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Review article

Persian Asafoetida vs. Sagapenum: Challenges and Opportunities

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Abstract

Asafoetida and sagapenum as valuable Iranian oleo-gum-resins from *Ferula* spp. (*F. assa-foetida*, *F. persica*, *F. foetida* and *F. alliacea*) have received interest during the history for producing valuable perfumes and common spices or as pharmaceutical agents. The aim of the present work was to characterize sources of asafoetida and sagapenum, according to botanical aspects, traditional and conventional medicine and phytochemical data. Available publications have been gathered from databases up to May 2019, and common Persian literatures were reviewed. We showed that sources for asafoetida and sagapenum should be differentiated botanically according to basal leaves, size of rays, fruits and petals. Furthermore, despite similarities, volatile sulfur components in *F. assa-foetida* are disulphides, in *F. persica* tri/tetra/pentasulphides, and in *F. alliacea* trisulphides. In the case of coumarins, conferol, conferone, farnesiferol A and B, samarcandin and samarcandin acetate are so far reported from *F. assa-foetida* and *F. persica*, and asacoumarin A from *F. assa-foetida* and *F. foetida* samples; while, persicaosides A-D have been reported only from *F. persica*. Moreover, farnesilferol C as the major coumarin in *F. assa-foetida* and mogoltavidin in *F. persica* would be new pharmacopeial markers. However, coumarins and essential oils similarities and differences among *Ferula* species should be more studied in a comparative research. Such studies would be essential for determining reliable sources and minimum requirements for standardizations of worldwide valuable wild growing medicinal and economical plants.

Keywords: asafoetida; *Ferula alliacea; Ferula assa-foetida; Ferula foetida; Ferula persica*

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Introduction

Ferula genus (Apiaceae) is one of the most economically and botanically important genera in Iran. This genus possesses about 170 species globally, comprising more than 30 species in Iran out of which 16 are endemic. Three main economically valuable products from *Ferula* genus are asafoetida ("Anghouzeh" in Persian), sagapenum ("Sakbinaj" in Persian) and galbanum

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(‘Barijeh” in Persian). Antitumor, cancer chemopreventive, antidiabetic and antileishmanial activities have been reported in the literature [1,2]. In traditional medicine of different nations, these are reported as anticonvulsant, anti-swelling, anti-spasm and expectorant agents. Asafoetida has been specially used as a flavoring agent, condiment, as a fixative in perfume industries and as a medicinal herb [1].

Iran as a major producer of Asafoetida [3], officially exports *ca* 200000 kg annually (table 1). Asafoetida is being exported to different countries such as India, UAE, Afghanistan, China, Vietnam, France, Austria, Tunisia, Hong Kong and Jordan [4].

Table 1. Export level of asafoetida from Iran (2016-2019) [4]

Year	Quantity (kg)	Value (US$)
2016	272,889	4,035,865
2017	204,953	3,752,679
2018	172,590	3,701,447
2019 (First trimester)	41,287	1,198,299

There are many forms of asafoetida and sagapenum oleo-gum-resin available in the market including pure tears, mass forms, sweet or bitter forms probably depending on purity or being mixed with related species, adulterations or external impurities. Pharmaceutical standardization of this product has many challenges, since the oleo-gum-resin doesn’t have any specific microscopic organs for identification and also botanically identification of *Ferula* species are still challenging [5].

In the traditional and official markets two types of oleo-gum-resin called as asafoetida and sagapenum, are available. These products which are available as bitter or sweet forms are collected from various and not well botanically and phytochemicaly recognized sources [6]. The main resources for such related products in Iran are *F. assa-foetida*, *F. persica*, *F. foetida* and *F. alliacea* [6,7]. The aim of this work was characterizing and discussing challenges on common Iranian *Ferula* spp., sources for producing asafoetida and sagapenum according to botanical characteristics, traditional medicine, pharmacological, therapeutical and phytochemical data.

