Research Journal of Recent Sciences _____ ISSN 2277-2502
Vol. 4**(IVC-2015),** 16-22 **(2015)** *Res. J. Recent. Sci.*

Oleo-gum-resin of *Ferula asafoetida*: A traditional culinary spice with versatile pharmacological activities

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Available online at: www.isca.in, www.isca.me
Received th 2015, revised th 2015, accepted th 2015

Abstract

Ferula asafoetida (family: Umbelliferae) is a monoecious, herbaceous, perennial plant. Oleo-gum-resin of Ferula asafoetida is exudates obtained from the rhizome of this plant. Asafoetida is inhabitant to central Asia, eastern Iran to Afghanistan. However, asafoetida is not inhabitant of India. It is grown chiefly in Afghanistan and Iran, and from these areas it is exported to the entire world. Asafoetida is in use from ancient times in Indian medicine and cookery as a spice. It is also used in folk phytomedicine since antiquity in traditional medicine for the treatment of several neurological (epilepsy, paralysis, hysterias and depression), gastrointestinal (intestinal parasites, flatulence, weak digestion, stomach ache), respiratory (influenza, asthma), and reproductive disorders (premature labour, unusually painful, difficult and excessive menstruation, leucorrhoea, and infertility). Traditionally, it has carminative, antispasmodic, digestive, aphrodisiac, emmenagogue, sedative and diuretic properties. Recently, antispasmodic and hypotensive, antinociceptive, antioxidant, anxiolytic, aphrodisiac, antiviral, antidiabetic, gastric anti-ulcer, antiseptic, nephroprotective, neuroprotective and anticancer properties are proven pharmacologically and biologically in animal models and humans. This article is an attempt to explore and assemble the various pharmacological actions of the oleo-gum-resin of Ferula asafoetida reported till date.

Keywords: *Ferula asafoetida*; Pharmacological activities; Oleo-gum-resin; Traditional medicine.

Introduction

Ferula assafoetida L. *is a monoecious, herbaceous, perennial plant* and one of the most important among the thirty species of Ferula.[1] *Hilteet* or *hing* (asafoetida) is oleo-gum-resin which is obtained from the rhizome and root of the plant *Ferula asafoetida*[2]. Asafoetida, the Latin name ferula means "carrier" or "vehicle". *Asa* is a Latinized form of Farsi *asa* "resin", and Latin foetidus means "smelling fetid". Asafoetida's English and scientific name is derived from the Persian word for resin (asa) and Latin foetida, which refers to its strong sulfurous odor. Ancient texts describe it as *hingu* and several centuries of its constant use have bestowed upon it the peculiarity of a tempting spice and trusted medicine[2]. It was described by a number of Arab and Islamic scientists and pharmacists. Ibn Sina (Avicenna) mentioned the effects of asafoetida on digestion. Ibn al-Baitar and Fakhr al-Din, al-Razi discussed some positive medicinal effects of it on the respiratory system[1]. As such *hing* has been referred as the "Food of the Gods"[3]. Asafoetida is in use from ancient times in Indian medicine and cookery as a spice. It is also used in folk phytomedicine since antiquity in traditional medicine for the treatment of several neurological (epilepsy, paralysis, hysterias and depression), gastrointestinal (intestinal parasites, flatulence, weak digestion, stomach ache), respiratory (influenza, asthma), and reproductive disorders (premature labour, unusually painful, difficult and excessive menstruation, leucorrhoea, and infertility) [2, 4, 5-12].

