



Journal of Medicinal Herbs

journal homepage: www.jhd.iaushk.ac.ir



Dracocephalum kotschy Boiss.: An Iranian endemic medicinal plant; A review

Elham Foroozandeh, Hossein Ali Asadi-Gharneh*

Department of Horticulture, College of Agriculture, Isfahan (Khorasgan) Branch, Islamic Azad University, Isfahan, Iran;

*Email: h.asadi@khuif.ac.ir

ARTICLE INFO

Type: Review Article

Topic: Medicinal Plants

Received June 21th2020

Accepted October 05th2020

Key words:

- ✓ *Dracocephalum kotschy* Boiss.
- ✓ Biochemical compound
- ✓ Xanthomicrol
- ✓ Spinal-Z

ABSTRACT

Background & Aim: Iran with about 8000 plant species and 1728 endemic species; is one of the most important sources of medicinal plants. *Dracocephalum kotschy* Boiss, belonging to the Lamiaceae family, is one of the endemic plants in Iran. It grows in regions of Chaharmahal and Bakhtiari, Esfahan, Gorgan, Mazandaran, Hamedan, Kermanshah, Lorestan, Tehran, Fars and the northern heights of Semnan. In this review, the botany, traditional uses, phytochemical and pharmacological properties of *Dracocephalum kotschy* Boiss are discussed.

Experimental: In the current review keywords including *Dracocephalum kotschy* Boiss. and medicinal properties were searched in scientific websites such as PubMed, Science Direct and Google Scholar to compile the botanical and medicinal properties of *Dracocephalum kotschy* Boiss.

Results: According to the literature review, *Dracocephalum kotschy* Boiss. with high concentration of essential oil, flavonoids and other secondary metabolites is a valuable endemic plant. It has been shown immunomodulatory, anti-hyperlipidemic and anti-spasmodic activities and is effective in treatment of headaches, congestion, and liver disorders. In addition, anti-cancer properties of this plant are related to presence of xanthomicrol and Spinal-Z compounds in the leaves of this plant.

Recommended applications/ industries: *Dracocephalum kotschy* Boiss. with high amount of biochemical components and pharmacological effects can be used as a valuable herbal drugs. Its cultivation for industrial and pharmaceutical purposes can help to improve the production of anti-cancer drugs in Iran.

1. Introduction

The vast plateau of Iran is one of the special geographical units, which have different climates and environments. In this plateau, most of the distribution of plant communities belongs to Iran and among the rich flora of Iran, which includes more than 8000 plant species, there are a large number of medicinal plants. The use of many of these medicinal plants has a long history and in recent years, despite the presence of chemical and laboratory-synthesized drugs; Iranians prefer to use herbal medicines. Many of these medicinal plants have become endangered due to their

significant medicinal values, people's interest in using herbal medicines, excessive harvesting and lack of planning for cultivation (Omidbeigi, 2018).

Dracocephalum kotschy Boiss., belonging to the Lamiaceae family, is one of the endemic plants in Iran. *Dracocephalum* with 186 species is one of the most important genus of Lamiaceae family. Eight species of them are found in Iran and *D. kotschy* Boiss. is one of the valuable rare medicinal plant among them. The Zagros region (2000- 3200 m altitude) is the most well-known places of its growth, but it has a wide distribution in Iran. It is exposed to destruction due to

its medicinal value, heavy grazing and uncontrolled harvesting before flowering, and its density has decreased in its natural habitat (Fig. 1) (Rechinger, 1986).



Fig 1. *Dracocephalum kotschyi* Boiss. in natural habitat in Semrom region in Iran (Photo by Nasim Khansarifar, 2018)

It usually grows in the mountainous heights of Chaharmahal and Bakhtiari, Esfahan, Gorgan, Mazandaran, Hamedan, Kermanshah, Lorestan, Tehran (Alborz mountain), Fars (Dena mountain) and the northern heights of Semnan (Mozaffarian, 2008) (Fig. 2).



Fig 2. Distribution of *Dracocephalum kotschyi* Boiss. in Iran (<https://wwwnc.cdc.gov/travel/destinations/traveler/none/iran>).