Methods

Available publications were gathered from databases such as PubMed (*F. assa-foetida* and *F. foetida* (69 publications), *F. persica* (11 publications), *F. alliacea* (3 publications)), Scopus (*F. assa-foetida* and *F. foetida* (74 publications), *F. persica* (26 publications), *F. alliacea* (1 publication), , Web of Science (*F. assa-foetida* and *F. foetida* (51 publications), *F. persica* (17 publications), *F. alliacea* (1 publication), ScienceDirect (*F. assa-foetida* and *F. foetida* (119 publications), *F. persica* (5 publications), and SID (*F. assa-foetida* and *F. foetida* (60 publications), *F. persica* (13 publications), *F. alliacea* (3 publications) up to December 2019 with *F. assa-foetida*, *F. persica*, *F. foetida* and *F. alliacea*, coumarin, and essential oil and related keywords. Publications on biological or pharmacological effects as well as those on identification of coumarins or essential oils were selected for this study.

For traditional literatures, manuscripts were studied with terms of “Anghouzeh” and “Heltit” (traditional names for “asafoetida” oleo-gum-resin), “Sakbinaj” (traditional name for sagapenum), and “Anjedan” (traditional name for herbal source of asafoetida) [8-13].

Results and Discussion

To the best of our findings, common sources for Persian Asafoetida and Sagapenum are *F. assa-foetida*, *F. persica*, *F. foetida* and *F. alliacea.*

Ferula assa-foetida L.

Botany

Ferula assa-foetida, the well-known source for collecting asafoetida exudates, is an indigenous species to Iran (center and south) and Afghanistan. The botanical description of *F. assa-foetida* is indicated in (table 2) [14]. This species is often growing in mountainous foothills and cliffs and oleo-gum-resin is excreted from dissected roots [14]. Collection of asafoetida is performed by cutting of the rootstock and pulling out brush-like mass. After 2-3 days, a slightly deeper cut is made and the mass is collected for 10-30 cycles. Tears form is produced at the first harvest and mass form in subsequent blades [3].

Traditional medicine

Asafoetida has been traditionally called “Heltit” in Persian medical and pharmaceutical manuscripts [8].

Table 2. Botanical differentiation of common Persian *Ferula* spp. as sources for asafoetida or sagapenum [14]

Species	Height (up to)	Basal leaves	Ray/umbel	Petal	Fruit
Ferula assa-foetida	2 m	2-Ternate-pinatisect, grow up to 35 cm; segments pinnate-lobate	17–25	Yellow	Glabrous
F. persica	1.5 m	3-4 Pinnate, grow up to 35 cm; segments lobate	17–25	Yellow	Glabrous
F. foetida	1.5 m	Large, bipinnate, pubescent, grow up to 40 cm; segments oblong, entire	14–35	White To Creamy	Pubescent
F. alliacea	1.2 m	3-Pinnate, grow up to 45 cm; segments oblong-ovate or linear-cuneate	30–35	Yellow	Glabrous

It has also been called "Angezad", "Angoshtgande" [8], "Angojhad", "Angedanjhad" (names for oleo-gum-resin) [9], "Anjodan", "Shajarat al-Heltit", "Majrooth", "Oshtorghar", "Zanjabeel al-Ajam", Persian "Zanjabeel" [10] (names for plant's source). "Heltit" has two types: a high grade called as "Tayeb" (odoriferous) which is extracted from white "Anjedan" ("Kool-e par"), and an inferior grade called "Mantan" (malodorous) which is collected from black "Anjedan" ("Komat") growing in Harat. The desirable type is described as clear, red color sharp smell and making milk-like liquid in water. The undesirable type possesses green color, Chives like smell and unfavorable taste. For adulteration, "Sakbinaj" and bean flour are added [8]. Temperament is reported as hot in 4th degree and dry in 3rd degree ("Mantan") and 2nd degree ("Tayeb") [8]. "Tayeb" type of "Heltit" is produced in Iran, Libya and Levant. Unpleasent smell of asafoetida can be masked by the essence of bitter almond [11]. It has been used for hoarseness, throat harshness, toothache and neurological disorders that are caused by cold nature like: paralysis, tremor, epilepsy, insensibility, tension, infantile convulsion and hysteria. It is also reported to be useful for flatulent gripes, colic, hemorrhoid, body weakness and as a carminative [8,11]. Comparative traditional pharmaceutical effects and respective dosage forms have been presented in table 3 [8,11].