Vernacular names: Arabic: *Zallouh; Anjadan; Hilteet*;[5-8] *Simagh-ul-mehroos* [5, 8-11]; Assamese: *Hin.*[7] Bengali: *Hing; Hingra*[7, 11]; English: Asafoetida [7, 11]; Europeans: Devil's dung[8]; Gujarati: *Hing; Vagharni*[7, 11]; Hindi: *Hingra; Hingu* [5, 6, 7,11]; Kannada: *Higu; Ingu; Hing*[7, 11]; Marathi: *Hing; Hira*[7,11]; Oriya: *Hengu; Hingu*[7,11]; Persian: *Angoza; Angzoo; Amma; Anksar; Nagoora; Nagsatgudha.*[1, 5,11]; Punjabi: *Hing*[7]; Sanskrit: *Ramatta; Bhutnasan; Hingu; Sulansan; Bahleeka* [7, 11]; Suraini: *Halteesa*[5, 9]; Telugu: *Ingura; Inguva; Ing*[7, 11,12] ; Turkish: Şeytantersi (devil's sweat), şeytan boku (devil's shit) or şeytanotu (the devil's herb)[1]; Urdu: *Hilteet, Hing*[5-7]

Scientific Classification: Kingdom: Plantae, Division: Magnoliophyta, Class: Magnoliopsida, Family: Umbelliferae, Genus: Ferula, Species: Foetida[3].

Ethno-botanical description: *F. asafoetida* is a small perennial herb with strong carrot shaped roots 5-6 inches in diameter at the crown when 4-5 years old. To obtain the oleo-gum-resin, in the month of March and April, before the flowering start, the upper part of the root is open bare and an incision is made at the lowest part of the stem close to the crown of the root. Milky white oleo-gum-resin exudates from the incised area which hardens and turns brown on contact to air[11] which is collected after some days and fresh incision is made. The process of collection of oleo-gum-resin and making incision is repeated until root stops exudation. This period may extend up to 3

month since the first incision and yield 2 lb. or more of gum resin. Three forms of asafoetida are available in market, viz. tears, mass and paste. The tears is the purest form of oleo-gum-resin, i.e. rounded or flattened in shape and 5-30 mm. in size with greyish color. Mass asafoetida is the most common form available in the market consists of stuck tears of oleo-gum-resin and form a mass mixed with fragments soil etc. Likewise paste form also contains soil and woody matter[11]. Asafoetida has distinctive bitter taste and sulphurous pungent odour[4].

Habitat: Asafoetida is inhabitant to central Asia, eastern Iran to Afghanistan. However, asafoetida is not inhabitant of India. It is grown chiefly in Afghanistan and Iran, and from these areas it is exported to the entire world[2].

Part used: Leaves, stem, root and gum resin[12]

Action

Gum-resin: Aphrodisiac, antispasmodic, anthelmintic, carminative, diuretic, emmenagogue, expectorant, mild laxative and nervine tonic; used in croup, asthma, bronchitis; colic pain, flatulence, and spasmodic movement of the bowels and infantile convulsions; an important ingredient in compounding medicinal preparations prescribed in habitual abortion, liver troubles, indigestion, diarrhoea, flatulence; applied externally to ringworm[10-12].

Chemical constituents: *F. asafoetida* contains carbohydrates 67.8% per 100 g, moisture 16.0%, protein 4.0%, fat 1.1%, minerals 7.0% and fiber 4.1%. Its mineral contents includes iron, phosphorus, substantial calcium and vitamin contents include carotene, riboflavin and niacin. Its calorific value is 297, contains 40-64% resinous material composed of ferulic acid, umbelliferone, farnesiferols A, B, and C, asaresinotannols etc., about 25% gum composed of rhamnose, galactose, glucose, l-arabinose, and glucuronic acid and volatile oil (3-17%) [2, 13] consisting of disulfides as its major components, notably 2-butyl propenyl disulfide (E-and Z-isomers), with monoterpenes (α- and β-pinene, etc.), valeric acid, free ferulic acid, and traces of vanillin (LAF). The disagreeable odor of the oil is reported to be due mainly to the disulphide $C_{11}H_{20}S_2$[2]. It also contains triterpenoids, and saponins[12]. Asafoetida consists resin (40-64%), gum (25%) and essential oil (10-17%)[11] as three main constituents. The various sesquiterpene coumarins present in asafoetida are assafoetidnol A and assafoetidnol B. There are various newly isolated sesquiterpene coumarins which are colladonin, 8-acetoxy-5- hydroxyumbelliprenin, epi-conferidone, karatavicinol, and asacoumarin free ferulic acid is present in the oleo-gum-resin. Free umbelliferone is absent in the drug which is a unique characteristic as compared to galbanum. Ferulic acid action with hydrochloric acid is changed into umbellic acid that further looses water to form umbelliferone. Galbanic acid is also one of the usually present sesquiterpene in resin portion of the drug[3].

