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Biological activities and medicinal properties of Asafoetida: A review

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ABSTRACT

Ferula asafoetida Linn. is a main source of asafoetida, a strong, tenacious and sulfurous odor, and oleogum resin of medicinal and nutritional importance. Asafoetida has been consumed as a spice and a folk medicine for centuries. Recent studies have shown several promising activities particularly relaxant, neuroprotective, memory enhancing, digestive enzyme, antioxidant, antispasmodic, hypotensive, hepatoprotective, antimicrobial, anticarcinogenic, anticancer, anticytotoxicity, antiobesity, anthelmintic and antagonistic effect. This review effectively deals with phytochemistry and various pharmacological and clinical studies of asafoetida.

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1. Introduction

Spices are used for thousands of years as food accessories to enhance the sensory quality of food. By imparting pleasant flavor, color and pungency, they can transform an otherwise dull food preparation into an attractive, appetizing meal. Spices are used not only alone, but also in the form of mixtures known as curry powders to math different tastes and preparations.¹ Spices are known to possess several medicinal properties. A number of health favorable physiological effects of dietary spices have been experimentally documented in recent decades.^{2–4}

Asafoetida is used as a flavoring agent in food and as a traditional medicine for many diseases in many parts of the world. Asafoetida (*Ferula asafoetida*) is an oleo-gum-resin obtained from the stems of *Ferula* plants belonging to the family *Umbelliferae*. Out of more than 170 species, sixty spices of *Ferula* are widely distributed in Central Asia, particularly West Afghanistan, Iraq, Turkey and Eastern Iran, Europe and North Africa.⁵ *F. asafoetida* is one of the important species of *Ferula* and is more native to Afghanistan and Iran than grows about 2 m in height and is in two types bitter and sweet.⁶ Asafoetida is called Hing or Hingu in India.³ Other names in different languages are given in Table 1. Asafoetida is extracted from the *Ferula* plants which have massive taproots or carrot-shaped roots, around 15 cm in diameter at the crown when they are 4–5 years old. Before the plants flower, the upper part of the living rhizome root is laid bare and the stem cut off close to the crown. A dome-shaped structure made of twigs and earth covers the exposed surface. A milky juice exudes from the cut surface. The exudates are scraped off and a fresh slice of the root cut when more latex exudes, sometimes the resin is removed along with the slice. The collection of resin and slicing of the root are repeated until exudation ceases.⁷

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Asafoetida has a strong, tenacious and sulfurous odor. Nowadays it is a popular ingredient in the Indian cuisine, most probably because its odor is reminiscent of the flavor of garlic and onion, two sprouting vegetables, as well as meat. Asafoetida is traditionally used for the treatment of different diseases, such as whooping cough, asthma, ulcer, epilepsy, stomachache, flatulence, bronchitis, intestinal parasites, antispasmodic, weak digestion and influenza.^{8–11} Asafoetida is an effective remedy for several diseases of the stomach. The digestive stimulant actions of asafoetida are the most commonly experimented beneficial physiological effect via enhanced secretion of saliva and activity of salivary amylase. It plays an important role in the digestion of dietary lipids by stimulating bile flow and enhances the bile acid secretion and also enhances the activities of digestive enzymes of the pancreas and small intestine. Moreover, it is used for low acid levels in the stomach, stomach pressure, flatulence and loose stools. It is specially considered an ailment for women. It is used as a treatment of several problems such as unwanted abortion, unusual pain,

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Table 2 (continued)

Table I	Та	ble	1
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Various names of asafoetida in different countries.

Country	Name
Afghanistan	Kama, Anguza
Bangladesh	Hing
China	A-wei
Denmark	Dyvelsdrak
England	Asafetida
Finland	Asafetida, Hajupihka, Pirunpaska, Pirunpihka
France	Asafetide, Assa foetida, Ferule persique, Merde du diable
Germany	Asafetida, Asafotida, Asant, Stinkasant, Teufelsdreck
Greece	Aza
Hungary	Ordoggyoker
India	Hengu, Hing, Hingu, Ingu, Inguva, Kayam, Perungayam,
	Perunkaya, Raamathan
Iran	Rechina fena, Zaz
Italy	Assafetida
Myanmar	Sheingho
Netherlands	Asafetida, Duivelsdrek, Godenvoedsel, Sagapeen
Norway	Dyvelsdrekk
Pakistan	Anjadana, Kama, Anguza
Poland	Asafetida, Zapaliczka cuchnaca
Russia	Asafetida
Spain	Asafetida
Sri Lanka	Perunkayan
Sweden	Asafetida, Dyvelstrack
Tanzania	Mvuje
Tibet	Shing-kun
Turkey	Setan bokosu, Seytan tersi
United States	Asafetida, Devil's dung, Stinking gum

sterility, difficult and excessive menstruation and leucorrhoea. Recent pharmacological and biological studies have also shown several activities, such as antioxidant,^{12,13} antimicrobial,^{14–18} antiviral,¹⁰ antifungal,^{19–22} cancer chemopreventive,²³ anti-diabetic,²⁴ anticarcinogenesis,^{23,25} antispasmodic and hypotensive,²⁶ relaxant effect,^{27,28} neuroprotective^{29,30} and molluscicidal³¹ from this asafoetida. The present review deals with phytochemistry and various pharmacological and clinical studies of asafoetida.

2. Methods

Systematic literature searches were carried out in the terms: *F. asafoetida*, biological activities, umbelliprenin, bioavailability, antioxidant and relaxant effects. Information on *F. asafoetida* was collected via search and studies in electronic databases including Web of Science, Medline/Pubmed, Scifinder, Scopus, Embase and Google Scholar and also locally available books.

3. Chemical constituents

In general, Asafoetida consists around 68% of carbohydrates, 16% of moisture, 4% protein, 1% of fat, 7% of minerals and 4% of fiber.¹⁰ It consists of three main fractions, including resin (40–64%), gum (25%) and essential oil (10–17%).⁸ The resin fraction contains ferulic

Table 2

Phytochemical constituents of Ferula asafoetida.

Major chemical constituents	References
Coumarins and sesquiterpene coumarins Umbelliprenin 5-Hydroxyumbelliprenin 8-Hydroxyumbelliprenin Tadshiferin	34,35
Galbanic acid 8-Acetoxy-5-S-hydroxyumbelliprenin Conferol Gummosin	34–36 34,35 37

Table 2 (continued)	
Major chemical constituents	References
Epi-samarcandin	
Epi-samarcandin acetate	
Franesiferol A Franesiferol B	38,39
Franesiferol C	
Asacoumarin A	36
Assafoetidin	40
Ferocaulicin	41
Assafoetidinol A Assafoetidinol B	41
Polyanthinin	
Kamolonol	42
Foetidine	43
Saradaferin 10-R-Acetoxy-11-hydroxyumbelliprenin	32,41
10-R-Karatavicinol	
Methyl galbanate	
Lehmferin	
Feselol	
Ligupersin A Epi-conferdione	
Microlobin	
Umbelliferone (7-hydroxycoumarin)	
Sulfur containing compounds	0.33
2-Butyl 1-propenyl disulfide 1-(Methylthio) propenyl disulfide	8,32
2-Butyl 3-(methylthio)-2-propenyl disulfide	
2-Methyl-2-propanethiol	
2,3-Dimethylthiirane	
1-Methylthio-(Z)-1-propene 1-Methylthio-(E)-1-propene	
Dimethyl disulfide	
S-Methylpropanethioate	
2-(Methylthio) butane	
3,4-Dimethylthiophene Methyl (Z)-1-propenyl disulfide	
Methyl (E)1-propenyl disulfide	
Dimethyl trisulfide	
2-Butyl methyl disulfide	
Dipropyl disulfide 2,3,4-Trimethylthiophene	
2-Butyl vinyl disulfide	
2-Butyl 1-propenyl disulfide	
Methyl 1-(methylthio)propyl disulfide Di-2-butyl disulfide	
Methyl 1-(methylthio)ethyl disulfide	
1-(Methylthio)propyl propyl disulfide	
1-(Methylthio)propyl 1-propenyl disulfide	
Asadisulfide	36 44
2-Butyl methyl trisulfide Di-2-butyl trisulfide	44
Di-2-butyl tetrasulfide	
Foetisulfide A	7,9
Foetisulfide C Diterpenes	
7-Oxocallitristic acid	9
Picealactone C	
15-Hydroxy-6-en-dehydroabietic acid	
Phenolics Vanillin	45
3,4-Dimethoxycinnamyl-3-(3,4-diacetoxyphenyl) acrylate	45
Sesquiterpenes	
Taraxacin	35
Fetidone A Fetidone B	
Other compounds	
Falcarinolone	46
Oleic acid	47
β-Sitosterol Galactose	9,48
Arabinose	
Glucuronic acid	
Rhamnose	
Luteolin 7-β-D-glucopyranoside Ferulic acid	
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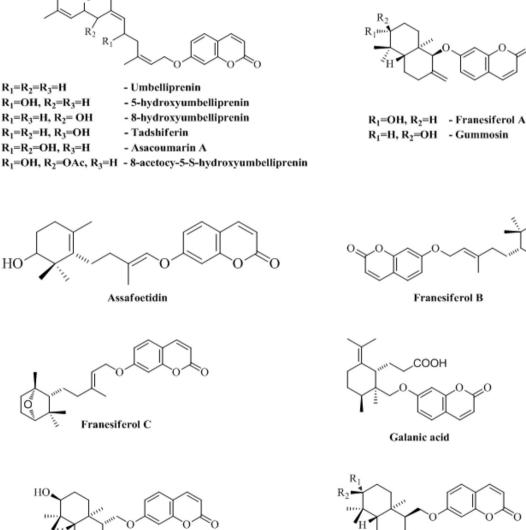
acid and its esters, coumarins, sesquiterpene coumarins and other terpenoids. The gum includes glucose, galactose, 1-arabinose, rhamnose, glucuronic acid, polysaccharides and glycoproteins, and the volatile fraction contains sulfur-containing compounds, monoterpenes and other volatile terpenoids.³² Sulfur compounds in F. asafoetida resin show various biological activities and can be valuable in medicine.³³ Three major sulfur constituents that have been identified include 2-butyl 1-propenyl disulfide. 1-(methyl thio) propyl 1-propenyl disulfide and 2-butyl 3-(methyl thio)-2-propenyl disulfide.⁸ The major constituents of *F. asafoetida* are well characterized and given in Table 2. Chemical structures of important sesquiterpene coumarins and sulfur-containing compounds present in F. asafoetida are given in Figs. 1 and 2 respectively.