Biological, pharmacological and therapeutical activities

The major biological and pharmacological activities reported for *F. assa-foetida* include anti-diabetic, anti-fertility, antifungal, antiobesity, antispasmodic, antitumor, antiviral, antiulcerogenic, cancer chemopreventive, digestive enzyme inhibitor, hepatoprotective, antihypotensive, memory enhancing, molluscicidal, and neuroprotective properties [1,3,15]. In phytotherapy, asafoetida is included as an analgesic, expectorant, diuretic, antispasmodic and vermifuge agent that has been used for treating various diseases including whooping cough, asthma, bronchitis, gastrointestinal disorders, intestinal parasites, diabetes, viral infections and various neurological conditions [6,7].

Table 3. Traditional pharmaceutical effects of "Heltit" and "Sakbinaj" [8,11,13]

	Indications/Uses	Preparation
"Heltit"	Toothache	With honey
	Otitis	With olive oil
	Miscarriage	Incense and vaginal
	Corns and warts	Cerate
	Alopecia	Plaster
"Sakbinaj"	Dislocating foreign objects	Plaster form with vinegar
	Back pain	With flaxseed
	Dry eyes	Ophthalmic ointment

Phytochemistry

Asafoetida oleo-gum-resin consists of three main parts including resin (40-60%), gum (25%) and essential oil (4-20%) [1,3]. The volatile fraction contains sulfur-containing compounds, mostly disulfide form, monoterpenes and related terpenoids. In different studies on root and oleo-gum-resin essential oils of *F. assa-foetida*, three major compounds including *sec*-butyl-(E,Z)-propenyl disulphide, 1-(methylthio) propyl 1-propenyl disulfide and di-and 2-butyl-3-methylthioallyl disulphide (both as mixtures of diastereomers) have been detected [1,3]. Other major components have been reported as 10-*epi*-γ- eudesmol, α-pinene, β-pinene, (*Z*)-β-ocimene and undecyl sulfonyl acetic acid.

For instance, volatile analysis of a sample from Lar area, Fars province (main gathering region for "Anghouzeh" during the history up to present) is shown in table 4 [16]. The major ingredients are Bis (1- methyl thio) propyl disulfide (29.68%), propenyl sec-butyl disulfide ((Z)-1-) (19.34%) and Propenyl sec-butyl disulfide ((E)-1-) (15.73%) (table 4, figure 1).

Table 4. Common volatile ingredients from Persian *Ferula* spp. as sources for asafoetida and sagapenum

