HING (Ferula foetida Regel): A potent Unani Herb with its descriptive parameters of pharmacognosy and pharmacology: A Review

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ABSTRACT

Hing (Family- Umbelliferae) or asafoetida is the latex obtained from living rootstocks or taproots of several species of Ferula, e.g. F. alliaceae Boiss, F. rubricaulis Boiss, F. asafoetida Linn and F. narthe Boiss found in central Asia. Asafoetida occurs in three forms, viz Tears, Mass and Paste. Hing has shown diverse biological and pharmacological activities. It has been used in Unani Medicine (Tibb-e-Unani) and other Traditional Systems of Medicine from time immemorial and it is described as diuretic, anti-diabetic, emmenagogue etc. The present review highlights the botanical description, traditional uses, pharmacognosical features, pharmacological properties and pharmacological studies conducted on this medicinal plant used in Unani system of medicine.

Keywords: Hing; Ferula foetida; Unani Medicine; Traditional Uses; Pharmacological Properties

INTRODUCTION

Hing (Family- Umbelliferae) is the latex obtained from living rootstocks or taproots of several species of Ferula, e.g. F. alliaceae Boiss, F. rubricaulis Boiss, F. asafoetida Linn and F. narthe Boiss found in central Asia. Ferula asafoetida Linn. is a main source of Hing or asafoetida. It is an oleo-gum resin of medicinal and nutritional importance having a strong, tenacious and sulfurous odor. Asafoetida has been consumed as a spice and a folk medicine for centuries. Hing is a coarse umbelliferous plant growing up to 7 feet high, large fleshy root covered with bristly filares, stem 6 to 10 feet, numerous stem leaves with wide sheathing petioles; flowers pale greeny yellow, fruit oval, flat thin, fuleaceous, reddish brown with pronounced vittae, it has a milky juice and a strong foetid odor. Asafoetida occurs in three forms, viz Tears, Mass and Paste. The tears, 0.5-3 cm in size constituting the purest form of the resin, are rounded or flattened, 5-30 mm in diameter and greyish dull yellow in colour. Mass asafoetida is the common commercial form. It consists of tears agglutinated into a more or less uniform mass usually mixed with fragments of root, earth, etc. The paste form also contains extraneous matter. It is bitter in taste, yellowish-white changing to reddish-brown in colour, and has intense, persistent, penetrating and alliaceous odour. It is mostly found in Afghanistan, Kashmir, Punjab, Iran, Turkistan and Pakistan.

1.0 BOTANICAL DESCRIPTION

It was first found in the sandy desert of Aral in 1844, but has been known since the twelfth century. Several species of Ferula yield asafoetida. The bulk of the drug comes from the official plant, which is indigenous to Afghanistan and grows from two to four thousand feet above sea level. These high plains are arid in winter but are thickly covered in summer with a luxuriant growth of these plants. The great cabbage-like folded heads are eaten raw by the natives.
1.1 Collection

In the month of June the juice is collected from plants that are about four years old. The roots of plants which have not flowered are exposed and slashed, then shaded from the sun for five or six weeks and left for the gummy oleoresin to leak out and harden. It is then scraped off in reddish lumps and put into leather bags and sent to Herat, where it is adulterated before being placed on the market. A very fine variety of Asafoetida is obtained from the leaf bud in the centre of the root and is only used in India, where it is known in the Bazaars as Kandaharre Hing. It appears in reddish-yellow flakes and when squeezed gives out an oil [3, 6, 6].

1.2 Adulteration

Asafoetida is admittedly the most adulterated drug in the market. Besides being largely admixed with inferior qualities Asafoetida is added with following things to increase the weight.

1.3 Adulterants

Gum Arabic, other gum resins, Rosin, Gypsum, Red clay, Chalk, Barely, Sand, Stones, Wheat flour, Slices of potatoes etc.

2.0 IMPORTANT PROPERTIES OF HING AS PER UNANI SYSTEM OF MEDICINE

Hing has shown diverse biological and pharmacological activities. It has been used in Unani Medicine (Tibb-e-Unani) and other Traditional Systems of Medicine from time immemorial.

2.1 Pharmacological Actions (Table-A)

The drug Hing (Ferula foetida Regel) is described in detail in ethnobotanical and classical Unani literature and various actions of the drug have been reported such as nervine stimulant, emmenagogue, carminative, anti-inflammatory, aphrodisiac, diuretic, anthelmintic, expectorant, laxative, antispasmodic, antidote, antiseptic, lithotriptic, analgesic, appetizer, abortifacient, astringent, demulcent, antipyretic, digestive, voice purifier 1-15.