4. Pharmacological and clinical studies of asafoetida

Various scientific investigations of asafoetida into physiological and pharmacological activities and critical evaluations of its various activity effects were discussed (Table 3). Schematic representation of various biological activities of asafoetida is shown in Fig. 3.

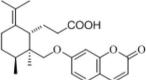
4.1. Relaxant effect

The relaxant effects of various preparations of *F. asafoetida* and its constituents on different types of smooth muscles were demonstrated. The relaxant effect of the asafoetida on tracheal smooth muscle of guinea pigs and its probable mechanisms were investigated by three cumulative concentrations of the aqueous extract (2, 5 and 10 mg/mL), theophylline (0.25, 0.50 and 0.75 mM) and saline were examined on non-incubated tracheal smooth muscle of guinea pig precontracted by 10 µM methacholine in group 1, pre-incubated tissues by propranolol and chlorpheniramine, contracted by methacholine in group 2 and pre-incubated tissues by propranolol contracted by methacholine in group 3. All concentrations of theophylline in group 1 and all concentrations of

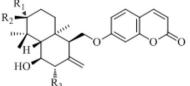


Conferol

Franesiferol B



Galanic acid



R1=OH, R2=R3=H - Assafoctidinol A R1=H, R2=OAc, R3=OH - Assafoetidinol B

Fig. 1. Chemical structures of important sesquiterpene coumarins present in Ferula asafoetida.

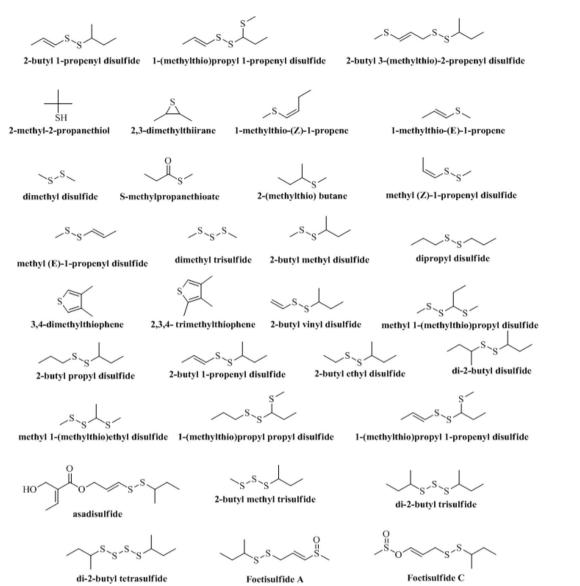


Fig. 2. Chemical structures of important sulfur compounds present in Ferula asafoetida.

the extract in the further three groups showed considerable relaxant effects compared to that of saline. Significant positive correlations have shown between the relaxant effects of the extract with their concentrations in all three groups. It is clearly indicated that a potent relaxant effect of the asafoetida extract on tracheal smooth muscle, which is perhaps due to muscarinic receptor blockade.⁴⁹ Bayrami et al⁵⁰ investigated the relaxant effects of oleogum-resin of asafoetida and its coumarin constituent umbelliprenin on tracheal chains of guinea pigs. The relaxant effects of three cumulative concentrations of the aqueous extract umbelliprenin, theophylline and saline were examined by their relaxant effects on pre-concentrated tracheal chains of guinea pig by 60 mM/L KCl in group 1 and 10 µM/L methacholine in group 2. In group 1 all concentrations of theophylline and the highest concentration of the extract showed significant relaxant effects compared with that of saline. In group 2, relaxant effects of all concentrations of theophylline, extract and two higher concentrations of umbelliprenin differed significantly compared with saline. The relaxant effect of the aqueous extract in group 2 was considerably greater than that of group 1. The relaxant effect of the extract was significantly more potent than umbelliprenin in both groups. It is indicated that a potent relaxant effect of the asafoetida extract on tracheal smooth muscle, which is due to its constituent umbelliprenin. The relaxant effect of asafoetida and essential oil from asafoetida seed was investigated by Bagheri et al²⁷ in isolated ileum of rat after three doses. Asafoetida produced an antispasmodic effect on acetylcholine (Ach) induced contraction in 0.2% and 0.3%. Spasmolytic evaluation showed that the essential oil derived from F. asafoetida seed in concentrations of 0.2 and 0.3%, significantly reduced Ach from 10 to 4 M induced concentrations. Exposure to the 0.2 and 0.3% asafoetida, reduced statistically significant, the percentage of maximum contraction induced by 10-4 M Ach to 43% and 12% respectively. Asafoetida can be used as an antispasmodic therapeutic agent. Khazdair et al²⁸ investigated the effect of asafoetida on muscarinic receptors of tracheal smooth muscle for relaxant effect. The effects of three cumulative concentrations of aqueous extract of F. asafoetida (2.2, 5 and 10 mg/mL), 10 nM atropine and saline on muscarinic receptors were tested in tracheal smooth muscle samples. The maximum responses to methacholine in the presence of higher concentration of the extract (10 mg/mL) were significantly lower than that of saline. Because of F. asafoetida or its constituents may bind to muscarinic receptor of tracheal smooth

Table 3

Pharmacological studies on Ferula asafoetida.

Pharmacological and clinical activities	Model used and study design	Type of extract	Observations	Reference
Relaxant effects	Guinea pigs (400—700 g, both sexes) — tracheal smooth muscle	Aqueous extract <i>Ferula asafoetida</i> (2, 5 and 10 mg/ ml) and theophylline anhydrous (0.25, 0.5 and 0.75 mM)	All concentrations of theophylline and the extract showed relaxant effect in comparison with saline which was not significantly different with that of theophylline. A potent relaxant effect for the asafoetida extract on tracheal smooth muscle which is perhaps due to muscarinic receptor blockade.	49
Relaxant effects	Precontracted tracheal chains of guinea pig by 60 mmol/L KCl and 10 μmol/L methacholine	Aqueous extract (2, 5 and 10 mg/mL), umbelliprenin (0.04, 0.2 and 0.4 mg/mL), theophylline (0.05, 0.1 and 0.15 mg/mL) and saline	The relaxant effect of the extract was significantly more potent than umbellipreni.	50
Relaxant effects	Male Wistar rats (250—350 g)	0.1, 0.2 and 0.3% of asafoetida aqueous extract	Essential oil derived from <i>F. asafoetida</i> seed in concentrations of 0.2% and 0.3% significantly reduced Ach ($10-4$ M) induced contractions. Exposure to the 0.2% and 0.3% asafoetida, reduced the percentage of maximum contraction induced by 10 -4 M Ach to $43%$ and $12%$ respectively.	27
Relaxant effects	Guinea-Pig Tracheal Smooth Muscle	Aqueous extract of <i>Ferula asafoetida</i> (2.5, 5 and 10 mg/mL), 10 nM atropine, and saline	The maximum responses to methacholine in the presence of 10 mg/mL concentration of the extract were significantly lower than that of saline. The values of CR-1, obtained in the presence of the extract, were significantly lower compared to atropine in the experimental group.	28
Neuroprotective effect	7-d rat brains and cerebellar granule neurons	80% methanol extract of Ferula asafoetida (100 $\mu g/$ ml)	<i>F. asafoetida</i> extract displayed neuroprotective effects in glutamate-induced neurotoxicity. The extract exerted antiapoptotic activity in cerebellar granule neurons due to cell cycle arrest in GOG1 phase, which explain the beneficial effects of <i>F. asafoetida</i> extract as therapies for neurologic disorders.	29
Neuroprotective effect	Sciatic nerves of adult male Balb/c mice	Aqueous extract of oleo gum resin of <i>Ferula</i> asafoetida (0.1 mg/kg, 1 mg/kg and 10 mg/kg).	Aqueous extract of oleo gum rein of asafoetida increased the amplitude and decreased the latent period of nerve compound action potential (CAP). Nerve conduction velocity (NCV) and amplitude of CAP also improved in asafoetida treated animals. Histological and behavioral studies showed that asafoetida was able to facilitate the healing process in peripheral nerves.	51
Memory enhancing activity	Male inbred albino rats	Aqueous extract of <i>Ferula asafoetida</i> (200 and 400 mg/kg)	Significant improvement in memory score and dose- dependent improvement of transfer latency Memory enhancing potential of <i>F. asafoetida</i> can be attributed to acetylcholinesterase inhibiting and antioxidant properties.	52
Memory enhancing activity	Dementia induced by ${\scriptscriptstyle D}\mbox{-}galactose$ and $NaNO_2$ in mice	100 mg/kg/d aqueous extract of asafoetida	Asafoetida could prevent and treat amnesia may be due to the presence of biologically active compounds such as sulfur containing and sesquiterpene coumarin.	53
Digestive enzyme activity	Adult female Wistar rats	14 spices with 50 mg of asafoetida	Fenugreek, mustard, and asafoetida affected chymotrypsin and trypsin activities.	54
Digestive enzyme activity	Adult female Wistar rats	14 spices with 50 mg of asafoetida	Positive influence of in vitro analysis on the activity of enzymes may have an additional role in the overall digestive stimulant action of spices to enhance the titers of digestive enzymes in pancreatic tissues.	55
Antispasmodic and hypotensive activity	Sprauge—Dawley rats and guinea-pigs	Aqueous extract of <i>Ferula asafoetida</i> (0.3–2.2 mg/ 100 g)	Ferula asafoetida gum extract is effective in reducing blood pressure in anaesthetized normotensive rats. The extract also decreased contractions induced by acetylcholine, histamine and KCl in the isolated guinea- pig ileum.	26

