2010). Wolff (1913) grouped the species into 34 sections and numerous subsections. He also recognized two major informal groups: *Species gerontogeae* and *Species americanae and australiensis*, the former representing twelve sections from the Old World, and the latter 22 sections from the Americas and Australia. *E. creticum* with *E. planum* and *E. caeruleum* belongs to Plana section (Wolff, 1913). A new subgeneric classification of the genus was presented by Wörz (2005). It recognizes five subgenera. The classification was based on morphology and did

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not reflect phylogeny or solve problems of infrageneric relationships (Wörz, 2005). The other paper dealt with the Balkan species. The classification of the Balkan species of *Eryngium* was based on conventional morphological characteristics. The basal leaves provided the main characteristics. Specialization, the high rate of endemism, sectional diversity, and distribution patterns suggest relatively old age of most Balkan *Eryngium* species. The topographical and climatic diversity resulted in isolation and some ecological adaptations. Exceptions to the old age species are probably the 3 widespread species including *E. creticum* which are migratory. Within the Circum-Mediterranean Plana section, *E. creticum* is the only Balkan species. The closest relative is the Caucasian *E. caeruleum* (Wörz, 2006). The study carried out by Calvino et al. (2008), based on phylogenetic analyses of DNA sequences from three non-coding chloroplast DNA loci and the nuclear ribosomal DNA internal transcribed spacer region, was useful in corroborating the monophyly of *Eryngium*, dividing it into redefined and monophyletic subgenera (*E.* subgenus *Eryngium* and *E.* subgenus *Monocotyloidea*), and identifying clades that shared several morphological, biogeographical and/or ecological traits (Calvino et al., 2008).

E. creticum Lam. (*E. cyaneum* Sibth. & Sm., *E. syriacum* Lam., eryngo, flat holly, blue sea holly) was described by Jean-Baptiste Pierre Antoine de Monet de Lamarck in 1798. It is known by several local names, but the most recognizable are: Qors Aanneh used in Lebanon and Qarsa'na (Palestine). Eryngo is a species that belongs to Apiaceae family (Umbellifereae) and it can be found in the Eastern Mediterranean region, mostly in Lebanon, Palestine, Jordan and Syria. It grows at low altitudes, in sunny places. It is commonly found in fallow fields, roadsides, waste places, and, occasionally, even in the understory of olive groves. In Syria it was found in various environments, which indicates its adaptability and abiotic stress tolerance (Jawdat et al., 2010). The species is also found in the Alpine and sub-Alpine calcareous grasslands in the high mountains of northern and central Greece. The soils are usually deep and relatively rich in nutrients (Tutin et al., 1968; Wörz, 2006; Caballero et al., 2009).

The Hebrew name of *E. creticum* – Charchevina–Makchila, is based on the fact the plant grows in dry weather; the root name is H-R-V which means dry, while the second word means "turning blue". Despite its name, Charchevina is actually listed in the Mishnah, the 2nd C. AD books of Jewish practices, as one of the Passover bitter herbs (Passachim 2: 6).

E. creticum is a spiny perennial, or sometimes biennial or annual, glaucous and globrous herb, reaching up to 50 cm in height and it has erect branched stems. Stem leaves are sessile and palmately divided into 3–8 prickly lobes. Winter rosette leaves are quickly withering, bluish, long petioled, not prickly, entire to dentate, or lobed. Inflorescences are repeatedly forked; umbels of 0.7–1 cm, head-like, with an involucre of 5 long, blue, spiny bracts 2–5 times as long as the head, spreading, linear, boat-shaped, prickly at base or along the long margin. Fruits are scaly-bristly, obscurely ribbed (Konig and Sims, 1806; Don, 1831; Muschler, 1912; Tutin et al., 1968; Mayer-Chissick and Lev, 2014).