2.1.2 Therapeutic Uses (Table-B)

It is therapeutically used in various diseases such as paralysis, epilepsy, convulsions, tetanus, eye tonic, worm infestation, toothache, dry cough, jaundice, scatica, arthritis, dysuria, ascites, flatulence, hysteria, asthma, oilitis, abscess, ring worm, cataract, intestinal ulcer, fever, scorpion bite, tininitus, hiccup, alopecia, cholera etc.1-10, 12, 14, 16, 17.

2.1.3 Mizaj (Temperament)

| Mizaj          | References |
|---------------|------------|
| Hot and Dry   | 11, 12, 13, 15, 14, 18 19 |
| Hot and Dry   | 11, 20     |
| Hot and Dry   | 9, 18      |
| Hot and Dry   | 11,18      |
| Hot and Dry   | 10         |
| Hot and Dry   | 11         |

2.1.4 Muzir Asaraat (Adverse Effects)

| Adverse effect                                      | References |
|-----------------------------------------------------|------------|
| Harmful to liver and brain in hot temperament persons | 15, 18     |
| Harmful to liver and stomach                        | 10, 13, 18 |
| Harmful to liver                                    | 9          |
| Stomach                                             | 12         |

2.1.5 Musleh (Correctives)

| Musleh (Correctives) | References |
|----------------------|------------|
| Anarain (Punica granatum) | 15, 18     |
| Anissoon (Pimpinella anisum) | 15, 18     |
| Kateera (Cochlospermum religiosum) | 15, 18    |
| Banafsha (Viola odorata) | 15, 18     |
| Nilofar (Nymphaea alba) | 15, 18     |
| Seb (Malus sylvestris) | 15         |
| Sandal (Santalum album) | 15       |
| Zarishik (Berberis vulgaris) | 9, 18     |
| Zeerah (Carum carvi) | 18         |

2.1.6 Badal (Substitute)

| Badal (Substitute) | References |
|--------------------|------------|
| Jaosheer (Ferula galbaniflua) | 15, 18 |
| Salbeenaj (Ferula persica) | 15, 18   |
| Zeerah (Carum carvi) | 18       |
| Tuhkm-e Gazar (Daucus carota) | 18 |

2.1.7 Miqdar – E-Khurak (Therapeutic Dose)

| Miqdar – e- Khurak | References |
|--------------------|------------|
| 0.5-1gm            | 19         |
| 1 gm               | 18         |
| 1.75 gm            | 10         |
| 1-2 gm             | 18         |
| 2-2.25 gm          | 15         |
| 3 gm               | 18         |

2.1.8 Mashhoor Murakkabat (Famous compound formulation)

| Mashhoor Murakkabat | Reference |
|---------------------|----------|
| Sharbat Haif Roza   | 21       |
| Habbe-e-Halteet     | 19       |
## Table-A: Afa‘al (Pharmacological Actions)

| Actions                  | Unani Reference | Ethno medical References |
|--------------------------|-----------------|--------------------------|
| Muharrrik-e Aasab (Nervine Stimulant) | 9, 10           | 1, 3, 4, 6, 22           |
| Mudir-e Haiz (Emmenagogue) | 9, 10, 11, 12, 13, 14, 15, 19 | 1                       |
| Kasir-e Riyah (Carminative) | 11, 12, 14, 19, 20 | 1, 3, 5, 6, 7, 8, 22    |
| Muhallil (Anti-inflammatory) | 9, 13, 19       | -                       |
| Muqawwi-e Meda (Stomachic) | 9, 14           | 7                       |
| Muqawwi-e Bah (Aphrodisiac) | 9, 11, 12, 13, 14, 15 | 1                       |
| Mudir-e Baul (Diuretic) | 9, 10, 11, 12, 13, 14, 19 | 1                       |
| Qatile-Kirm (Anthelmintic) | 9               | 1, 22                    |
| Munaffis (Expectorant)   | 14              | 1, 4, 5, 8, 22           |
| Mulayyn (Mild laxative)  | 18              | 1, 5, 6, 22              |
| Dafa-e Tashannuj (Antispasmodic) | 14, 19         | 1, 5, 22                 |
| Fad-e Zehar (Antidiote) | 9, 10, 13       | -                       |
| Dafa-e Taftun (Antiseptic) | 14, 19          | 1                       |
| Mufattit-e Hisat Gurd (Lithotriptic) | 20              | -                       |
| Musakkin (Analgisic)     | 10, 11, 13, 15  | -                       |
| Mushahi (Appetizer)      | -               | 1                       |
| Musaqit (Abortifacient)  | 11, 15          | 1                       |
| Qabiz (Astringent)       | 10, 13          | -                       |
| Insecticidal             | 10              | -                       |
| Muhmmir (Rubefacient)    | 14, 19          | -                       |
| Jali (Detergent)         | 9               | -                       |
| Munawwim (Sedative)      |                 | 7                       |
| Mufathee (Deobstruent)   | 9               | -                       |
| Mulattif (Demulcent)     | 9               | -                       |
| Dafa-e Humma (Fever)     | 9               | -                       |
| Hazim (Digestive)        | 9, 10           | -                       |