(continued on next page)

Pharmacological and clinical activities	Model used and study design	Type of extract	Observations	References
Hepatoprotective effect	Carbon tetrachloride-induced liver toxicity in Wistar rats	Petroleum either, chloroform, benzene, ethanol and aqueous extracts of <i>Ferula asafoetida, Momordica</i> <i>charantia</i> and <i>Nardostachys jatamansi</i> (Three different formulations were prepared)	Formulation 3 (containing chloroform, petroleum ether and aqueous extracts of <i>Ferula asafoetida</i> , petroleum ether and ethanol extracts of <i>Momordica charantia</i> Linn. and petroleum ether and ethanol extracts of <i>Nardostachys jatamansi</i>). It has shown significant hepatoprotective effect by reducing the elevated serum enzyme levels such as glutamate oxaloacetate transaminase, glutamate pyruvate transaminase and alkaline phosphatase.	56
Antimicrobial and antioxidant activity	Two food borne Gram-negative bacteria [Salmonella typhi PTCC 1609 and Escherichia coli PTCC 1330], two food borne Gram-positive bacteria [Staphylococcus aureus PTCC 1112 and Bacillus subtilis PTCC 1023], and two food borne fungi [Aspergillus niger PTCC 5010 and Candida albicans PTCC 5027]. ROS, NO, H ₂ O ₂ and TBARS scavenging assay	Essential oils obtained from <i>Ferula asafoetida</i> oleo- gum resins in different collections times	Essential oil obtained from the earlier stages of <i>F. asafoetida</i> growth could be used as safe and effective natural antioxidants in food industry to improve the oxidative stability of fatty foods during storage. Essential oil obtained from the later stages of <i>F. asafoetida</i> growth could be used in health industry as a safe and effective source of antimicrobial agents.	13
Antimicrobial activity	E. coli MTCC-443, Pseudomonas aeruginosa MTCC- 4673, Staphylococcus aureus MTCC-3160, Bacillus subtilis MTCC-441, Aspergillus niger MTCC-1344	Petroleum ether, acetone, carbon tetrachloride, methanol, ethanol and aqueous extracts of <i>Ferula</i> asafoetida	Alcoholic and aqueous extracts of Asafoetida showed significant effect against B. subtilis, S. aureus, E. coli, P. aeruginosa and Aspergillus niger.	14
Antimicrobial activity	Bacterial strains of Staphylococcus aureus, Yersinia enterocolitica, Salmonella typhi, Bacillus cereus, Bacillus subtilis, Listeria monocytogenes, Escherichia coli and Salmonella paratyphi	Volatile oils of two varieties of Ferula asafoetida (Pathani and Irani)	Pathani oil was found to be a good antibacterial agent. Irani oil was found to be a good fungicidal agent.	15
Antibacterial and antifungal activity	Antibacterial activity – Bacillus subtilis, Staphylococcus aureus, Klebsiella pneumonia and Escherichia coli Antifungal activity – Aspergillus niger and Candida albicans	Chloroform, ethyl acetate, ethanol, methanol and aqueous extracts of asafoetida	Ethyl acetate, ethanol, and methanol extract has significant antimicrobial and antifungal activity and highest activity was reported with methanolic extract.	17
Antibacterial activity	Gram negative — E. coli and K. pneumonia, Sh. flexneri Gram positive — S. aureus and E. faecalis	Red and white forms of <i>Ferula asafoetida</i> extracts in hot water, hexane, ethanol and petroleum ether	Highest antibacterial activity was shown by hexane extract against <i>Shigella flexineri</i> and <i>S. aureus</i> .	18
Antifungal activity	Aspergillus niger, Candida albicans, Candida blanki, Candida cylindracea, Candida glabrata, Candida krusei, Candida tropicalis, and Saccharomyces cerevisiae	Essential oils derived from 20 spices including asafoetida	Asafoetida oil showed inhibitory activity toward all fungal strains, but activity was strong toward Candida tropicalis, Candida albicans, Saccharomyces cerevisiae, and Aspergillus niger.	19
Antifungal activity	Aspergillus niger, A. flavus, Fusarium oxysporum, F. moniliforme, F. nivale, F. semitectum, Drechslera hawiinesis and Alternaria alternata	Essential oils extracted from the seeds of neem, mustard, black cumin and asafoetida	Asafoetida oil at 0.1% and 0.15% significantly inhibited the growth of all test fungi except <i>A. flavus</i> and <i>Nigella</i> sativa.	57
Antifungal activity	Sclerotium rolfsii ITCC 5226 and Macrophomina phaseolina ITCC 0482	Ninety formulations of neem oil, nicotinic acid and <i>Ferula asafoetida</i> at different concentrations with α , β -unsaturated carbonyl compounds	The formulations having <i>F. asafoetida</i> as the natural component showed significant antifungal activity.	20
Antifungal and allelopathic effects	Trichoderma harzianum and Pleurotus spp.	Methanol extract of Asafoetida oleo-gum-resin	Asafoetida showed fungicidal activity against <i>T. harzianum</i> strains and <i>Pleurotus</i> spp. at higher concentrations. Antagonistic activity of <i>T. harzianum</i> against the <i>Pleurotus</i> spp. was moderate.	21
Antifungal activity	Bipolaris sorokiniana, Verticillium sp, Fusarium graminearum, Fusarium solani and Aspergillus niger	Asafoetida seed essential oil	<i>Bipolaris sopokiniana</i> growth completely inhibited. Other species growth also increased with increase of essential oil concentration.	22
Antiprotozoa activity	Blastocystis hominis	Asafoetida (oleo-gum-resin) as powder and oil- form	Asafoetida decreased counts and viability of all tested isolates of <i>Blastocystis hominis</i> . The degree of the inhibitory effect was dependent on the concentration and time of incubation with asafoetida extracts.	58