Current biological and pharmacological studies have also shown several properties including antifungal, antioxidant, antidiabetic, antispasmodic, anticancer, hypotensive etc from oleo-gum-resin[4].

Current biological and pharmacological studies

Neuro-pharmacological studies: Anxiolytic, analgesic and sedative effect: Alqasoumi studied the anxiolytic, analgesic and sedative properties of asafoetida in rodents, using elevated plus maze, hole-board test as models of anxiety, hot plate, and locomotor motor activity meter for analgesic and sedative activity. He used diazepam as a reference anxiolytic agent. The results showed a dose-dependent anxiolytic and analgesic activity of aqueous extract of asafoetida, with a mild sedative effect in high doses in rodents at dose of 250mg/kg and 500mg/kg. He found peak analgesic effect after 60 min of drug administration. The author concluded that compared to diazepam, the asafoetida seems to be a better alternative for the treatment of anxiety disorders. However, further experimental and clinical studies are warranted to accurately assess its safety and efficacy for treatment of chronic anxiety[4].

Antinociceptive effect: The analgesic activity of asafoetida (25, 50 and 100 mg/kg) was compared with that of sodium diclofenac (30 mg/kg) or morphine sulfate (8 mg/kg) by using hot plate and acetic acid induced writhing tests. The authors found that asafoetida reduced the number of acetic acid induced writhes in an inverse dose dependent manner [lower (25 mg/kg) and moderate (50 mg/kg) doses] produced an analgesic effect comparable to that of the sodium diclofenac. A considerable effect of the asafoetida at all doses were found 15 min after treatment in the hot plate test and in general analgesic pattern of the most effective dose (50 mg/kg) was very comparable to morphine sulfate. They assumed that the analgesic effect of asafoetida was because of its action to the inhibit production/action of prostaglandins or to its action on visceral receptors sensitive to acetic acid. Hence, the analgesic effect of asafoetida in hot plate test may be correlated to the opioid pain inhibitory pathways[13]. Further the authors discussed that the antinociceptive activity of asafoetida may be due to the phenolic compounds such as ferulic acid which are present in a high contents in asafoetida[14]. One probable mechanism of action for the active principles of this oleo-gum-resin could be linked to lipooxygenase and/or cyclooxygenase in the arachidonic acid flow at the peripheral route. Umbelliprenin of asafoetida can inhibit the activity of 5-lipooxygenase and shows the anti-inflammatory action[15] as it has been established that sesquiterpene coumarins are the most bioactive components of asafoetida[16] and Umbelliprenin is one of sesquiterpene coumarin. The authors concluded that asafoetida exhibited a significant antinociceptive effect on chronic and acute pain in mice which most likely involves central opioid pathways and peripheral anti-inflammatory action[13].