***Ferula assa-foetida* [16]**	**%**	***Ferula persica* [17]**	**%**	***Ferula alliacea* [18]**	**%**
Bis (1-methyl propyl disulfide)	0.10	Aristolene	1.0	Agarofuran (α-)	1.2
Bis (1- methyl thio) propyl disulfide	**29.68**	Barbatene (α-)	3.1	Butenyl-sec-butyl trisulphide (sec-)	0.1
Cadina- 1(6), 4-diene	0.32	Bornyl acetate (exo-)	1.2	Butyl disulphide (di-sec-)	0.1
Dihydroagarofuran (4-epi-cis-)	3.11	Butyl methyl trisulphide	1.1	Eremoligenol	2.0
Dihydroagarofuran (α-)	0.57	Copaene (α-)	1.0	Eudesmol (α-)	3.6
Eremoligenol	0.58	Decadienal ((*E,Z*)-2,4-)	1.3	Eudesmol (5-epi-7-epi-α-)	4.7
Eudesmol (5-epi-7-epi-γ-)	0.34	Decanoic acid	1.0	Eudesmol (7-epi-α-)	2.4
Eudesmol (10-epi-γ-)	3.99	Dimethyl pentasulphide	1.2	Eudesmol (10-epi-γ-)	**22.3**
Guaiol	0.74	Dimethyl tetrasulphide	**7.6**	Farnesal (2Z-6Z)	2.3
Humulene (α-)	0.86	Dimethyl trisulphide	**18.2**	Farnesyl acetate (2Z–6Z)	1.8
Myrcene	0.37	Elemicin	1.8	Guaiol	7.3
Ocimene (E- β-)	1.27	Funebrene (β-)	1.4	Hinesol	**8.3**
Ocimene (Z- β-)	6.09	Lavandulyl acetate	1.7	Hinesol acetate	1.4
Pinene (α-)	8.15	Lavandulyl 2-methyl butanoate	3.7	Methyl-1-(methylthio) propyl disulphide	0.1
Pinene (β-)	1.33	Methyl 1-(methylthio)propyl disulphide	0.5	Propenyl-1-(methylthio) propyl disulphide (Z-)	1.0
Propenyl sec-butyl disulfide ((E)-1-)	**15.73**	Myristicin	**8.9**	Propenyl-propyl trisulphide (E-)	0.3
Propenyl sec-butyl disulfide ((Z)-1-)	**19.34**	Nonanoic acid	1.0	Propenyl-propyl trisulphide (Z-)	0.3
Propyl sec-butyl disulfide	0.54	Terpinyl acetate	1.8		
Selinene (α-)	0.58	Terpinylisopentanoate (α-)	3.5	Propenyl-sec-butyl disulphide (E-1-)	1.9
Valerianol	0.97	Terpinyl*n*-pentanoate (α-)	5.8	Propenyl-sec-butyl disulphide (Z-1-)	2.2
				Propenyl-sec-butyl trisulphide (E-)	2.7
				Propenyl-sec-butyl trisulphide (Z-)	6.5
				Valerianol	**12.5**

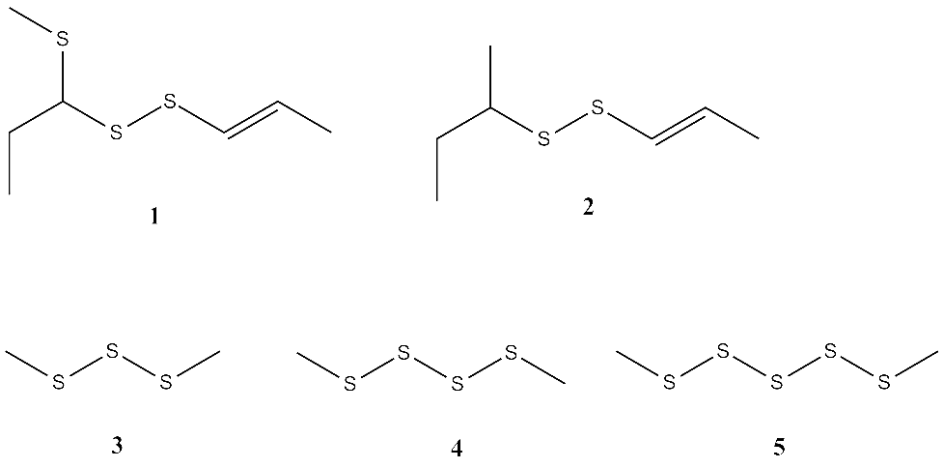

Figure 1. Chemical structure of major sulfur constituents from Persian *Ferula* spp. as sources for asafoetida and sagapenum. 1: bis (1- methyl thio) propyl disulfide; 2: propenyl sec-butyl disulfide; 3: dimethyl trisulphide; 4: dimethyl tetrasulphide; 5: dimethyl pentasulphide