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Anticarcinogenic activity	Swiss albino mice	70% ethanol extract of Ferula asafoetida	Asafoetida extract inhibited two stage chemical carcinogenesis induced by 7,12 dimethyl benzanthracene and croton oil on mice skin with	59
Anticarcinogenic activity	Swiss albino mice	Petroleum ether, benzene, ethyl acetate, acetone, methanol and aqueous extracts of <i>Ferula asafoetida</i>	significant reduction in papiloma formation. The pretreatment of animals with asafoetida recovered the antioxidant level and reversed the induced ODC activity and DNA synthesis significantly.	23
Anticarcinogenic activity	Sprague—Dawley rats	Asafoetida (1.25 and 2.5%w/w in diet)	A significant decrease in tumor multiplicity after asafoetida treatment.	25
Anticancer activity	Spargue—Dwaley rats (120—150 g)	Asafoetida orally daily (10 and 20 mg/100 g bw)	A striking reduction in the number of terminal end buds during mammary gland differentiation. Asafoetida supplementation attenuates DMH induced deleterious effects in of rats.	60
			Medium dose of 10 mg/100 g bw exhibited more pronounced effect as it constantly influenced all the tested biochemical parameters.	
Anti-quorum sensing activity	Pseudomonas aeruginosa	Essential oil extracted from Ferula asafoetida (25 $\mu\text{g}/\text{mL})$	Fully abolished the violacein production by <i>C. violaceum</i> . Pyocyanin, pyoverdine, elastase and biofilm production were decreased in Ferula oil treatments.	61
Antihyperglycemic effect	Male Wistar rats (280—320 g)	Aqueous extract of oleo gum resin of <i>Ferula</i> asafoetida (50 mg/kg)	Blood glucose level in streptozotocin induced diabetic animals is reduced	62
Farnesyltransferase inhibition	Oncogenic ras-transformed NIH3T3/Hras-F cells	Coumarin-derived sesquiterpene galbanic acid, karatavicinol, umbelliprenin, farnesiferol B, and farnesiferol C	Galbanic acid demonstrated potent inhibition of the proliferation of oncogenic ras-transformed NIH3T3/ Hras-F in a dose-dependent manner	63
Protein and metabolic activity	Male Wistar albino rats (230–250 g)	Nigella sativa (50–400 mg/kg), Trigonella foenum- graecum (25–600) and Ferula asafoetida (50–450)	Asafoetida significantly inhibited the mRNA and protein expression levels of CYP2C11 in a dose-dependent manner.	64
			The in vitro enzyme metabolic activity study showed a significant decrease in the formation of 4-hyroxy-tolbutamide, a tolbutamide metabolite, at the higher doses.	
Anti-cytotoxicity activity	Male NMRI mice (18–28 g)	<i>Ferula asafoetida</i> oleo-gum resin at doses of 300 mg/ kg	Oleo-gum-resin of <i>F. asafoetida</i> exhibited cytotoxic effect with LC_{50} values in the range of $6-321 \mu g/mL$.	65
Anti-obesity and fat lowering effect	Male Wistar rats (285–300 g)	Ferula asafoetida oleo-gum resin at doses of 25 or 50 mg/kg	Administration of Ferula asafoetida significantly decreased body weights, abdominal fat and size of epididymal adipocyte compared to untreated rats. Levels of serum leptin were significantly decreased in	66
Anxiolytic effect	Swiss albino mice (20–25 g) and Wistar albino rats (140–180 g)	Asafoetida orally daily (0.1, 0.3, 1, 1.5 and 2 g/kg)	treated rats. A dose-dependent anxiolytic and analgesic activity of asafoetida, with a mild sedative effect in high doses. Compared to diazepam, the asafoetida seems to be a better alternative for the treatment of anxiety disorders.	67
Anthelmintic activity	Pheretima postuma-adult Indian earthworms	Aqueous extract from <i>Ferula asafoetida</i> (25, 50, 100 mg/mL)	The extract has exhibited significant anti-helmintic activity at the highest concentration of 100 mg/mL.	68
Anthelmintic activity	Liver fluke Fasciola gigantic	Acetone, ether, chloroform and ethanol extract from Ferula asafoetida (2–10 mg/mL)	The ethanol extract of <i>F. asafoetida</i> (2 h; LC ₅₀ 3.94 mg/mL) was high toxic against <i>Fasciola gigantic</i> .	69
Spermatic and testicular histopathology	Male Wistar rats (230–250 g)	Asafoetida orally daily (25, 50, 100 and 200 mg/kg)	Asafoetida significantly increased the number and viability of sperms Spermatogenesis process and numbers of Leydig cells were increased with increasing	70
Antagonistic Effect	Guinea pigs (600–800 g)	Aqueous extract from <i>Ferula asafoetida</i> (2.5, 5 and 10 mg/mL)	the dose. Competitive antagonistic effect of <i>F. asafoetida</i> at muscarinic receptors.	71

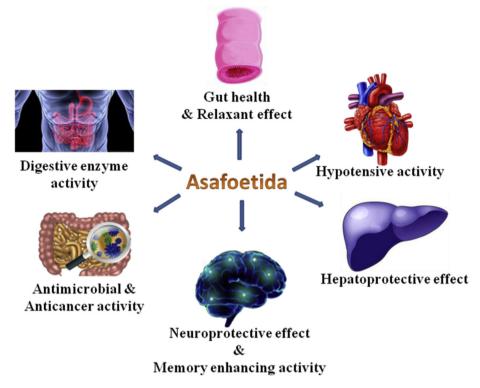


Fig. 3. Schematic representation of various biological activities of asafoetida.

muscle and put off the binding of methacholine to this receptor, it suggested the competitive antagonistic effect of *F. asafoetida* at muscarinic receptors.

4.2. Neuroprotective effect

Traditional usages and some recent findings suggested that F. asafoetida can exert some effects on the function of the nervous system particularly in neuroprotective and nerve stimulating effects. F. asafoetida extract treatment on glutamate-induced cell damaged in primary culture of rat cerebellar granule neurons was investigated by Tayeboon et al.²⁹ Cerebellums and cerebellar granule neurons were collected from seven days rat brains and eight days culture respectively. Cerebellar granule neuron cells were treated with *F. asafoetida* extract at 100 µg/mL concentration before, after and during exposure to 30 µM glutamate. Neuroprotective effects of extracts of F. asafoetida against glutamateinduced neurotoxicity confirmed by increased glutamate-induced reduction in cellular viability and attenuated glutamate-induced apoptotic/necrotic cell death. The extract exerted antiapoptotic activity in cerebellar granule neurons due to cell cycle arrest in GOG1 phase, which explain the beneficial effects of F. asafoetida extract as therapies for neurologic disorders.²⁹ In vitro studies were carried out by Moghadam et al⁵¹ to identify the response of isolated sciatic nerves to various concentrations of oleo gum resin of asafoetida solved in Lock's solution. In vivo studies were also conducted to evaluate its effect on amelioration of peripheral neuropathy in mice. In vitro experiments authenticated that incubating the nerves in aqueous extract of the oleo-gum-resin of asafoetida increased the amplitude and decreased the latent period of nerve compound action potential. Nerve conduction velocity and amplitude of compound action potential improved in asafoetida treated animals. The ability of asafoetida to facilitate the healing process in peripheral nerves is also confirmed by the histological and behavioral studies. In vitro experiments showed that asafoetida is a nerve stimulant and its management in neuropathic mice exerted neuroprotecting effects through stimulating axonal regeneration and remyelination and decrement of lymphocyte infiltration.⁵¹

4.3. Memory enhancing activity

Loss of memory is the first symptom to manifest in majority of the people suffering from Alzheimer's disease around the world. Vijayalakshmi et al^{52} investigated the effect of the *F. asafoetida* extract on learning and memory in rats. Learning and memorization were evaluated using elevated plus maze and passive avoidance paradigm after the oral administration of two doses (200 and 400 mg/kg) of F. asafoetida aqueous extract with rivastigmine as positive control. The extract produced significant improvement in memory score and dose-dependent improvement of transfer latency in elevated plus maze model. Dose-dependent inhibition of brain cholinesterase and significant improvement in antioxidant levels were also noted. Memory enhancing potential of F. asafoetida can be attributed to acetylcholinesterase inhibiting and antioxidant properties. Dietary usage of *F. asafoetida* is beneficial and can also be employed as an adjuvant to existing anti-dementia therapies. The effect of asafoetida on preventive treatment of Dementia induced by D-galactose and NaNO2 in mice was investigated by Bagheri et al.⁵³ Animals were divided into four different groups such as normal control (NC), dementia control (DC), dementia prophylactic (DP) and dementia treated (DT). The groups DP, NC and DT were significantly shown greater memory retention ability than the DC group. Because of asafoetida could prevent and treat amnesia may be due to the presence of biologically active compounds such as sulfur containing and sesquiterpene coumarins. The anti-epileptic and anti-oxidant properties of the F. asafoetida gum extract, using the pentylenetetrazole (PTZ) kindling method. Considerable reduction of MDA and NO levels and increased the SOD level in the plant extract treatment groups compared to the PTZ group implies that probably F. asafoetida gum extract causes a

decrease in oxidative damage and lipid peroxidation due to its antioxidant properties. The lowering effects of hydro-alcoholic *F. asafoetida* gum extracts on the PTZ-induced seizures are probably due to its antioxidant properties and decrease of oxidative stress.

4.4. Digestive enzyme activity

In general spices have been considered to strengthen salivary flow and gastric juice secretion and support in digestion. The digestive stimulating action of the spices is most likely through a stimulation of activities of enzymatic participate in digestion. A few common spices or their active principles were examined for their possible influence on digestive enzymes of the pancreas in experimental rat. Groups of animals were maintained for 8 weeks on the following spice diets are curcumin (0.5 mg), capsaicin (15 mg), piperine (20 mg), ginger (50 mg), cumin (1.25 mg) fenugreek (2 mg), mustard (250 mg) and asafoetida (250 mg). Among these spices, asafoetida prominently enhanced pancreatic lipase activity and also stimulated pancreatic amylase. The positive influence of the pancreatic digestive enzymes exerted by a good number of spices consumed in diet could be a factor contributing to the well recognized digestive stimulant action of spices.⁵ Ramakrishna Rao et al⁵⁵ also examined the *in vitro* influence of fourteen spices with asafoetida on the activities of digestive enzymes of rat pancreas and small intestine by including them in the reaction blend at two dissimilar concentrations. A majority of spices enhanced the activity of pancreatic lipase and amylase when they are directly in contact with the enzyme. It is inferred that this positive influence on the activity of enzymes may have a supplementary role in the overall digestive stimulant action of spices, besides causing an enhancement of the titers of digestive enzymes in pancreatic tissue.