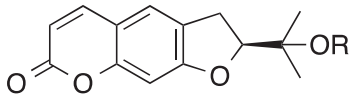
It is cultivated for use as a vegetable, mainly in salads. Its young leaves are eaten fresh and thick roots are eaten raw or cooked (Mayer-Chissick and Lev, 2014). An ethnobotanical survey of wild edible plants of Cyprus (Paphos vine zone and Larnaca mixed farming zone) revealed that young stems and leaves of eryngo preserved in vinegar were eaten as appetizers with several kinds of food (Della et al., 2006). The freshly harvested, simple leaves on long stalks of *E. creticum* and deeply lobed leaves of *E. glomeratum* are made into pickles by Greek Orthodox monasteries in Cyprus (Lardos, 2012). In Lebanon, eryngo is consumed mainly when freshly gathered and prepared mainly raw as a salad. Most information shows that the plant is appetizing and it is described as bitter in taste. According to an ethnobotanical survey of edible plants in northeast Lebanon, eryngo is consumed about three times a week (Jeambey et al., 2009).

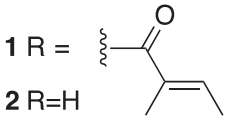
Phytochemistry

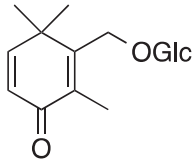
Unfortunately, the literature on phytochemistry of *E. creticum* is still scarce. There are some studies on the chemical composition of the essential oil. However, the knowledge about their non-volatile chemical constituents is limited.

The phytochemical screenings of aqueous, ethanolic, and methanolic extracts of *E. creticum* indicated the presence of different bioactive compounds, mainly sesquiterpenes, monoterpenes, aldehydes, coumarins, sitosterols, tannins, resins and sugars. On the other hand, screening for metal by means of spectroscopy showed that this plant contains metals such silver, zirconium, nickel, selenium, niobium and molybdenum, iron, calcium, manganese and copper (Al-Khalil, 1994; Ayoub et al., 2003; Celik et al., 2011; Farhan et al., 2012; Dammous et al., 2014; Dirani et al., 2014; Rammal et al., 2015; Erdem et al., 2015).

One of the first phytochemical investigations of the roots of *E. creticum*, which grows wildly in Jordan, led to the isolation and characterization of nine compounds: two coumarins – deltion (**1**) and marmesin (**2**), cyclic alcohol – quercitol, monoterpene glycoside 3-(β-D-glucopyranosyloxymethyl)-2,4,4-trimethyl-2,5-cyclohexadien-1-one (**3**), phloroglucinol glycoside (1-(β-D-glucopyranosyloxy-3-methoxy-5-hydroxy benzene)) (**4**), β-sitosterol and its glycoside (β-sitosterol-β-D-glucopyranose), and two sugars – mannitol and dulcitol (Al-Khalil, 1994).







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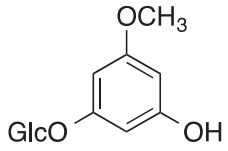

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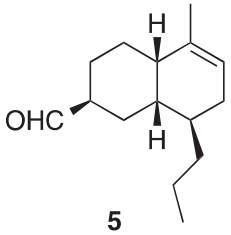
The unique 1-*n*-propyl-perhydronaphthaline 1,2,4a,5,6,7,8,8a-octahydro-4-methyl-1-propyl-naphthalene-7-carbaldehyde (eryng-9-en-15-al) (**5**), a compound which possesses an unusual sesquiterpene carbon skeleton, was isolated and identified, together with the new natural methyl ketone eicos-8,11-dien-18-ol-2-one (**6**), from the hexane: ether (1:1) extract of the aerial parts of *E. creticum* growing in Egypt. The structures of those compounds were established by conventional methods of analysis and confirmed by DEPT, COSY, HMQC and HMBC spectral analysis (Ayoub et al., 2003).



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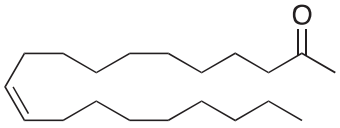

6