The gum part mainly includes glucose, galactose, L-arabinose, rhamnose, glucuronic acid, polysaccharides and glycoproteins. The resin fraction contains ferulic acid and related esters (60%), coumarins, sesquiterpene coumarins (table 5) and various terpenoids [1,5]. Sesquiterpene coumarins are included as acyclic sesquiterpene substituent, monocyclic sesquiterpene substituent, and bicyclic sesquiterpene substituent (figure 2). In our previous study, we found Farnesiferol C as the major compound in an extract of *F. assa-foetida* roots from Lar [19].

Table 5. Coumarins and sesquiterpene coumarins of common Persian *Ferula* spp. as sources for asafoetida and sagapenum

Ferula assa-foetida	**Ref.**	***Ferula persica***	**Ref.**	***Ferula foetida***	**Ref.**
Asacoumarin A	[20]	Badrakemone	[21]	Asacoumarin A	[22]
Asacoumarin B	[20]	Conferone	[23]	Colladonin	[22]
Assafoetidin	[24]	Conferol	[23]	Conferdione	[22]
Assafoetidinol A	[25]	Farnesiferol A	[26]	Karatavicinol	[22]
Assafoetidinol B	[1]	Farnesiferol B	[21]	8-acetoxy-5-hydroxyumbelliprenin	[22]
Badrakemin	[25]	Farnesiferone A	[21]		
Conferdione (*epi*-)	[1]	Ferulone C	[27]		
Conferol	[1]	Gummosin	[21]		
Conferone	[28]	Persicaosides A	[29]		
Farnesiferol A	[30]	Persicaosides B	[29]		
Farnesiferol B	[30]	Persicaosides C	[29]		
Farnesiferol C	[30]	Persicaosides D	[29]		
Ferocaulicin	[24]	Samarcandin	[23]		
Feselol	[28]	Samarcandin acetate	[23]		
Foetidine	[31]	Umbelliferone	[27]		
Galbanic acid	[32]	Umbelliprenin	[2]		
Gummosin	[25]				
Isosamarcandin	[28]				
Kamolonol	[1]				
Lehmferin	[1]				
Ligupersin A	[33]				
Methyl galbanate	[34]				
Microlobin	[34]				
Neveskone	[25]				
Polyanthinin	[25]				
Samarcandin	[25]				
Samarcandin acetate	[1]				
Saradaferin	[35]				
Tadshiferin	[34]				
Umbelliferone	[36]				
Umbelliprenin	[36]				
8-acetoxy-5-hydroxyumbelliprenin	[36]				
5-hydroxyumbelliprenin	[36]				
8-hydroxyumbelliprenin	[36]				
10-R-acetoxy-11-hydroxyumbelliprenin	[36]				