4.5. Antispasmodic and hypotensive activity

In 2004, Fatehi et al²⁶ demonstrated that *F. asafoetida* gum extract was effective in reducing blood pressure in anaesthetized normotensive rats. The effects of F. asafoetida gum extract on the contractile responses of the isolated guinea-pig ileum stimulated by histamine, acetylcholine, and KCl, and on the mean arterial blood pressure of rat were investigated. The average amplitude of spontaneous contractions of the isolated guinea-pig ileum was decreased when compared with control. Exposure of the precontracted ileum by acetylcholine to F. asafoetida gum extract caused relaxation in a dose-dependent manner. F. asafoetida gum extracts significantly reduced the mean arterial blood pressure in anaesthetized rats. It strength be concluded that the relaxant compounds in F. asafoetida gum extract interfere with a variety of histaminic receptor and muscarinic adrenergic activities or with the mobilization of calcium ions required for smooth muscle contraction nonspecifically.

4.6. Hepatoprotective effect

In 2008, Dandagi et al⁵⁶ explored the hepatoprotective activity of a variety of extracts of *Momordica charantia* Linn., *Nardostachys jatamansi* and *F. asafoetida* against experimental hepatotoxicity. These extracts were formulated as polyherbal suspensions and they were showing significant activity and evaluated for both hepatoprotective and physicochemical activity in evaluation with LIV-52 as standard. Three different formulations were prepared, among these Formulation 3 (containing chloroform, petroleum ether and aqueous extracts of *F. asafoetida*, petroleum ether and ethanol extracts of *M. charantia* Linn. and *N. jatamansi*) has shown a significant hepatoprotective effect by decreasing the elevated serum enzyme levels such as glutamate pyruvate transaminase, glutamate oxaloacetate transaminase and alkaline phosphatase. Experimental data also suggested that treatment with Formulation 3 enhances the recovery from hepatotoxicity induced by carbon tetra chloride.

4.7. Antimicrobial activity

Antimicrobial activity of spices depends upon the several factors such as class of species, composition and concentration of spices and its level of occurrence, composition of substrate, processing conditions and storage. Asafoetida is a spice and herbal medicine used to treat against various fungi and bacteria. Crude extracts of asafoetida were evaluated for their antimicrobial activity against various fungal and bacterial strains. It was observed that alcoholic and aqueous extracts of asafoetida showed significant effect against Bacillus subtilis, Staphylococcus aureus, Escherichia coli, Pseudomonas aeruginosa and Aspergillus niger by the agar disc diffusion method. The crude extract showed a broad spectrum of antimicrobial activities by inhibiting the respective fungi and bacteria. Agar disc diffusion assay for antimicrobial activity yielded the inhibitory zone of 4-16 mm diameter for asafoetida extracts. Asafoetida can be recommended for therapeutic and medicinal purposes.¹⁴ Essential oils obtained from F. asafoetida oleo-gum resins (OGRs) in different collections times named as OGR1, OGR2 and OGR3 had different chemical compositions, antioxidant, ROS, RNS, H₂O₂ and TBARS scavenging. The essential oil from OGR1 was constituted high levels of bicyclic sesquiterpenes [10-epi- γ -eudesmol] and acyclic sulfurcontaining compounds [(E)-1-propenyl sec-butyl disulfide and (Z)-1-propenyl sec-butyl disulfide] showed the highest radical scavenging and the lowest antifungal and antibacterial activities. Essential oil from OGR2 was constituted high levels of acyclic sulfur-containing compounds [(Z)-1-propenyl sec-butyl disulfide and (E)-1-propenyl sec-butyl disulfide] and bicyclic monoterpenes $[\beta$ -pinene and α -pinene] and showed moderate radical scavenging, antifungal and antibacterial activities. Essential oil from OGR3 was constituted high levels of bicyclic monoterpenes [β -pinene and α pinene] and heterocyclic disulfide [1,2-dithiolane] and showed the lowest radical scavenging and the highest antibacterial and antifungal activities. The essential oil obtained from the earlier stages of F. asafoetida growth could be used as safe and effective natural antioxidants in the food industries to get better oxidative stability of fatty foods during storage, while the essential oil obtained from the later stages of *F. asafoetida* growth could be used in the health industry as a safe and effective source of antibacterial agents.¹³ Volatile oils of two varieties of F. asafoetida, namely Pathani and Irani, isolated by hydro-distillation were studied for their antimicrobial properties against various food-borne bacterial and fungal organisms. Pathani was more effective against bacteria such as E. coli and B. subtilis. The volatile oil of Irani showed 70 and 75% inhibition of growth of Aspergillus ochraceus and Penicillium chrysogenum respectively, whereas volatile oil of Pathani exhibited 49 and 45% inhibition. Pathani oil was found to be a good antibacterial agent while Irani oil a fungicidal agent.¹⁵ Bhatnager et al¹⁸ used two kind of F. asafoetida such as red and white gum to screen their antimicrobial activity against five dissimilar bacterial strains. Hexane extracts of both red and white asafoetida has shown the highest antibacterial activity against Shigella flexneri and S. aureus was found to be least affected by other extracts. Extracts of both red and white forms showed comparable antibacterial activities, so it may have the same chemical composition. F. asafoetida has broadspectrum antibacterial activity because it showed the potential inhibitory effect against the tested strains of bacteria. Bioactive substances from this plant can therefore be worked in the formulation of antibacterial agents for the treatment of various bacterial infections mainly related to the digestive system. The antibacterial and antifungal activity of chloroform, ethyl acetate, ethanol, methanol and aqueous extracts of asafoetida were studied by Patil et al¹⁷ Antibacterial activity was carried out against *B. subtilis, E. coli, Klebsiella pneumonia, S. aureus* and the antifungal activity was evaluated against *A. niger* and *Candida albicans*. Ethyl acetate, ethanol and methanol extract has significant antimicrobial activity due to the occurrence of a mixture of phytoconstituents and it could be a source of new antibiotic compounds.

Essential oils derived from 20 different spices were investigated for their antifungal activity against A. niger, C. albicans, Candida cylindracea, Candida blanki, Candida krusei, Candida glabrata, Candida tropicalis and Saccharomyces cerevisiae using the disc diffusion method. The sensitivity of fungi to various essential oils was compared with standard ketoconazole and an activity index was determined. Among the selected spices, asafoetida oil showed inhibitory activity toward all fungal strains, but activity was strong toward C. tropicalis, C. albicans MTCC-227, S. cerevisiae and A. niger while moderate toward C. blanki, C. glabrata, C. krusei, C. cylindracea, C. albicans MTCC-3017 and C. albicans NCIM-3100. Essential oils extracted from the seeds of neem, mustard, black cumin and asafoetida were evaluated by Sitara et al⁵⁷ for their antifungal activity in 0.5, 0.1 and 0.15% against eight seed borne fungi viz., Aspergillus flavus, A. niger, Fusarium moniliforme, Fusarium oxvsporum. Fusarium nivlae. Fusarium semitectum. Drechslera hawaiiensis and Alternaria alternate. Ridomyl gold (MZ 68% WP) was used for comparison. All the oils extracted except mustard. showed variation of degree of fungicidal activity against experimental species. Asafoetida oil significantly inhibited the growth of all test fungi except.⁵⁷ The antifungal and allelopathic effects of the methanol extract of asafoetida oleo-gum resin concentrations against Pleurotus spp. and Trichoderma harzianumand were investigated in dual culture experiments on an agar-based medium. It showed fungistatic and fungicidal properties against T. harzianumand and Pleurotus spp. at higher concentrations.²¹ Ninety formulations of neem oil, nicotinic acid and F. asafoetida at different concentrations with α , β -unsaturated carbonyl compounds were screened for in vitro analysis against Sclerotium rolfsii ITCC 5226 and Macrophomina phaseolina ITCC 0482. The formulations having F. asafoetida at a dose level of 66 mg/L as a natural product may be an effective novel alternative approach to control pathogenic fungi.²⁰ Mostafa et al²² investigated the antifungal effect of asafoetida seed essential oil on some of plant pathogens fungi including: Bipolaris sorokiniana, Fusarium graminearum, Verticillium sp, A. niger and Fusarium solani based on completely randomized design and an in vitro method. Asafoetida seed essential oil compared with controls significantly inhibited the growth of all tested fungal species. B. sorokiniana growth completely inhibited by asafoetida seed essential oil, but inhibiting effect of other species was highly dose dependent. El Deeb et al evaluated the activity of asafoetida against the in vitro growth of Blastocystis sp. Both powder and oil form of asafoetida extracts were incubated with isolates of Blastocystis sp. subtype 3 and compared to the reference antiprotozoan drug metronidazole. Both powder and oil form of asafoetida decreased counts and viability of all tested isolates of *Blastocystis* sp. subtype 3. The degree of the inhibitory effect was highly dependent on the concentration, form and time of incubation with asafoetida extracts. The lowest concentration of both powder and oil form of asafoetida that caused complete inhibition of Blastocystis growth and highest percentage inhibition of development was 16 and 40 mg/ mL respectively. Asafoetida can potentially be used as a potent natural alternative Phytomedicine for treatment of Blastocystis sp. infection.58