It is known in different parts of Iran by the other names such as Zarringiah, Badrandjboie-dennaie, Palang-moshk, Faranj-moshk, Zarabi, Giahe-ahovan

(Mozaffarian, 2008) and is locally used as an aromatic vegetable for taste and scent of yogurt and foods (Moridi Farimani *et al.*, 2017).

2. Botany

Dracocephalum kotschyi Boiss. is a semi-woody plant with 23 to 33 cm length, perennial with numerous woody stems, oval-shaped leaves; white or yellowish-white flowers integrated in cycles located in stem bands in the form of terminal clusters that appear from early May to July. The seeds ripen gradually at the time of flowering (Mozaffarian, 2008). The results of phenological studies have shown that its leaves remain green at the base of the plant in winter. In spring, new stems and branches are formed after the increase of temperature. Flowering, which continues gradually in different regions, starts from May 20 to July. One week after flowering, the seeding stage begins and usually two seeds and sometimes 1, 3 and 4 healthy seeds are formed in each fruit.

Results of the root study have shown that the root of *Dracocephalum kotschyi* Boiss. is spread on the soil, the depth of rooting is about 10 to 20 cm and the average length of the roots is about 25 cm. The average diameter of its canopy is about 20.69 cm and because of the presence of green leaves at the bottom of the plant in the fall, it can play a good protective role to prevent soil erosion (Asaadi and Khoshnood-Yazdi, 2010). In recent years, due to the medicinal importance of this plant as well as its economic properties in the production of medicine and the need for scientific researches, it has been cultivated in farms and greenhouses (Fig. 3).



Fig 3. Cultivated *Dracocephalum kotschyi* Boiss. in greenhouse condition for research purposes (Photo by Mozhddeh Alimaleki, 2019 and Mostafa Shirmardi, 2020).

3. Ecological Requirement

Dracocephalum kotschyi Boiss. grows in high rock areas at an altitude of 2300 to 3000 meters above sea

level. It needs cool summers and high relative humidity. The needs for special microclimatic conditions such as highlands and rocks with high rainfall has led to the distribution in small and separate populations. Therefore, by modeling the microclimatic conditions and providing natural-like conditions, *Dracocephalum kotschyi* Boiss. could be adapted to cultivate. In addition, collecting different ecotypes of this plant can be used in plant breeding processes.

Meteorological and topographic data have shown that this plant requires highlands and rocks with moderate temperatures in summer, high relative humidity and rainfall between 400-600 mm (Asaadi and Khoshnood-Yazdi, 2010).

The vegetative growth of *Dracocephalum kotschyi* Boiss. has started from the end of March and reaches its maximum growth in April. Flowering stage begins in May with the appearance of single flowers on the plants. From mid-June to early July, the plant is in full bloom stage. In August, the seeds of this plant ripen and in September and before the rains, while the seeds are still ripening, the plant buds begin to grow. It is resistant to winter cold. In winter, the plant growth is slow and the reduced plant growth happens in the months of autumn to late March. Drought, overgrazing, uncontrolled and unprincipled harvesting by human, special climatic conditions of the habitat, steep habitat slope, shallow soil, irregular germination due to seed dormancy and poor plant establishment in the first year reduce population of *Dracocephalum kotschyi* Boiss. Also, uncontrolled harvesting of this plant during the flowering stage prevents seed production and as a result makes this plant a rare herbaceous one (Otroshy and Moradi, 2012)

4. Propagation and cultivation of *Dracocephalum kotschyi* Boiss.

Given the limited natural sources of medicinal plants, cultivation of medicinal plants and researches on appropriate environmental conditions in agricultural systems can help to produce plants with rich secondary metabolites. *Dracocephalum kotschyi* Boiss. is propagated by the seeds. According to the researches, the seeds of *Dracocephalum* genus, despite being healthy and mature, may not germinate due to their dormancy (Chang *et al.*, 2009; Hatami *et al.*, 2019). Despite the distribution of *Dracocephalum kotschyi* Boiss. in the western and central regions of Iran, this

plant has been introduced as endangered species because of hard seedcoat and irregular germination due to seed dormancy (Jalali and Jamzad, 1999). The seeds of wild species usually show more dormancy than the cultivated species, and this is one of the main problems in the widespread cultivation of medicinal plants (Kochaki and Sirmainea, 2000). In a study by Hatami *et al.* (2019), a significant increase in seed germination of *Dracocephalum kotschyi* Boiss. was reported from the interaction effect of mechanical scraping with sandpaper and the use of gibberellic acid. It is reported that the use of gibberellic acid alone has no significant effect on germination rate, which is probably due to the hard coat of the seeds and the high accumulation of mucilage that prevents the hormone absorption by the seeds (Hatami *et al.*, 2019).