Neuroprotective effect: Moghadam et al., studied the neuroprotective and neurotoxic effects of aqueous extract of gum-resin of asafoetida. The results demonstrated that asafoetida gum resin predominantly with 0.01 and 1 µg/ml concentrations showed improvement in survival rate of neurons, whereas 10 µg/ml was toxic[17]. Further the authors discussed that neuroprotective effects could be ascribed to presence of flavonoids, phenolic acids, and polysulfide compounds. Several mechanisms are elucidated for antioxidative effects of the aforementioned compounds. Certain flavonoids could inhibit Nitric oxide (NO) production by reducing inducible nitric oxide synthase (iNOS) expression and previous reports also showed surviving effect of polysulfide compounds on neurons derived from mouse embryo. The principal mode of neuroprotection of sulfur containing neutraceuticals is via activation of endogenous antioxidant systems, including gene targets of the Nrf2/ARE (Nrf2-antioxidant response element) transcription factor pathway. In addition, various other components are also neuroprotective such as sodium ferulate, sesquiterepene coumarins, and ferulic acid. Ferulic acid may perhaps improve survival rate of neurons through inhibiting ICAM-1 mRNA expression. Hence, inhibition of NO production by sesquiterepenes and flavonoids powerfully removes NO from microenvironment and augments endurance of neurons in culture. The authors concluded that gum-resin of asafoetida improves survival rate and has neuroprotective effect on neurons in low doses, however in higher concentrations it is toxic for neurons[17].

Nerve stimulant and neuroprotective activity: The researchers investigated *in-vitro* and *in-vivo* studies to identify response of isolated sciatic nerves to different concentrations of oleo-gum-resin of asafoetida solved in Lock′s solution and to evaluate its effect on amelioration of peripheral neuropathy in mice respectively. Peripheral neuropathy was induced by intraperiotoneal injection of high doses of pyridoxine in adult Balb/c male mice. Tail flick tests were performed to identify the incidence of neuropathy in animals. After 10 days treatment with asafoetida, the efficiency of treatment was assessed by behavioral, electrophysiological and histological studies. The authors found that *in-vitro* experiments established that incubating the nerves in oleo-gum-resin aqueous extract 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. They concluded that in vitro experiments showed that use of asafoetida in neuropathic mice exerted neuroprotecting effects via stimulating axonal regeneration, remyelination and decrement of lymphocyte infiltration[18] because of nerve stimulant effect.

Effect on cardio-vascular system

Antihypertensive effect: Dried gum-resin water extract of asafoetida at different doses, intravenously to dogs, showed antihypertensive activity. Another study showed that intravenously tincture of the gland to rabbits, produced significant hypotensive effects[2]. Fatehi et al., studied the effects of *F. asafoetida* gum extract on the mean arterial blood pressure of Sprauge Dawley rat. The extract (0.3-2.2 mg/100g body weight) considerably reduced the mean arterial blood pressure in anaesthetised rats. The authors concluded that the extract of asafoetida impedes with a variety of adrenergic, muscarinic, and histaminic receptor activities or with the mobilisation of calcium ions required for smooth muscle contraction non-specifically thereby have relaxant activity[19].

Effect on blood vessels and blood: Water extract of the dried gum resin showed vasodilation effect in frogs. Significant smooth muscle relaxant effect was observed when administered to rabbits probably helpful in lowering the blood pressure[2].

Anti haemolytic effect: Water extracts of the gum at variable doses, administered intravenously to dogs and rats, showed anti-coagulant activity. Ether extracts of the dried gum and gum resin showed fibrinolytic activity in 10 healthy subjects [2].

Effect on gastrointestinal tract

Antispasmodic effect: Fatehi et al., studied antispasmodic effect of gum extract of *F. asafoetida* on the isolated guinea-pig ileum. The average amplitude of spontaneous contractions of the isolated guinea-pig ileum was decreased to 54 ± 7% of control at dose of 3 mg/ml extract. Further they noted that gum extract of *asafoetida* caused relaxation in a concentration-dependent manner of precontracted ileum by acetylcholine (10 microM). Likewise relaxatory effect of extract on the precontracted ileum by histamine (10 microM) and KCl (28 mM) was also observed [19].