4.8. Anticarcinogenic activity

Tumor reducing activity of extract of asafoetida was studied by Unnikrishnan and Kuttan⁵⁹ in mice transplanted intraperitoneally with Ehrlich ascites tumor. Asafoetida extract inhibited two stage chemical carcinogenesis induced by croton oil and 7.12-dimethyl benzanthracene on mice skin with considerable reduction in papiloma formation. It indicates the potential use of asafoetida as anticancer agents as well as antitumor promoters. Saleem et al²³ investigated the potential of antioxidant and anticarcinogenic activity of asafoetida in Swiss albino mice. The pretreatment of animals with asafoetida recovered the antioxidant level and reversed significantly the induced ornithine decarboxylase activity and DNA synthesis. Asafoetida can be an effective Chemopreventive agent and capable of alleviating cutaneous carcinogenesis. Mallikarjuna et al^{25} were studied to ascertain the modulatory influences of *F*. asafoetida on the mammary epithelial tissue differentiation, hepatic drug metabolizing enzymes, antioxidant outlines and N-methyl-Nnitrosourea-induced mammary carcinogenesis in Sprague-Dawley rats. A significant decrease in tumor multiplicity after asafoetida treatment can be explained in light of the fact that the carcinogenic effect was suppressed to a considerable extent as evidenced by the strengthening of drug metabolizing and antioxidant enzymes, and also a striking reduction in the number of terminal end buds during mammary gland differentiation. The Chemopreventive potential of asafoetida was reflected in the reduced number of tumors per tumor bearing rat.

4.9. Anticancer activity

In 2015, Panwar et al⁶⁰ investigated the chemopreventive potential of different doses of *F. asafoetida* oleo-gum-resin on 1,2dimethylhydrazine induced rat colon carcinogenesis by evaluating tumor size, tumor multiplicity and tumor incidence, serum total sialic acid levels as well as histoarchitecture of the colons of rats subjected to various treatment. The study revealed that asafoetida supplementation attenuates 1,2-dimethylhydrazine induced deleterious effects in of rats. The minimum dose of asafoetida (10 mg/100 g) exhibited more prominent effect as it continuously influenced all the tested biochemical parameters, which can be used as a promising chemopreventive agent against colon carcinogenesis.

4.10. Anti-quorum sensing activity

F. asafoetida was tested for its anti-quorum sensing activity against *P. aeruginosa*. Essential oil of *F. asafoetida* exhibited antiquorum activity at 25 μ g/mL of concentration and fully abolished the violacein production by *Chromobacterium violaceum*. Pyocyanin, pyoyerdine, elastase and biofilm production were decreased in *F. asafoetida* oil treatments. Expression analysis of quorum sensing dependent genes confirmed asafoetida as novel anti-quorum sensing and virulence inhibitors.⁶¹

4.11. Antihyperglycemic effect

Akhlaghi et al⁶² evaluated the hypoglycemic activity of the asafoetida extract in streptozotocin induced diabetic rats. The asafoetida extract administration at dose of 50 mg/kg for 4 weeks has shown the hypoglycemic activity in streptozotocin-diabetic rats during 2nd week and 4th week of treatment period. Blood glucose level in streptozotocin induced diabetic animal is reduced may be at least in part by the presence of the phenolic acid and tannins in the extract.

4.12. Farnesyltransferase inhibition, protein and metabolic activity

Farnesylation of the activated ras oncogene product by protein farnesyltransferase (FTase) is a critical step for its oncogenic function. The isolation of the coumarin-derived sesquiterpene galbanic acid from *F. asafoetida* extract as an active principal for FTase inhibitory action, collectively with the four structurally related sesquiterpenes such as karatavicinol, umbelliprenin, farnesiferol B and farnesiferol C. The 50% inhibitory concentration (IC₅₀) of galbanic acid against FTase in an enzyme-based assay was calculated as 2.5 µM. It also demonstrated potent inhibition of the proliferation of oncogenic ras-transformed NIH3T3/Hras-F in a dose-dependent manner. The IC₅₀ value of galbanic acid on the proliferation of oncogenic ras-transformed NIH3T3/Hras-F cells was calculated as 16.2 μ M, whereas its IC₅₀ value on control vector-transfected normal ras-containing NIH3T3/ZIPneo cells was 58.5 μ M.⁶³ Korashy et al⁶⁴ investigated the potential effects of 3 commonly used local herbal medicines such as Nigella sativa, Trigonella foenum-graecum and F. asafoetida on the expression of CYP2C11 gene at the mRNA, protein and metabolic activity levels in rat liver tissues. All the 3 herbs significantly inhibited the mRNA and protein expression levels of CYP2C11 in a dosedependent manner. The in vitro enzymes metabolic activity study showed a significant decrease in the formation of 4hydroxy-tolbutamide, a tolbutamide metabolite, at the higher doses. Asafoetida was a strong inhibitor of CYP2C11 expression that can lead to an objectionable pharmacological effect of clinically used CYP2C11 substrate drugs with a low therapeutic index.

4.13. Anti-cytotoxicity activity, anti-obesity and fat lowering effect

Cytotoxicity and anticonvulsant activity of the methanol extracts of some Ferula species particularly F. asafoetida were evaluated by Bagheri et al.⁶⁵ To evaluate general cytotoxicity, the brine shrimp (Artemia salina) was employed as a model assay system, it provided a suitable in-house pre-screening method. The methanol extracts of Ferula species and the oleo-gum resin of F. asafoetida exhibited cytotoxic effect with LC50 values in the range of 6-321 µg/mL and showed a dose-dependent cytotoxicity. Azizian et al⁶⁶ determined the effect of *F. asafoetida* on weight gain, fat accumulation, liver steatosis and leptin level in type 2 diabetic rats. Two treatment groups received F. asafoetida oleo-gum resin at doses of 25 or 50 mg/kg. Administration of F. asafoetida extensively decreased body weight, abnormal fat and size of epididymal adipocyte compared to untreated rats. Serum leptin levels were considerably decreased in treated rats. The results revealed that F. asafoetida gum has potent anti-obesity activities, fat lowering and can prevent liver steatosis. F. asafoetida gum can be a good candidate for the treatment of diabetes-induced obesity and hepatosteatosis.

4.14. Anxiolytic effect and anthelmintic activity

In 2012, Algasoumi⁶⁷ examined the anxiolytic, analgesic and sedative properties of asafoetida in rodents, using hole-board test, elevated plus maze, hot plate and motor activity meter. Diazepam was utilized as a reference anxiolytic agent. The results have shown a dose-dependent anxiolytic and analgesic activity of asafoetida, with a calm sedative outcome in high doses. Evaluated to diazepam, the asafoetida appears to be a better alternative for the treatment of anxiety disorders. The low doses of asafoetida can be a therapeutic alternative to the presently used anxiolytic drugs.

In 2013, Gundamaraju⁶⁸ evaluated the anthelmintic activity of three different concentrations of aqueous extract of *F. asafoetida*

against *Pheretima posthuma* that involved the determination of time of paralysis and death of the worm. The extract has exhibited considerable anthelmintic activity at the highest concentration of 100 mg/mL. It has also shown better significant activity than the standard drug of piperazine citrate.⁶⁸ The effect of dried *Allium sativum* clove powder, *F. asafoetida* dried latex powder and flower but dried powder of *Syzygium aromaticum* in *in vitro* treatment against liver fluke *Fasciola gigantic* were studied by Kumar and Singh.⁶⁹ The anthelmintic activities of all the three plants were both concentration and time dependent. Ethanol extract of *F. asafoetida* was highly toxic against *F. gigantic*. The dried root latex powder of *F. asafoetida* can be used as potent helminthicide.

4.15. Spermatic, testicular histopathology and antagonistic effect

In 2015, Bagheri et al⁷⁰ evaluated the effectiveness of asafoetida on spermatic parameters, blood testosterone levels and testis tissue. The asafoetida significantly increased the number and viability of sperms. Histological study showed that numbers of Leydig cells and spermatogenesis process were increased with increasing the dose. Johnsen score was found to be more when compared with experimental groups rather than the control group. Asafoetida has shown a positive effect on spermatic parameters even though the histopathological effects on the testis were observed, particularly at high doses.

