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Review

Artemisia sieberi Besser essential oil and treatment of fungal infections

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ABSTRACT

A. sieberi essential oil has been used for treatment of hardly curable infectious ulcers in Middle East Medicine and has been famous due to its wormicide effects. In this review, we evaluated the potency of *A. sieberi* essential oil in treatment of fungal infections. We searched in PubMed Central, Science direct, Wiley, Springer, SID, and accessible books, reports, thesis. There is a lot of mixed information on chemical compositions of *A. sieberi* essential oil, but most articles reported α, β-thujones as the main components of essential oils. *In vitro* studies confirmed the antifungal activity of *A. sieberi* essential oil against saprophytes fungi, dermatophytes, *Malassezia* sp. and *Candid*a sp. and these results were confirmed in six clinical studies. The clinical studies confirmed the superiority of *A. sieberi* essential oil (5%) lotion in improvement of clinical signs of fungal superficial diseases, and mycological laboratory examinations of dermatophytosis and pityriasis versicolor diseases than clotrimazole (1%) topical treatment. The recurrence rate of superficial fungal infections with dermatophytosis and pityriasis versicolor was statistically lower in *A. sieberi* essential oil (5%) lotion than clotrimazole. There are no adverse effects due to the application of *A. sieberi* essential oil in clinical studies. Despite, the efficacy of *A. sieberi* essential oil against *Candida* sp., there is no clinical study about their related infections. Investigation about the effects of *A. sieberi* essential oil on fungal virulence factors in order to identifying the exact mechanism of antifungal activity and clinical trials on *Candida* related diseases are recommended.

Contents

1. Introduction

Artemisia L. (Compositae family) has 34 herbaceous annual or perennial species in Iran. *A. sieberi* is called as “Terekh”, “Youshan”, or “Dermaneh” in Iran. *A. herba alba* Asso var. *laxiflora* Boiss; *A. sogdiana* Bunge; *A. oliveriana* J. Gay ex DC. are the synonyms of *A. sieberi* Besser [1].

A. sieberi is a famous medicinal plant in Middle East traditional medicine as an anthelmintic. In external use, the flowering shoots and leaves was boiled in normal saline and the extracted solution was used for treatment of gangrenous ulcers, infectious ulcers and inflammations [2]. *A. sieberi* is used for sheep as a feed and it is believed that if the sheep eat *A. sieberi*, it will get weight and meat. It was used as carminative, relieves the inflammation and

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abscesses and prevent leprosy [3]. The beneficial effects of *A. sieberi* essential oil on skin development [4,5], antimicrobial [6], insecticidal [7], nematocidal [8], anti-malaria [9] and anti-coccidiosis effects [10] were the subject of many studies. *A. sieberi* is used as feed supplement [11] and for treatment of diabetes [6] as its traditional believes.

Although, investigations on the biological activity of *A. sieberi* has been the subject of many studies [12–14], but the important application of *A. sieberi* in treatment of fungal diseases was not the subject of any review study. In this review, we evaluated the potency of *A. sieberi* in treatment of superficial fungal infections.

2. *A. sieberi* in traditional medicine

Shih in traditional medicine is used for different species of *Artemisia* and the same properties are attributed to these species. In India, Shih is known as the strongest intestinal anthelmintic and is effective against *Ascaris lumbricoides*. Shih is used for treatment of diabetes and it reduces the urine glucose. The temper of Shih is hot and dry. The traditional practitioners believed, shih removed the gases and killed the long worms and *Ascaris lumbricoides*. For removing the worm from belly, the traditional practitioners prescribed Shih with a purgative compound such as Senna (*Cassia fistula* L.). Shih was useful for difficulty breathing, hiccup, cramps and pain. Its poultice was applicable for scorpion poison and cold toxins. The oral dose for poisoning was 12 g and for other ailments was 8 g. Shih was harmful for stomach and nerve and believed to bring headache, therefore, it should be eaten with mastic and lupine. The poultice from Shih ash and olive oil (or lily oil) prohibited from hair loss and enhanced the hair growth. There are three different prescriptions (powder, decoction and syrup) for killing the worms. For preparing the powder formula, the cleaned closed buds of Shih were dried at 25 °C and were beaten to give a fine powder. 3–4 g of this powder was mixed with milk and used in the morning before breakfast.

Decoction was prepared by 10 g of powdered Shih in 500 ml boiling water. The syrup for removing the worm was prepared by 5 g senna, 5 g rhubarb, 5 g Shih, 5 g *Artemisia maritima* (sager), and 5 g *Artemisia ponticain* in boiling water. Then, the decoction was filtered and 250 g of it was mixed with 475 g sugar. A daily prescription of this combination is one spoon. Therefore, *Artemisia* sp. can be a good candidate for killing the intestinal worms.

Furthermore, *A. sieberi* was used for treatment of hard curable infectious ulcers; it can be a good medicinal plant for treatment of contagious fungal infections in human and animals. For this purpose, we concentrate our surveys on *A. sieberi* essential oil and before everything; we studied the chemical composition of its essential oil.