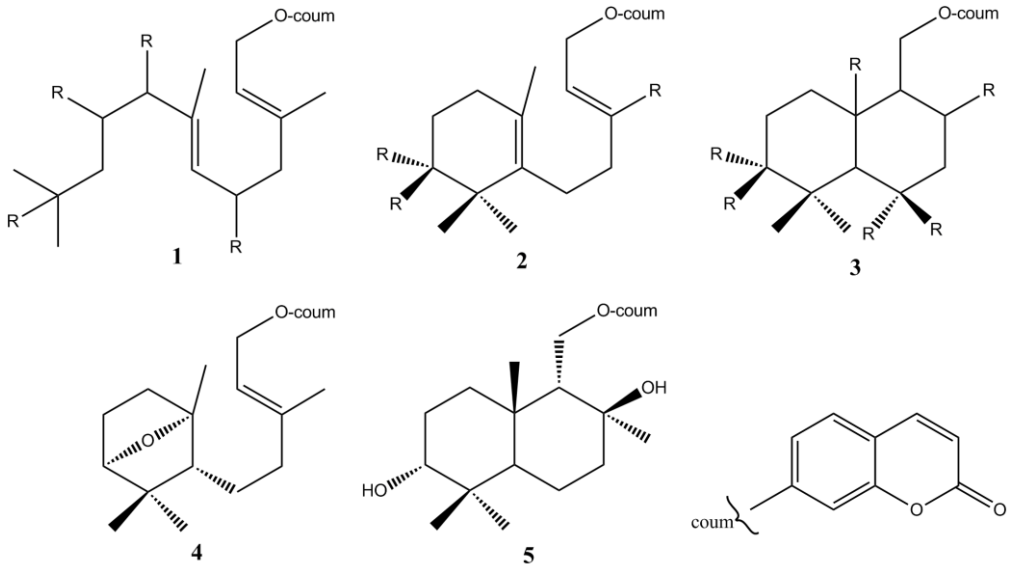

Figure 2. Chemical structure of some sesquiterpene coumarins from Persian *Ferula* spp. as sources for asafoetida and sagapenum. Coum: Coumarin moiety; 1: acyclic sesquiterpene substituent; 2: monocyclic sesquiterpene substituent; 3: bicyclic sesquiterpene substituent; 4: farnesiferol c; 5: mogoltavidin

***Ferula persica* Willd.**

Botany

Ferula persica is an endemic plant in Iran (north and center) growing up to 1.5 m height. The botanical description of *F. persica* has been presented in (table 2) [14].

Traditional medicine

Sagapenum has been traditionally called "Sakbinaj" in Persian medical and pharmaceutical manuscripts [8]. It is also reported as "Sakbineh", "Saghaphioon" [8], "Saghbin", "Gandeangojad", "Saghabinoon" [9], "Saghaphenoon" [10] and "Askbineh" [11]. The best type is reported as clear type without external materials. It has red or yellow appearance with white inside [8] and a smell like "Anjedan" gum or "Ghanne" and hot and bitter taste. Pure "Sakbinaj" is miscible with water. The gum is obtained by grooving the stem near the leaves [9]. Temperament is warm and dry in 3rd degree [8]. It has been used as mucolytic, alleviator of joint and gout pains, wormicide, diuretic, emmenagogue, antiepileptic, antiparalytic, antiurolithiasis, carminative, anti-hemorrhoid and as an aphrodisiac [8,13]. It is miscible with almond oil, Chives's water and rue's oil. Sagapenum can be replaced in therapy by galbanum ("Qinnah") or colophene ("Ratianj") [8]. Traditional pharmaceutical properties of "Heltit" and "Sakbinaj" have been described at table 3.

Biological, pharmacological and therapeutical activities

Biological and pharmacological activities reported so far are cytotoxicity, antibacterial, anti-fungal, anti-leishmanial, cancer chemopreventive, reversal of multi-drug resistance for enhancement of doxorubicin cytotoxicity in MCF-7/Adr cells, anti-inflammatory, lipoxygenase inhibitory activity, hypertensive effects and modulatory effect in morphin induce tolerance [2,37]. *Ferula persica* oleo-gum-resin is used as laxative, carminative, anti-hysteric, and for the treatment of diabetes and rheumatism [6,7].