## Table-B: Mawaqe-Istemaal (Therapeutic Uses)

| Uses                  | Unani References | Ethno medical References |
|-----------------------|-------------------|--------------------------|
| Faalij (Paralysis)    | 10-13, 15, 19, 20 | 1                        |
| Sara (Epilepsy)       | 10-13, 15         | 1, 4, 5                  |
| Raasha (Convulsions)  | 11, 15, 20        | -                       |
| Kuzaz (Tetanus)       | 10, 15            | -                       |
| Muqawwi-e Basr (Eye tonic) | 10-13, 15       | -                       |
| Kirm-e Ama (Worm infestation) | 10, 15, 21    | 1                       |
| Waja-ul Asnan (Toothache) | 11-13, 15, 21    | 1                       |
| Sual-e Yabis (Dry cough) | 10-15, 19        | 1                       |
| Mufall awaz (Voice purifier) | 10-13, 15      | -                       |
| Yarqan (Jaundice)     | 9, 10, 13, 15    | -                       |
| Irq-un-nasa (Sciatica) | 9               | 1                       |
| Wajaul Mafasl (Arthritis) | 9, 10          | -                       |
| Nisyam (Dementia)     | 9, 19             | -                       |
| Usr-ul Baul (Dysuria) | 9, 19             | 1                       |
| Istisqa (Ascites)     | 15                | -                       |
| Riyah (Flatulence)    | 11, 12, 14, 19, 20 | 1, 4, 5, 7, 22         |
| Ikhtinaq-ur-u Reham (Hystera) | 14, 19, 21     | 1                       |
| Zeeq-un Nafas (Bronchial Asthma) | 14, 19       | 4, 5, 22                |
| Qulañj (Colitis)      | 20, 21            | -                       |
| Warme Luhat (Uvulitis) | 10-13             | -                       |
| Dabeela (Abscess)     | 13                | -                       |
| Quba (Ring worm)      | 10, 12, 13       | 22                      |
| Nazoold-um maa (Cataract) | 10-13            | -                       |
| Qurood-e Ama (Intestinal Ulcer) | 13              | 1                       |
| Humma (Fever)         | 9, 10, 13        | -                       |
| Gazedagly-e Aqrab (Scorpion bite) | 9, 10, 13     | 1                       |
| Tanin (Tinnitus)      | 11                | -                       |
| Fuwwaq (Hicups)       | 9, 11             | -                       |
| Da-us- salab (Alopecia) | 12               | -                       |
| Haiza (Cholera)       | 1, 4, 5           | -                       |
3.0 VARIOUS PHARMACOLOGICAL STUDIES CONDUCTED SO FAR WITH SOME RECENT DEVELOPMENTS

On detailed search of the literature the following important pharmacological studies were found to be conducted on Hing (Ferula foetida Regel) so far. The details are as below-

3.1 Anti-diabetic and Anti-hyperlipidemic Activities

A study was conducted to investigate the hypoglycemic and hypolipidemic activity of ethanolic ferula asafoetida oleo-gum-resin extract (FAOGRETE) and also its effects on liver and kidney function in streptozotocin (STZ)-induced diabetic rats. The results of this study showed that FAOGRETE can regulate hyperglycemia and complications of diabetes. Antidiabetic and hypolipidemic activities of FAOGRETE are probably related to its antioxidant activity.

3.2 Transcipient and Genetic study

A 8-weeks feeding trial was conducted to examine the effects of different levels (0, 0.5, 1 and 2%) of dietary Ferula (Ferula assafoetida) on expression of antioxidant enzymes (GSR, GPX and GSTA), immune (TNF-alpha, I1B, Il- 8 and LY7) and growth (GH, IGF1 and Ghrl) genes as well as cutaneous mucus and serum non-specific immune response in common carp. The results revealed that Ferula significantly increased antioxidant gene expression (GSR and GSTA) in a dose dependent manner (P < 0.05). The expression of immune and growth related genes were significantly higher in Ferula fed fish as compared to control group (P < 0.05). The effects of Ferula on expression of genes were more pronounced in higher doses. These results indicated up-regulation of growth and health related genes in Ferula fed common carp.