Anti-helmintic effect: Gundamaraju studied anti-helmintic activity of aqueous extract of resin against *Pheretima postuma.* Extract at concentration of 25, 50 and 100mg/ml were studied. Piperazine citrate and distilled water was used as standard reference and control respectively in the same concentration as that of extracts. The outcome involved to determine time of paralysis and time of death of the worm. The author found that the extract exhibited significant anti-helmintic activity at the highest concentration of 100 mg/ml and showed considerable activity compared with standard. The extract confirmed paralysis (aqueous extract 6 min) as well as death (aqueous extract 18 min) of worms at a time similar to piperazine citrate (paralysis 8 min and death 20 min) in particular at higher concentration. Polyphenolic compounds (tannins) shows anthelmintic effect. Various synthetic phenolic anthelmintics compounds uncouples oxidative phosphorylation thereby interferes with energy generation in helminth parasites. The phenolic anthelmintics compounds are niclosamide, oxyclozanide and bithionol. The author postulated that tannins contained in the extracts of *F. foetida* produced analogous effects and further they can also bind to free protein in the gastrointestinal tract of host animals[20].

Antiulcerogenic effect: Alqasoumi et al., investigated the anti-ulcerogenic property of an aqueous suspension of asafoetida in ulcer models on Wistar albino rats. They reported that gastric ulceration induced by indomethacin, basal gastric acid secretion, and noxious chemicals was significantly improved with the suspension at doses of 250 and 500 mg/kg body weight, orally (i.p. in Shay rat model). Further, histopathological evaluation of gastric tissue and by the determination of gastric wall mucus (GWM) contents of the stomach also supported these results, as these factors showed protection of various indices and replenishing the depleted (GWM) level by the suspension treatment, respectively. Authors discussed it is not well know that which chemical constituents of asafoetida are accountable for gastroprotective activity. However, previous researches reported that asafoetida contains resinous material that consists of ferulic acid, other flavonoidal glycosides and coumarins. Ferulic acid is known to exert antioxidant activity by reducing vascular disorders in humans by strengthening the membranes It is well recognized that antioxidants play an significant role in preventing gastric mucosal damage by strong cell defence mechanisms, likely to stimulate the endogenous synthesis of prostaglandins or by a protective role as a membrane stabilizing agent and act by scavenging oxygen free radicals. Further, authors discussed that anticholinergic drugs shows inhibition of acid secretion and slow gastric motility and possibly this might be the one of the mechanism(s) by which the suspension of asafoetida offers its ulcer protective effect. In addition, many of the orally effective cytoprotective agents act by increasing generation of prostaglandins because of mild irritant action, a observable fact which has been described as 'adaptive cytoprotection'. The authors concluded that the ulcer protective effect of asafoetida may perhaps because of its anti-secretory action, antioxidative and cytoprotective through a prostaglandin mediated mechanism[21].

Hepatoprotective effect: Dandagi et al., (2008) explored the hepatoprotective effect of *Ferula asafoetida*, *Momordica charantia* Linn and *Nardostachys jatamansi* various extracts against experimental hepatotoxicity induced by carbon tetrachloride in Wister rats. Suspending agent and other excipients were used to prepare polyherbal suspensions by the trituration method. Polyherbal suspensions in comparison to LIV-52 (standard) was investigated for both physicochemical and hepatoprotective activity. The authors concluded that tested formulation (containing aqueous extracts, petroleum ether, and chloroform of *F. asafetida*, ethanol extracts and petroleum ether of *M. charantia* and *N. jatamansi*) confirmed significant hepatoprotective activity because of combined effect of all these extracts[22].