Kiyanmehr et al⁷¹ evaluated the effect of different concentrations of *F. asafoetida* extract, a muscarinic receptor antagonist, and saline on methacholine concentration-response curve in tracheal smooth muscles incubated with β -adrenergic and histamine (H1) [group 1], and alone β -adrenergic [group 2] receptors antagonists. The study showed a parallel right-ward shift in the concentrationresponse curve of methacholine and achievement of maximum response in the presence of *F. asafoetida*, which support the competitive antagonistic effect of *F. asafoetida* at muscarinic receptor. The absence of maximum response to methacholine in group 1, also suggest an inhibitory effect for the plant on histamine (H1) receptor of tracheal smooth muscles.

5. Toxic effect

A case of methemoglobinemia has been registered after intake of asafoetida in a 5 week old black male infant. He was recovered by the treatment of intravenous methylene blue from onset of tachypnea, grunting and cyanosis.⁷² Large dose intake of asafoetida can lead to swelling of the mouth, digestive illness such as flatulence and diarrhea, anxiety and headache. The intake of asafoetida is prohibited during the pregnancy.⁷³

6. Conclusion

On the basis of the available evidences in the literature, asafoetida can be used as different medicines by its phytochemical and biological activities. It is also widely used all over the world as an aroma spice in different foodstuff. Traditionally it is very much utilized for the treatment of a variety of diseases. In recent studies of pharmacological and biological activities have also shown that asafoetida acquire numerous activities such as a relaxant, neuroprotective, memory enhancing, digestive enzyme, antioxidant, antispasmodic, hypotensive, hepatoprotective, antimicrobial, anticarcinogenic, anticancer, anticytotoxicity, antiobesity, anthelmintic and antagonistic effect. Even though Asafoetida has very good medicinal significance, detailed studies are also very much needed.

Conflict of interest

None declared.

References

- Pruthi JS. Spices and Condiments: Chemistry, Microbiology, Technology. New York: Academic Press; 1980.
- Srinivasan K. Role of spices beyond food flavouring: nutraceuticals with multiple health efforts. *Food Rev Int*. 2005;21:167–188.
- Srinivasan K. Spices for taste and flavour: nutraceuticals for human health. In: De AK, ed. Spices: The Elixir of Life. New Delhi, India: Original Publications; 2011:43–62
- 4. Srinivasan K. Dietary spices as beneficial modulators of lipid profile in conditions of metabolic disorders and diseases. *Food Funct*. 2013;4:503–521.
- 5. Sahebkar A, Iranshahi M. Biological activities of essential oils from the genus *Ferula (Apiaceae). Asian Biomed.* 2010;4:835–847.
- Iran Herbal Pharmacopeia Edition Committee. Iran Herbal Pharmacopeia. Ministry of Health & Medical Education, Food and Medicine Deputy Office Publication; 2002.
- 7. Duan H, Takaishi Y, Tori M, et al. Polysulfide derivatives from Ferula foetida. *J Nat Prod.* 2002;65:1667–1669.
- 8. Takeoka G. Volatile constituents of Asafoetida. In: Takeoka GR, Guntert M, Engel K-H, eds. *Aroma Active Compounds in Foods*. Washington, DC: American Chemical Society; 2001:33–44.
- 9. Lee CL, Chiang CL, Cheng LH, Liaw CC, et al. Influenza A (H1N1) antiviral and cytotoxic agents from *Ferula asafoetida*. J Nat Prod. 2009;72:1568–1572.
- Mahendra P, Bisht S. Ferula asafoetida: traditional uses and pharmacological activity. Pharmacogn Rev. 2012;6:141–146.
- Al-Jafari AH, Vila R, Freixa B, Costa J, Canigueral S. Antifungal compounds from the rhizome and roots of F. hermonis. Phytother Res. 2012. http://dx.doi.org/ 10.1002/ptr.4806.
- 12. Dehpour AA, Ebrahimzadeh MA, Fazel NS, Mohammad NS. Antioxidant activity of the methanol extract of *Ferula asafoetida* and its essential oil composition. *Grasas Aceites*. 2009;60:405–412.
- Kavoosi G, Rowshan V. Chemical composition, antioxidant and antimicrobial activities of essential oil obtained from *Ferula asafoetida* oleo-gum-resin: effect of collection time. *Food Chem.* 2013;138:2180–2187.
- Shrivastava V, Bhardwaj U, Sharma V, Mahajan N, Sharma V, Shrivastava G. Antimicrobial activities of Asafoetida resin extracts (a potential Indian spice). J Pharm Res. 2012;5:5022–5024.
- Divya K, Ramalakshmi K, Murthy PS, Rao LJM. Volatile oils from Ferula asafoetida varieties and their antimicrobial activity. LWT Food Sci Technol. 2014;59:774–779.
- Padhy S, Rai S, Lamba NNHK, Upadhyay M. Spices as potent antibacterial agents against Staphylococcus aureus. ARPN J Sci Technol. 2014;4:46–51.
- 17. Patil SD, Shinde S, Kandpile P, Jain AS. Evaluation of antimicrobial activity of asafoetida. Int J Pharm Sci Res. 2015;6:722–727.
- Bhatnager R, Rani R, Dang AS. Antibacterial activity of Ferula asafoetida: a comparison of red and white type. J Appl Biol Biotechnol. 2015;3:18–21.
- Kamble VA, Patil SD. Spice-derived essential oils: effective antifungal and possible therapeutic agents. J Herbs Spices Med Plants. 2008;14:129–143.
- 20. Rani A, Jain S, Dureja P. Synergistic fungicidal efficacy of formulations of neem oil, nicotinic acid and *Ferula asafoetida* with α, β-unsaturated carbonyl compounds against *Sclerotium rolfsii* ITCC 5226 & Macrophomina phaseolina ITCC 0482. J Pestic Sci. 2009;34:253–258.
- Angelini P, Pagiotti R, Venanzoni R, Granetti B. Antifungal and allelopathic effects of asafoetida against *Trichoderma harzianum* and *Pleurotus* spp. *Allelopath J.* 2009;23:357–368.
- Mostafa Z, Soheil P, Mahdi J, Mahmoodi S. Antifangal effects of asafoetida seed essential oil on *in vitro* growth of five species of plant pathogenic fungi. *Int Res J Appl Basic Sci.* 2013;4:1159–1162.
- 23. Saleem M, Alam A, Sultana S. Asafoetida inhibits early events of carcinogenesis: a chemopreventive study. *Life Sci.* 2001;68:1913–1921.
- 24. Abu-Zaiton AS. Anti-diabetic activity of *Ferula asafoetida* extract in normal and alloxan-induced diabetic rats. *Pak J Biol Sci.* 2010;13:97–100.
- 25. Mallikarjuna GU, Dhanalakshmi S, Raisuddin S, Ramesha Rao A. Chemomodulatory influence of *Ferula asafoetida* on mammary epithelial differentiation, hepatic drug metabolizing enzymes, antioxidant profiles and *N*-methyl-*N*nitrosourea-induced mammary carcinogenesis in rats. *Breast Cancer Res Treat*. 2003;81:1–10.
- **26.** Fatehi M, Farifteh F, Fatehi-Hassanabad Z. Antispasmodic and hypotensive effects of *Ferula asafoetida* gum extract. *J Ethnopharmacol.* 2004;91:321–324.
- 27. Bagheri SM, Hejazian SH, Dashti-R MH. The relaxant effect of seed's essential oil and oleo-gum-resin of *Ferula asafoetida* on isolated rat's ileum. *Ann Med Health Sci Res.* 2014;4:238–241.
- Khazdair MR, Boskabady MH. The relaxant effect of *Ferula asafoetida* on smooth muscles and the possible mechanisms. *J HerbMed Pharmacol*. 2015;4: 40–44.
- 29. Tayeboon GS, Tavakoli F, Hassani S, Khanavi M, Sabzevari O, Ostad SN. Effects of Cymbopogon citratus and Ferula asafoetida extracts on glutamate-induced neurotoxicity. In vitro Cell Dev Biol-Anim. 2013;49:706–715.