Phytochemistry

The oleo-gum-resin which is known as sagapenum, consists of resin (50-60%), gum (23-30%) and essential oil (3-11%) [2]. In a study on the root essential oil of *F. persica* from Iran, sulfur compounds (28.6 %), oxygenated monoterpenes (23.2%) and sesquiterpene hydrocarbons (11.1%) were reported as the major groups of compounds in the root oil. The major components have been dimethyl trisulfide (18.2 %), myristicin (8.9 %), dimethyl tetrasulfide (7.6 %), α-terpinyl*n*-pentanonate (5.8 %), lavandulyl 2-methyl butanoate (3.7 %), α-terpinylisopentanonate (3.5 %) and α-barbatene (3.1%) (table 4, figure 1) [17]. Also, two new sulfur containing derivatives, *t*-butyl 3-[(1-methylpropyl) dithio]-2-propenyl malonate, *t*-butyl 3-[(1-methylthiopropyl) thio]-2-propenyl malonate were isolated from root methanol extract [38]. Sesquiterpene coumarins are included as acyclic sesquiterpene, monocyclic sesquiterpene, and bicyclic sesquiterpene substituents (table 5, figure 2). In our previous research, mogoltavidin was isolated from a dichloromethane extract of *F. persica* roots (Yasouj, Iran) as the major component [19].

***Ferula foetida* (Bunge) Regal**

Botany

Ferula foetida like other *Ferula* species is growing in deserts, particularly in central Asia, Iran (northeast, center and south east), Pakistan and Afghanistan. The botanical description of *F. foetida* is indicated in table 2 [14].

Traditional medicine

The botanical description of "Heltit" in traditional texts is equal to *F. assa-foetida*; however, in traditional manuscripts it is indicated that asafoetida gum is collected from *F. assa-foetida* allied plants, too. Therefore, the traditional description for "Heltit" (refer to Heltit traditional description [8,9]) can be developed to *F. foetida* as a traditional source for asafoetida gum [39].

Biological, pharmacological and therapeutical activities

Ferula foetida possesses powerful nervine and bowel stimulant which has been used in the nervous disorders as hysteria and constipation. Also it has a mild intestinal disinfectant effect [39]. The major biological and pharmacological activities reported so far are antioxidant, antihaemolytic, antihypertension properties and reversing gentamicin-induced nephrotoxicity [40-

43]. It has also shown therapeutic properties such as analgesic, anthelmintic, antispasmodic, diuretic and laxative activities. Furthermore, the oleo-gum-resin can be used for treating asthma, bronchitis, gastrointestinal disorders, hysteria, seizures, rheumatism and various neurological conditions [6,40].

Phytochemistry

In various studies, a number of compounds including sulfur-containing compounds, thiophene derivatives (foetithiophenes C-F) and sesquiterpene coumarins have been reported from *F. foetida*. Sesquiterpene coumarins are acyclic sesquiterpene and bicyclic sesquiterpene derivatives (table 5, figure 2). Several studies have reported the components found in the essential oil of aerial parts. For instance, monoterpene hydrocarbons (6.1%), sesquiterpene hydrocarbons (0.7%), organosulfur compounds (76.6%) and phenylpropanoids (13.9%) are reported from essential oils [44]. Six sulfide derivatives, (*E*)-3-methylsulfinyl-2-propenyl *sec*-butyl disulfide (foetisulfide A), (*Z*)-3 methylsulfinyloxy- 2-propenyl *sec*-butyl disulfide (foetisulfide B), (*E*)-3-methylsulfinyloxy-2-propenyl *sec*-butyl disulfide (foetisulfide C), bis(3-methylthio-2 *E*-propenyl) disulfide (foetisulfide D), 3,4,5-trimethyl-2-thiophenecarboxylic acid (foetithiophene A), 3,4,5-trimethyl-2-(methylsulfinyloxymethyl) thiophene (foetithiophene B) have been reported from the ethyl acetate-soluble portion of a methanol extract of *F. foetida* roots [45].

***Ferula alliacea* Boiss.**

Botany

Ferula alliacea as an endemic species to Iran (north east), is a perennial herb up to 120 cm height. The botanical description of *F. alliacea* has been presented in (table 2) [14].

Traditional medicine

Simillar to *F. foetida*, the traditional description for "Heltit" (refer to "Heltit" traditional description [8,9]) can be developed to *F. alliacea* as a traditional source for asafoetida gum [7].