Respiratory system

Relaxant effect: Gholamnezhad et al., (2011) investigated the relaxant effects of the asafoetida on tracheal smooth muscle of guinea pigs and its probable mechanism(s). The relaxant effects of three cumulative concentrations of the aqueous extract (2, 5 and 10 mg/ml), theophylline (0.25, 0.5 and 0.75 mM) and saline were examined on non-incubated tracheal smooth muscle of guinea pig precontracted by 10 μM methacholine (group 1); preincubated tissues by propranolol and chlorpheniramine, contracted by methacholine (group 2) and preincubated tissues by propranolol, contracted by methacholine (group 3). They reported that all concentrations of theophylline in group 1 and all concentrations of the extract in the other three groups showed significant relaxant effects compared to saline. Authors discussed that results of this study demonstrated that the therapeutic effect described for asafetida on asthma disease perhaps because of its relaxant effect causing bronchodilation. The probable mechanism of action of this drug is because of a muscarinic receptor blockade and a small contribution of histamine (H1) receptor inhibitory property of asafoetida and on other hand, β-adrenoceptor stimulation effect of the extract did not contribute to its relaxant effect. Authors concluded that asafoetida showed a relaxant effect on tracheal smooth muscle of guinea pigs which was comparable to that of theophylline, which is possibly due to muscarinic receptor blockade[23].

Genito-Urinary System

Aphrodisiac effect: Kassis et al., (2009) in their study, investigated the safety and efficacy of extracts from *F. asafoetida* L in enhancing male libido on male fertility and sexual functioning in rats and in man. They reported high levels of safety of Masculine on rats with LD 50 of 5 g/kg and cultured human fibroblasts. Further, antioxidant properties were significant at a concentration of 50μg/ml both in rat liver cells and in human sperm cells. They also observed that Masculine is a potent vasodilator because of endothelial mediated effect. Significant augmentation of episodes of penile erection was observed in Masculine treated group of rats.

Moreover, in human experiment, the first group (n = 60) consists patients of incomplete azospermia which was medically untreatable, and the second group (n = 25) consists patients of erectile dysfunction and impotence of no treatable cause. Patients were recruited from fertility clinics and administered one Masculine tablet daily for 3 months. No side effects were reported and were well tolerated by all men. The results showed after two months of treatment quantitative and qualitative improvements of sperm counts in 17% in first group and 60% in the second group. Moreover, 60% of the second group showed notable improvements in both their libido and erectile function. Authors discussed that Masculine is a sexual tonic, and safe. Masculine extract has an endothelial-mediated action and a secondary direct effect on arterial smooth muscle cells. Asafoetida gum extracts, *in-vitro* have shown to interfere with various adrenergic, muscarinic and histaminic receptor activities. Asafoetida sesquiterpene coumarines may act like Ferula hermonis sesquiterpenes (ferutinin, teferdin, and tenuferidine) that have been shown to have estrogenic activity, and may contribute to its aphrodisiac activity[24].

Anti-infertility effect: Methanol extract of the resin, orally at a dose of 400 mg/ kg daily for 10 days, administered to Sprague–Dawley rats prevented pregnancy in 80% of the rats. Mean number of implantations were markedly reduced by lower doses of the extract [2].

Nephroprotective effect: Javaid et al., (2012) investigated the nephroprotective effects of *F. foetida* extracts on gentamicin-treated rats. In rats, serum creatinine, blood urea nitrogen (BUN), and thiobarbituric acid reacting substances (TBARS), as an indicator of renal disorder were markedly increased on subcutaneous administration with Gentamicin (100 mg/kg). The rise in blood urea nitrogen (BUN), serum creatinine and TBARS in rats were inhibited by eight days treatment of methanol soluble (70 mg/kg) and insoluble (350 mg/kg) fractions of *F. foetida*, including gentamicin administration on 4th day. Further, both doses showed similar effect. Further, post treatment the histopathological evaluation of the gentamicin-treated rat kidney tissues demonstrated marked reduction in peritubular congestion, glomerular congestion, tubular casts, blood vessel congestion, epithelial desquamation, interstitial edema and inflammatory cells. This proves nephroprotective effect of asafoetida[25].