In the cultivation of medicinal plants, in addition to trying to maintain and increase the secondary metabolites, it is necessary to pay attention to hygienic principles and minimal use of toxic industrial and chemical compounds. In the research by Mafakheri *et al.* (2018), 26 compounds were identified in the *Dracocephalum kotschyi* Boiss. essential oil and among them Limonene and Verbenone showed the highest accumulation. In greenhouse cultivation, the use of vermicompost in comparison with chemical fertilizer can significantly increase the essential oil content of *Dracocephalum kotschyi* Boiss. (Mafakheri *et al.*, 2018).

Different levels of drought stress affect the growth, physiological and biochemical traits of species of the Lamiaceae family (Karimi *et al.*, 2020) as well as the profile of the essential oil (Kulak, 2020), but little researches have been conducted on *Dracocephalum kotschyi* Boiss.. According to Kiani *et al.*, (2020) the chlorophyll content in the flowering stage is higher than the vegetative stage and drought stress reduces the amount of photosynthetic pigments in *Dracocephalum kotschyi* Boiss.. In general, it seems that it is more sensitive to drought stress during the flowering stage and *P5CS* gene expression and proline accumulation in the flowering stage, under drought stress, show a greater increase (Kiani *et al.*, 2020).

In production and processing of medicinal plants, the use of the maximum amount of secondary metabolites is intended for consumers of these plants. In this regard, Moradi *et al.*, (2019) analyzed the antioxidant, phenol and flavonoids contents of *Dracocephalum*

kotschy Boiss. in different ages (two, three, and six). Their research showed that the highest antioxidant activity, total phenol, and total flavonoids belonged to the flower of six age plants and the flowers are the mainly organs with the highest accumulation of these compound compared to leaves (Moradi *et al.*, 2019).

In general, in order to propagate this plant, in addition to eliminating seed dormancy in the first step, it is necessary to pay attention to fertilizer and plant nutrition, temperature and irrigation conditions and plant harvesting age to maintain and increase secondary metabolites in later steps.

5. Biochemical component and therapeutic properties

5.1. The components of essential oil

In recently decades, the therapeutic effects of essential oils of plants have been considered in many studies (Aziz *et al.*, 2018; Plant *et al.*, 2019; Zhang and Yao, 2019) and there are some studies focusing on the medicinal usages of Lamiaceae family essential oils. For example, it is reported that Peppermint (*Mentha × Piperita* L.) essential oil with high levels of menthol/menthone and its effective properties in neurotransmitters can beneficially modulate performance on demanding cognitive tasks and in healthy adults can attenuate the increase in mental fatigue associated with extended cognitive task performance (Kennedy *et al.*, 2018). The other studies are focused on the anti-diabetic and neuro-protective effects of essential oils derived from lavender flower, lemon myrtle, oregano, peppermint, sage, and rosemary leaves (Romero Rocamora *et al.*, 2020), anticonvulsant, anxiolytic, antioxidant, anti-inflammatory, and antimicrobial activities of lavender (*Lavandula angustifolia*) (Cardia *et al.*, 2018) and wound healing activity and antioxidant property of essential oil of *Lavandula aspic* L. (Ben Djemaa *et al.*, 2016). According to the studies on samples collected from different areas of Iran, *Dracocephalum kotschy* Boiss. has immunomodulatory, anti-hyperlipidemic and anti-spasmodic activities (Sadraei *et al.*, 2016; Sajjadi *et al.*, 1998; Amirghofran *et al.*, 2000) and is effective for headaches, congestion, and liver disorders (Zargari, 1995). It contains essential oils, flavonoids, monoterpene glycosides, tannins, phenolic acids, caffeic acid, chlorogenic acid and rosmarinic acid (Gohari *et al.* 2003; Monsef-Esfahani *et al.* 2007). The

structures of some main components of *Dracocephalum kotschy* Boiss. are presented in Fig 4.