Biological, pharmacological and therapeutical activities

Oleo-gum-resin of *F. alliacea* is used for the treatment intestinal infections, hysteria, epilepsy, lung infections, asthma and whooping cough. Furthermore, it recommended as an appetite enhancer, carminative, anti-flatulence, uterus stimulant and antispasmodic [6,18].

Phytochemistry

Chemical study on the composition of *F. alliacea* is scare. The main components in the root oil have been reported to be 10- epi-γ-eudesmol (22.3%), valerianol (12.5%), hinesol (8.3%), guaiol (7.3%) and Z-propenyl-sec-butyl trisulphide (6.5%) (table 4 figure 1) [18].

There is very little information about the pharmacognostic quality controls of asafoetida or sagapenum in the world pharmacopeias [46]. For instance, Iranian Herbal Pharmacopeia indicated general information including the maximum amount of impurities and total ash or determination of a flavonoid (rutin) as an estimation of asafoetida oleo-gum-resin quality which is not adequate and should be updated [5]. Microscopic detection of the oleo-gum-resin using plant organs is also not plausible. Furthermore, there are still many complications on the botanical identifications of *Ferula* species. Here we showed that at least 4 Iranian species, as the major sources for asafoetida and sagapenum, should be differentiated botanically according to basal leaves, size of rays, fruits and petals (table 2). It seems that types of compounds in the essential oils of such *Ferula* spp. should be helpful for identification. For instance, volatile sulfur compounds in *F. assa-foetida* are disulphides, in *F. persica* are tri/tetra/pentasulphides, while, in *F. alliacea* trisulphides are found (table 4, figure 1).

In the case of coumarins, conferol, conferone, farnesiferol A and B, samarcandin and samarcandin acetate have been so far reported from *F. assa-foetida* and *F. persica*, and asacoumarin A from *F. assa-foetida* and *F. foetida* samples. While, persicaosides A-D have been reported only from *F. persica* which can be used as a dentification marker. Farnesilferol C as the major coumarin in *F. assa-foetida* or mogoltavidin in *F. persica* would be new specific pharmacopeial markers (table 5, figure 2). However, coumarins and essential oils similarities and differences among *Ferula* species should be more studied in the similar conditions (plant's part, extraction and purification methods).

Conclusion

Asafoetida and sagapenum as oleo-gum-resins of *Ferula* spp. have received interest during the

history regarding producing valuable perfumes to common Indian spices or as pharmaceutical agents. Nevertheless, there aren't still reliable monographs available due to many reasons. The main challenges for at least Persian asafoetida and sagapenum can be itemized as followings:

- There is no well described botanical literature available on Persian *Ferula* species producing asafoetida or sagapenum. Furthermore, scattering seeds of *F. assa-foetida* and *F. persica* from their wild growing habitant and also cultivating seeds in a quite different climate, has probably amplified such botanical complications. Among botanical reports on Iranian *Ferula* species which is attributed to *F. assa-foetida* -now we know- only species which are growing in Lar (Fars province) should be botanically *F. assa-foetida*. While, in the case of miscellaneous reports on *F. assa-foetida* from other regions, further precise botanical studies should be performed. Here, we tried to differentiate four major *Ferula* species producing asafoetida or sagapenum; however, there are still many botanical questions which affect the phytochemical results of at least those publications which are attributed to asafoetida.
- Up to present the phytochemical studies of oleo-gum-resin of these *Ferula* species are inadequate. Although, essential oil is a classic route for identification of *Ferula* spp. source, but coumarins type molecules which have been recently isolated from *Ferula* spp. could be more specific indicators. Such components would be adequate markers for detecting adulterations as well as for quality control.

Similar studies would be essential for determining reliable sources and adjusting minimum requirements for standardizations of wild growing valuable medicinal and economical plants worldwide.

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Author contributions

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Declaration of interest

The authors declare that there is no conflict of interest. The authors alone are responsible for the accuracy and integrity of the paper content.

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Abbreviations

Coum: Coumarin; spp. species