- Moghaddama M, Farhadi N. Influence of environmental and genetic factors on resin yield, essential oil content and chemical composition of *Ferula asafoetida L.* populations. J App Res Med Aromat Plants. 2015;2:69–76.
- Kumar P, Singh DK. Molluscicidal activity of Ferula asafoetida, Syzygium aromaticum and Carum carvi and their active components against the snail Lymnaea acuminata. Chemosphere. 2006;63:1568–1574.
- Iranshahy M, Iranshahi M. Traditional uses, phytochemistry and pharmacology of asafoetida (*Ferula asafoetida* oleo-gum-resin) – a review. J Ethnopharmacol. 2011;134:1–10.
- **33.** Iranshahi M, Amin G, Salehi Sourmaghi M, Shafiee A, Hadjiakhoondi A. Sulphur-containing compounds in the essential oil of the root of *Ferula persica* willd. var. *persica. Flavour Frag J.* 2006;21:260–261.
- 34. Appendino G, Tagliapietra S, Mario Nano G, Jakupovic J. Sesquiterpene coumarin ethers from asafetida. *Phytochemistry*. 1993;35:183–186.
- Appendino G, Maxia L, Bascope M, et al. A meroterpenoid NF-κB inhibitor and drimane sesquiterpenoids from asafetida. J Nat Prod. 2006;69:1101–1104.
 Kaiimoto T, Vabiro K, Nobara T, Sesquiterpenoid and disulphide derivatives
- Kajimoto T, Yahiro K, Nohara T. Sesquiterpenoid and disulphide derivatives from Ferula asafoetida. Phytochemistry. 1989;28:1761–1763.
- Nassar MI, Abu-Mustafa EA, Ahmed AA. Sesquiterpene coumarins from Ferula asafoetida L. Pharmazie. 1995;10:766–767.
- Caglioti L, Naef H, Arigoni D, Jeper O. Zur Kenntnis der Sesquiterpene und Azulene. 126. Mitteilung. Über die Inhaltsstoffe der Asa foetida I. Farnesiferol A. Helv Chim Acta. 1958;41:2278–2292.
- Caglioti L, Naef H, Arigoni D, Jeper O. Zur Kenntnis der Sesquiterpene und Azulene. 127. Mitteilung. Über die Inhaltsstoffe der Asa foetida II. Farnesiferol B und C. Helv Chim Acta. 1959;42:2557–2570.
- Banerji A, Mallick B, Chatterjee A, Budzikiewicz H, Breuer M. Assafoetidin and ferocolicin, two sesquiterpenplatoid coumarins from *Ferula asafoetida* regel. *Tetrahedron Lett.* 1988;29:1557–1560.
- **41.** Abd El-Razek MH, Ohta S, Ahmed AA, Hirata T. Sesquiterpene coumarins from the roots of *Ferula asafoetida*. *Phytochemistry*. 2001;58:1289–1295.
- **42.** Hofer O, Widhalm M, Greger H. Circular dichroism of sesquiterpeneumbelliferone ethers and structure elucidation of a new derivative isolated from the gum resin "Asa Foetida". *Monatsh Chem.* 1994;115:1207–1218.
- **43.** Buddrus J, Bauer H, Abu-Mustafa E, et al. Foetidin, a sesquiterpenoid coumarin from *Ferula asafoetida*. *Phytochemistry*. 1985;24:869–870.
- 44. Rajanikanth B, Ravindranath B, Shankaranarayana ML. Volatile polysulphides of asafoetida. *Phytochemistry*. 1984;23:899–900.
- Abd El-Razek MH. A new ester isolated from Ferula asafoetida L. Biosci Biotechnol Biochem. 2007;71:2300–2303.
- 46. Christensen LP, Brandt K. Bioactive polyacetylenes in food plants of the Apiaceae family: occurrence, bioactivity and analysis. J Pharm Biomed Anal. 2006;41:683–693.
- Pangarova TT, Zapesochnaya GG. Flavonoids of Ferula asafoetida. Chem Nat Compd. 1975;9:768.
- Zargari A. Medicinal Plants. Sixth ed. Tehran: Tehran University Publications; 1996.
- 49. Gholamnezhad Z, Byrami G, Boskabady MH, Iranshahi M. Possible mechanism(s) of the relaxant effect of asafoetida (*Ferula asafoetida*) oleo-gum-resin extract on guinea-pig tracheal smooth muscle. Avicenna J Phytomed. 2012;2: 10–16.
- Bayrami G, Boskabady MH, Iranshahi M, Gholamnezhad Z. Relaxant effects of asafoetida extract and its constituent umbelliprenin on guinea-pig tracheal smooth muscle. *Chin J Integr Med*. 2013:1–6.
- Moghadam FH, Dehghan M, Zarepur E, et al. Oleo gum resin of *Ferula asafoetida* L. ameliorates peripheral neuropathy in mice. J Ethnopharmacol. 2014;154: 183–189.
- 52. Vijayalakshmi, Adiga S, Bhat P, Chaturvedi A, Bairy KL, Kamath S. Evaluation of the effect of *Ferula asafoetida* Linn. gum extract on learning and memory in Wistar rats. *Indian J Pharmacol.* 2012;44:82–87.
- Bagheri SM, Dashti-R MH. Influence of asafoetida on prevention and treatment of memory impairment induced by p-galactose and NaNO₂ in mice. Am J Alzheimers Dis Other Demen. 2015;30:607–612.
- 54. Platel K, Srinivasan K. Influence of dietary spices and their active principles on pancreatic digestive enzymes in albino rats. *Nahrung*. 2000;44:42–46.
- Ramakrishna Rao R, Platel K, Srinivasan K. In vitro influence of spices and spiceactive principles on digestive enzymes of rat pancreas and small intestine. Nahrung. 2003;47:408–412.
- Dandagi PM, Patil MB, Mastiholimath VS, Gadad AP, Dhumansure RH. Development and evaluation of hepatoprotective polyherbal formulation containing some indigenous medicinal plants. *Indian J Pharm Sci.* 2008;70:265–268.
- Sitara U, Niaz I, Naseem J, Sultana N. Antifungal effect of essential oils on in vitro growth of pathogenic fungi. Pak J Bot. 2008;40:409–414.
- El Deeb HK, Al Khadrawy FM, Abd El-Hameid AK. Inhibitory effect of Ferula asafoetida L. (Umbelliferae) on Blastocystis sp. subtype 3 growth in vitro. Parasitol Res. 2012;111:1213–1221.
- Unnikrishnan MC, Kuttan R. Tumour reducing and anticarcinogenic activity of selected spices. *Cancer Lett.* 1990;51:85–89.
- Panwar R, Rana S, Dhawan DK, Prasad KK. Chemopreventive efficacy of different doses of *Ferula asafoetida* oleo-gum-resin against 1,2-dimethylhydrazine (DMH) induced rat colon carcinogenesis. *J Phytopharm*. 2015;4: 282–286.
- Sepahi E, Tarighi S, Ahmadi FS, Bagheri A. Inhibition of quorum sensing in *Pseudomonas aeruginosa* by two herbal essential oils from *Apiaceae* family. *J Microbiol.* 2015;53:176–180.

- Akhlaghi F, Rajaei Z, Hadjzadeh M, Iranshahi M, Alizadeh M. Antihyperglycemic effect of asafoetida (*Ferula asafoetida* oleo-gum-resin) in streptozotocininduced diabetic rats. World Appl Sci J. 2012;17:157–162.
- 63. Cha M-R, Choi YH, Choi CW, et al. Galbanic acid, a cytotoxic sesquiterpene from the gum resin of *Ferula asafoetida*, blocks protein farnesyltransferase. *Planta Med.* 2011;77:52–54.
- 64. Korashy HM, Al-Jenoobi FI, Raish M, et al. Impact of herbal medicines like Nigella sativa, Trigonella foenum-graecum, and Ferula asafoetida, on cytochrome P450 2C11 gene expression in rat liver. Drug Res. 2015;65:366–372.
- Bagheri SM, Sahebkar A, Gohari AR, Saeidnia S, Malmir M, Iranshahi M. Evaluation of cytotoxicity and anticonvulsant activity of some Iranian medicinal *Ferula* species. *Pharm Biol.* 2010;48:242–246.
- 66. Azizian H, Rezvani ME, Esmaeilidehaj M, Bagheri SM. Anti-obesity, fat lowering and liver steatosis protective effects of *Ferula asafoetida* gum in Type 2 diabetic rats: possible involvement of leptin. *Iran J Diabetes Obes*. 2012;4: 120–126.

- Alqasoumi S. Anxiolytic effect of Ferula asafoetida L in rodents. J Pharmacogn Phytother. 2012;4:86–90.
- Gundamaraju R. Evaluation of anti-helmintic activity of Ferula foetida "Hing- A natural Indian spice" aqueous extract. Asian Pac J Trop Dis. 2013;3:189–191.
- Kumar P, Singh DK. In vitro anthelmintic activity of Allium sativum, Ferula asafoetida, Syzygium aromaticum and their active components against Fasciola gigantic. J Biol Earth Sci. 2014;4:B57–B65.
- Bagheri SM, Yadegari M, Porentezari M, et al. Effect of *Ferula asafoetida* oleo gum resin on spermatic parameters and testicular histopathology in male Wistar rats. J Ayurveda Integr Med. 2015;6:175–180.
- Kiyanmehr M, Boskabady MH, Khazdair MR, Hashemzehi M. Possible mechanisms for functional antagonistic effect of *Ferula asafoetida* on muscarinic receptors in tracheal smooth muscle. *Malays J Med Sci.* 2016;23:35–43.
- Kelly KJ, Nue J, Camitta BM, Honig GR. Methemoglobinemia in an infant treated with the folk remedy glycerited asafetida. *Pediatrics*. 1984;73:717–719.
- 73. Emami A, Fasihi S, Mehregan I. Medicinal Plants. Tehran: Andisheh Avar; 2010.