Essential oils are one of the most important secondary metabolites with antioxidant properties and *Dracocephalum kotschy* Boiss. is one of the most valuable plants with essential oil of the Lamiaceae family. Its vegetative parts contain very fragrant yellow essential oil and its main components are limonene, geranial, Alpha-terpineol, verbenone and caryophyllene, limonene-10-al (Sadraei *et al.*, 2017). According to the previous studies, the major components in the essential oil of wild *Dracocephalum kotschy* Boiss. were limonene (29.1%), methyl geranate (17.7%), geranial (15.8%) and neral (11.9%) whereas in the oil of cultivated sample the main components were limonene (23.6%), geranial (14.3%) myrthenol (30.1%), and neral (9.3%) (Najafpour-Navaei and Mirza, 2007).

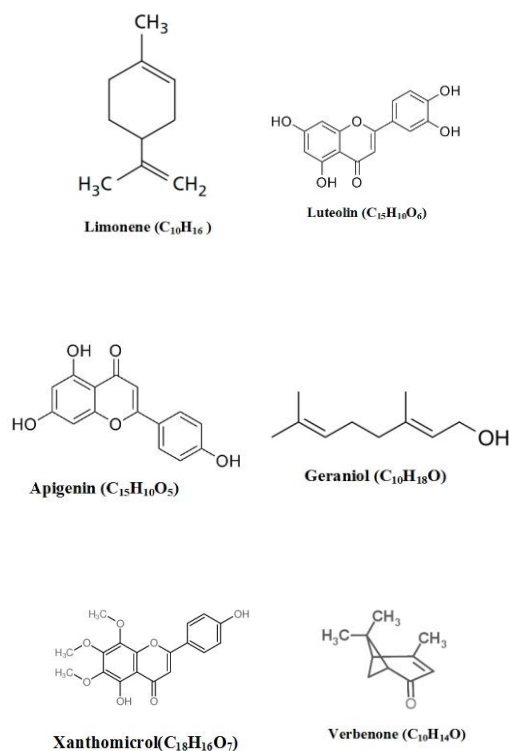


Fig. 4. The structures of some main components of *Dracocephalum kotschy* Boiss.

Limonene, as bitter substances in citrus fruit (Taiz and Zeiger, 2010), is known with its antitumor activities and its protective effect against many types of

cancer has been approved in many researches (Crowell, 1999; Mario *et al.*, 2009). Limonene, a natural colorless cyclic monoterpene and major component of the essential oil of *Dracocephalum kotschy* Boiss., is effective as an inhibitor of angiotensin-converting enzyme, anti-tumor, anti-virus, bactericidal, antispasmodic and cancer-preventing agent, expectorant and fungal growth inhibitor (Mukhtar *et al.*, 2018; Han *et al.*, 2019).

Geraniol, the other main compounds in the essential oil of *Dracocephalum kotschy* Boiss., inhibits the synthesis of polyamines in human cancer cells (Cho *et al.*, 2016; Lee *et al.*, 2016).

There are differences in the chemical composition of the essential oils depending on the ecological conditions of the region and the site, harvesting time, genetic, physiological factors and the chosen laboratory methods for extraction (Sadraei *et al.*, 2016; Nejad-Sadeghi *et al.*, 2015; Kamali *et al.*, 2014).

2. Phenolic substances

Free radical-scavenging activity of medicinal plant extracts and their mechanisms have been extensively studied (Gulcin *et al.*, 2006; Elbashir *et al.*, 2018; Sai *et al.*, 2019; Zhi Xiang *et al.*, 2020; Patle *et al.*, 2020). Flavonoids are phenolic substances with antioxidant activities due to their ability to reduce free radical formation and scavenge free radicals (Pietta, 2000; Guo *et al.*, 2020; Sammar *et al.*, 2019). In *Dracocephalum kotschy* Boiss. some flavonoids such as luteolin, apigenin, cirsimaritin, pendolitin, xanthomicrol and rosmarinic acid are found (Fattahi *et al.*, 2013).