Effect on Endocrine System

Anti-obesity effect: Azizian et al., (2012) conducted a study to find out the effect of *Ferula asafoetida* on weight gain, fat accumulation, liver steatosis and leptin level. Rats of control and treatment groups received daily tap water (P.O) as vehicle mixed with fructose 10%. Two treatment groups received oleo-gum resin of asafoetida at doses of 25 or 50 mg/kg (P.O). Normal rats received only tap water and standard chow food. Body weights, abdominal fat, size of epididymal adipocyte and serum leptin were recorded. Authors reported that administration of *F. asafoetida* notably decreases body weights, abdominal fat and size of epididymal adipocyte compared to untreated rats. Further serum leptin levels were also significantly decreased in treated rats and are associated with protective effects of *Ferula asafoetida* in obese diabetic rats. Authors discussed that asafoetida may perhaps decrease adipocyte proliferation in fat tissue such as abdominal area and reduce obesity. Previous studies reported that asafoetida administration at dose of 50 mg/kg shown anti-hyperglycemic however, antihyperlipidemic effects was not reported in streptozotocin diabetic rats. As antioxidative agents are implicated in attenuating the diabetes symptoms, the anti-diabetic, anti-obesity and liver seatosis preventing effects may be partly mediated by the phenolic acids such as ferula, tannins and umbelliprenin that present in the ferula gum. They concluded that *F. asafoetida* extract has anti-obesity, fat lowering effects and can prevent liver steatosis in type 2 diabetic rats[26].

Anti-diabetic effect: Akhlaghi et al., (2012) investigated the hypoglycemic activity of the asafoetida extract in streptozotocin induced diabetic rats. Male Wistar rats were randomly divided into control, diabetic and diabetics treated with the asafoetida extract at doses of 50, 100 and 300 mg/kg (5 groups). The animals were rendered diabetic by a single intraperitoneal injection of 60 mg/kg streptozotocin. The blood glucose and lipids were spectrophotometrically measured in all groups at weeks 0 (before diabetes induction), 2 and 4. Diabetic rats received the asafoetida extract daily in drinking water for 4 weeks. Diabetic rats showed an elevated serum glucose level over those of control rats at weeks 2 and 4. Treatment of diabetic rats with the asafoetida extract at dose of 50 mg/kg significantly lowered the serum glucose concentration in comparison to diabetic rats. Diabetes induction for 4 weeks did not change the triglyceride, total cholesterol and HDL-cholesterol concentrations in diabetic rats compared to controls concerned with serum lipids. Authors concluded that the asafoetida extract administration at dose of 50 mg/kg for 4 weeks showed hypoglycemic activity in streptozotocin-diabetic rats during 2 week and at the end of 4 week of treatment period. The authors discussed the probable mechanism of hypoglycaemic in diabetic rats might be because of potentiating the insulin release, which is also confirmed from previous reports.

This effect can be explained at least in part by the presence of the phenolic acids (ferulic acid) and tannins in the extract. Ferulic acid exerts its hypoglycaemic activity by increase plasma insulin level, antioxidant property. This decreased oxidative stress on the pancreas may help the beta cells to proliferate and secrete more insulin. Ferulic acid also inhibits the activity of alpha glucosidase that converts carbohydrates into monosaccharides that result in a high glucose level in diabetic subjects. Further, ferulic acid also increases the activity of glucokinase that facilitates the phosphorylation of glucose to glucose-6-phosphate. Moreover, the authors also discussed that tannin have shown antidiabetic activity[27].

Abu-Zaitun et al., (2010) have found that the injection of asafoetida extract for 14 days at a dose of 0.2 g/kg had the hypoglycemic and hyperinsulinemic effects on alloxan –diabetic rats[28].

Another study conducted by Helal et al., (2005) also reported hypoglycemic and hyperinsulinemic effects of Ferula (100mg/kg orally for 1 month) in alloxan induced diabetes[29].