3. Chemical composition of *A. sieberi* essential oil

Although, flavonoids (flavones, luteolin, apigenin), sesquiterpene lactones (Artemisin), cyclic sesquiterpens, bicyclic monoterpene glycosides, and sesquiterpene are found in *A. sieberi* plant [15–17], but the main part of *A. sieberi* is its essential oil.

The chemical composition of *A. sieberi* essential oil was the subject of different studies (Table 1).

According to the results of articles, the yields of essential oil extraction varied from 0.2-3% w/w. The chemical composition of *A. sieberi* essential oil showed different chemical profiles in different studies. Large studies on chemical composition of *A. sieberi* were performed in Iran. 10 studies reported the chemical composition of *A. sieberi* essential oil from different parts of Iran. β-thujone (19.8%), α-thujone (19.6%), and camphor (19.6%), were reported as the main components of *A. sieberi* aerial part essential oil at full flowering stage from northeastern of Iran (Southern part of Khorasan Province, Iran) [18]. The chemical composition of *A. sieberi* essential oil from this study was the same with the *A. sieberi* aerial part essential oil from Kashan city (central of Iran) with the main components of α- thujone (32.9%), β-thujone (13.3%), camphor (22.9%) [19,20] and Qom province (central part of Iran) with β-thujone (23%), camphor (19.5%) and α-thujone (15%) [21]. Although, the percent amounts of each component varied from one city to other city, but three main components are the same. Camphor (54.7%), camphene (11.8%) and 1,8-cineol (9.9%) were the main components of *A. sieberi* essential oil from southern part of Tehran, Iran. Although, β-thujone (5.7%) and α-pinene (2.5%) were found in this essential oil but they were not as the main components of essential oil [22].

Chrysanthenone (29.50%), camphor (19.80%), and 1,8-Cineol (14.50%) were the main components of *A. sieberi* aerial parts essential oil at full flowering stage from Karaj region, Iran [23]. Artemisine ketone (48.5%), 1,8-cineole (19.7%) were found in *A. sieberi* aerial parts essential oil at full flowering stage from north of Iran (Gorgan Province, Iran) [24]. Camphor (49.3%), 1,8-cineole (11.1%), bornyl acetate (5.8%) and neryl acetate (4.3%) were the main components of *A. sieberi* essential oil from Semnan-Damghan province, Iran [25].

1,8-cineol (0–48.7%), santolina alcohol (0–40.8%), α-thujone (0–2.6%), β-thujone (0–4.6%) and camphor (32.4-33.7%) were the main components of *A. sieberi* essential oil from south parts of Iran (Fars provine, Iran) [26], while santolina alcohol (40.8%), camphor (32.4%) and β-thujone (4.6%) were the components of *A. sieberi* essential oil gathering from Fars province in January [27].

β-thujone (25.1%), α-thujone (22.9%), 1,8-cineole (20.1%), and camphor (10.5%) was found in the full flowered *A. sieberi* aerial parts essential oil from Buseirah, South Jordan [28].

Camphene (4.7–13.4%), α-thujone (33.5–51.5%), β-thujone (5.7–6.9%), and camphor (32.3–42.9%) were the main components of *A. sieberi* essential oils from France [26,27].

Chrysanthenone (47.0%), camphor (24.0%), verbenone (7.2%), tridecane (3.3%), and borneol (2.7%) were found in Moroccan *A. sieberi* aerial parts essential oil at pre-flowering stage [29].

β-thujone (17.4–58.4%), α-thujone (7.2–44.4%), 1,8-cineole (5.6–17.1%), and camphor (4.1–11.3%), followed by chrysanthenone (2.5–7.2%) were the main components of *A. sieberi* essential oil from Tunisia [30].

1,8-cineole (3–9.8%), β-thujone (1.9–7.8%), α-thujone (6.9–28.1%), camphor (17.3–33.1%), and chrysanthenone (3.9–19%) were reported from Algerian *A. sieberi* essential oil [31].

The effects of harvesting time on chemical composition of *A. sieberi* essential oil were evaluated. For this purpose, *A. sieberi* aerial parts were gathered from Abuzeidabad country (Kashan, Iran) in different month (January, February, October, December) and the main components of essential oils were determined. The yield of essential oil extraction was higher in January, February (about 1.4%) than that of October, and December (0.5% w/w). α-thujone (52.3–62.1%),

β-thujone (10–11.1%), camphor (9.9–12.2%), and borneol (5.3–8.6%) were the main components of *A. sieberi* essential oils from January, February. 1,8-cineol (40.8%), camphor (33.7%), and

β-thujone (5.8%) were the main components of *A. sieberi* essential oil from October samples, while α-thujone (53.5%), borneol (12.8%), β-thujone (11.6%) were the main components of December samples [27].

The subjected organ for extracting of essential oil can affect on the chemical composition of essential oil.

α-pinene (34.3%), δ-cadinene (4.2%), β-pinene (3.9%), thymol (2.9%), and myrtenal (2.9%) were the main components of *A. sieberi* leaves and stems essential oil from Karkas Mountains, Kashan, Iran, while α-pinene (12.3%), α-amorphene (15.9%), thymol (7.3%), δ-cadinene (5.7%), and β-caryophyllene (4.9%) were identified in