According to the recently reports, luteolin modulates the expression of genes involved in stress response, and also in aging males dietary luteolin may be effective in leydig cell tumor chemoprevention (Couture *et al.*, 2020). According to Gadotti and Zamponi (2019), luteolin as a possible natural anxiolytic molecule without sedative effects, has therapeutic potential for the comorbidities involving peripheral inflammation, pain, mood and anxiety-related disorders. In an animal model the effectiveness of two flavones, luteolin and apigenin, in controlling blood cholesterol was examined and it was found that apigenin suppresses the biosynthesis of cholesterol, whereas luteolin promotes the elimination of cholesterol (Wong *et al.*, 2017). In animal models, the experimental findings approved that

apigenin treatment prevents cognitive deficit and reverses behavior impairments (Sharma *et al.*, 2020). Also the plants constituents including the flavones, apigenin, hispidulin and cirsimaritin; and the diterpenes 7-methoxyrosmanol may influence benzodiazepinereceptor activity in brain that may change cognitive functions (Kavvadias *et al.*, 2003), so it may be suggested that the secondary metabolites of *Dracocephalum kotschy* Boiss. may improve the cognitive functions.

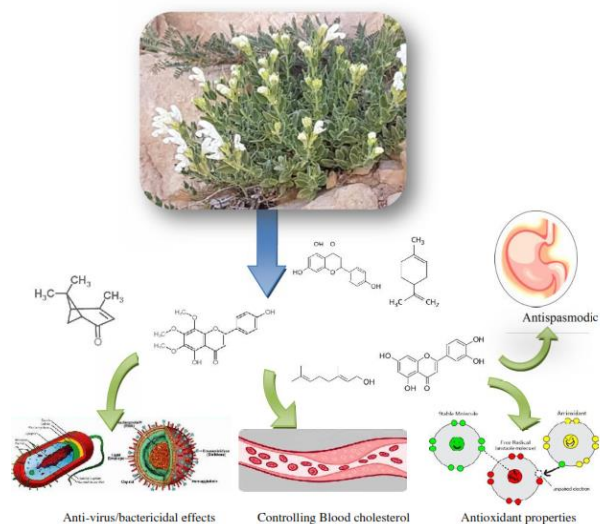


Fig. 5. Some of the therapeutic properties of *Dracocephalum kotschy* Boiss.

6. Herbal drugs of *Dracocephalum kotschy* Boiss.

Xanthomicrol is a compound in the leaves of *Dracocephalum kotschy* Boiss. and anti-cancer properties of this medicinal plant are related to this compound (Jahanian *et al.*, 2005; Fattahi *et al.*, 2014). Except xanthomicrol, methanolic compound from the dried seeds of *Peganum* (*Peganum harmala*) and the leaves of *Dracocephalum kotschy* Boiss. is available as oral capsules called Spinal-Z which has been used to treat various cancers. Spinal-Z has cytotoxic, anti-inflammatory, analgesic, anti-bacterial and anti-virus effects. In a study by Panahi *et al.*, (2018) the efficacy and safety of spinal-Z in patients with esophageal and stomach adenocarcinoma, and squamous cell carcinoma of the esophagus were examined. Spinal-Z therapy made significant differences in abdominal pain, heartburn, constipation and vomiting between experimental and control groups. The Spinal-Z capsule is a dried extract of harmala beans that has three

alkaloids (harman, harmine, harmaline) plus leaves of *Dracocephalum kotschyi* Boiss. that contain the flavonoid xanthomicrol. Xanthomicrol with anti-tumor properties, exerts its effect through inhibition of DNA isomerase (Panahi *et al.*, 2018).

7. Conclusion

In conclusion, *Dracocephalum kotschyi* Boiss. with high concentration of essential oil, flavonoids and other beneficial secondary metabolites is a valuable endemic plant in Iran. Its purposeful cultivation for industrial and pharmaceutical purposes can help to improve the production of anti-cancer drugs and therefore subvert its eventual elimination. Also, purposeful cultivation and its use as an additive to improve the taste and scent of tea, dairy and meat products can help to increase the physical health of people. It seems that considering the different types of medicinal compounds in *Dracocephalum kotschyi* Boiss., more researches need be conducted on its aromatic, edible and nutritional properties across Iran and around the worldwide.

8. Acknowledgement

The authors wish to thank Mrs. Nasim Khansari-far, Mozhdah Alimaleki and Mostafa Shirmardi for photos of *Dracocephalum kotschyi* Boiss.

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