Antihyperlipidemic effect: A hot mixture of *C. myrrha, N. sativa, F. asafoetida, Aloe vera,* and *B. serrata,* at a dose of 0.5 g/kg administered by gastric intubation to rats for 7 days has shown antihyperlipidemic activity against streptozotocin-induced hyperglycemia[30].

Anti-infective effect

Antifungal effect: Antifungal activity of oleo-gum-resin asafoetida was confirmed by different studies against *M. gypseum T. interdigitale,* and *A. parasiticus.*

Anti-Microbial effect: Aqueous and alcoholic extracts of asafoetida have showed anti-microbial activity e against various bacterial and fungal strains like *C. albicians, E. coli, S. aureus, B. subtilis, P. aeruginosa,* and *P. chrysogenum* by agar well diffusion method[3].

Antiviral effect: Three sesquiterpene coumarins badrakemin acetate (1), kellerin (2) and samarcandin diastereomer (3) were isolated from the gum resin of *F. asafoetida*. A comparative evaluation of cytotoxicity and antiviral activity showed that kellerin (2) could significantly inhibit the cytopathic effects and reduce the viral titre of the herpes virus type 1 (HSV-1) DNA viral strain KOS at concentrations of 10, 5 and 2.5 µg/ml[31].

Miscellaneous

Wound healing effect: This study investigated the wound healing property of aqueous extract of *F. asafoetida's* resin of diabetic ulcers in wister rats. Wistar rats (n=18) were divided into the normal control (1), diabetic control (2) and diabetics treated with aqueous extract of *F. assafoetida's* resin groups. Four wounds (4mm) were created in two lateral posterior parts of body in all groups. Topical treatment by extract and normal saline was applied 3 times a day for 2 days in experimental and control group respectively. Inflammatory cells, re-epithelization and vascularization were evaluated on the 4th, 8th and 10th day. The authors observed that average thickness of the epithelium, density of inflammatory cells and blood vessels increased significantly in groups 1 and 3. They concluded that aqueous extract of *F. asafoetida's* resin has a immense influence on the healing of diabetic ulcers by increasing epithelium[32].

Chemopreventive effect: A notable effect as cytotoxic agents for tumor cells was shown by the aqueous and alcoholic extracts of asafoetida, cardamom cinnamon, and ginger. Crude extract of asafoetida showed the maximum inhibitory effect as compared to the other[33]. The countries like Japan, Russia, China, Indonesia, where the asafoetida usage is not common, the rate of cancer is quite higher in the comparison of other countries as asafoetida has the ability to prevent the increasing incidences of cancer. The use of *F. asafoetida* also reduces the probability of side effects cause by allopathic treatment of cancer[34].

Anti-oxidant effect: Ferulic acid and umbellifedrone present in asafoetida are responsible for antioxidant activity. Aqueous and ethanol extracts of the leaf, stem and flower have been proven for antioxidant activity[3].

Acute toxicity: Asafoetida at doses used in the present study did not show any short or long term toxic effect. This was evidenced by the absence of tremor, paralysis, weight loss and autonomic behavioral changes in comparison with control group. Also there was no mortality in treated animals during 10 days of observations [13]. *F. asafoetida* solution up to a maximum dose of 2 g/kg was found to be safe, as the mice did not show any symptoms of toxicity and mortality during a period of 14 days of observation[4].

Conclusion

F. asafoetida is an old age herb especially used in Unani and Ayurvedic medicines in the treatment of several neurological, gastrointestinal, respiratory and reproductive disorders. Recent studies have proven that asafoetida have several activities such as neuroprotective, antispasmodic, antiulcerogenic, hepatoprotective, hypotensive, relaxant, nephroprotective, antiviral, antifungal, chemopreventive, antidiabetic and antioxidant. Aforementioned pharmacological activities of asafoetida are attributed to its phyto-chemical constituents such as saponins, steroids, glycosides, phenolic compounds such as tannins and flavonoids. However, clinical trials are scarce; therefore randomized controlled trials are recommended further to prove these actions of asafoetida in human.

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