3.3 Anti-Ulcer Activity

A water based ultrasound mediated gel-phase dispersion of Asafoetida gum on fenugreek derived soluble galactomannan fibre matrix was employed. Micro-encapsulated particles (1 ± 0.3 µm) of asafoetida was prepared as water dispersible free flowing powder (Asafin). Fourier-transform infrared spectroscopy (FTIR), scanning electron microscopy (SEM), accelerated stability and in vitro dissolution studies confirmed the stability, sustained release and microencapsulated structure of Asafin. Further investigations revealed significant (p < 0.01) reduction in acetic acid-induced writhings and inhibition of ethanol-induced ulcer (94.1%) in rats orally administered with Asafin at 250 mg kg−1 b.w. Asafin also exhibited anti-inflammatory effects (p < 0.01), in acute and chronic paw edema mice models. The safety of Asafin was further demonstrated by acute toxicity studies at 4 g kg−1 b.w. and by 28 days of sub-acute toxicity studies at 2.0 g kg−1 b.w.

3.4 Cytotoxicity and anticonvulsant activity

Cytotoxicity and anticonvulsant activity of the methanol extracts from several Ferula species were evaluated. For determination of the cytotoxicity of the extracts the oleogum-resin of F. assafoetida L., the brine shrimp (Artemia salina) was employed as a model assay system since it provides a convenient in-house pre-screening method for evaluating general cytotoxicity. The methanol extracts of different Ferula species and the oleo-gum-resin of F. asafoetida exhibited cytotoxic effect with LC50 values in the range of 6-321 μg/mL. For the anticonvulsant testing, seizure was induced by injection of pentylenetetrazole (PTZ), 90 mg/kg intraperitoneally (i.p.). All of the extracts and the oleo-gum resin of F. asafoetida showed dose-dependent cytotoxicity while methanol extracts and F. asafoetida oleogum resin did not possess anticonvulsant activity.

3.5 Anti-parasitic activity

The effect of F. asafoetida on Schistosoma mansoni in experimentally infected mice was investigated. F. asafoetida was given orally via intragastric tube in an oil-form and a powder-form in different concentrations. A highly significant statistical difference between the test groups was recorded in comparison to the infection control. The highest reduction in worm burden and egg counts was found with powder form of F. asafoetida (G3 III & IV) when compared to oil form as confirmed histopathologically and by ultrastructural profile alteration.

3.6 Pregnancy interceptive property

Ethanolic extract of Ferula assafoetida and chloroform fraction of Melia azedarach, both devoid of estrogenic activity, were examined for their pregnancy interceptive property. Treatment of rats from days 1 to 7 of pregnancy with either of the plant extracts resulted in pregnancy failure in about 65-85% of the animals. The possible role of energy metabolism in the antifertility action was investigated by measuring changes in activities of the key enzymes of carbohydrate metabolism in uterus on day 7 of pregnancy. It was observed that on the day 7 of pregnancy, one key enzyme of glycolytic pathway (phosphofructokinase) was significantly reduced in the uteri of treated rats as compared to controls. It was thus concluded that plants lacking phytoestrogens may intercept pregnancy by their ability to disrupt energy metabolism in rat uterus during implantation, especially the oxidative pathway.

3.7 Antispasmodic and hypotensive activity

The effects of Ferula foetida gum extract on the contractile responses of isolated guinea-pig ileum induced by acetylcholine, histamine and KCl on the mean arterial blood pressure of rat were investigated. Exposure of the precontracted ileum by acetylcholine (10 microM) to Ferula foetida gum extract caused relaxation in a concentration-dependent manner. Similar relaxatory effect of the extract was observed on the precontracted ileum by histamine (10 microM) and KCl (28 mM). However, when the preparations
were preincubated with indomethacin (100 nM) and different antagonists, such as propranolol (1 µM), atropine (100 nM), and chlorpheniramine (25 nM) then were contracted with KCL, exposure to the extract (3 mg/ml) did not cause any relaxation. Furthermore, Ferula asafoetida gum extract (0.3-2.2 mg/100g body weight) significantly reduced the mean arterial blood pressure in anaesthetised rats. It might be concluded that the relaxant compounds in Ferula asafoetida gum extract interfere with a variety of muscarinic, adrenergic and histaminic receptor activities or with the mobilisation of calcium ions required for smooth muscle contraction non-specifically.

3.8 Anti-Hypertensive Activity:

The present study was designed to evaluate the effects of hydroalcoholic extract of the stems of F. foetida in dexamethasone (Dex)-induced hypertension in rats. Hypertension was induced by subcutaneous injection of Dex (30 µg/kg) for 14 days. In a prevention study, rats received oral F. foetida extract (200, 400 and 800 mg/kg) for 4 days prior to Dex administration and during the test period (Days 1-18). Dexamethasone hypertension showed significant increases in SBP and in plasma H2O2 and decreases in the body and thymus weights and in Fluorescence recovery after photobleaching (FRAP) value (P<0.001). Administration of F. foetida extract significantly prevented and reversed hypertension at all doses. These results suggest antihypertensive and antioxidant effects of F. foetida stem extract in Dex-induced hypertension.

3.9 Anti-fungal activity

The effect of Asafoetida on growth of Trichomonas vaginalis in vitro was studied and compared to metronidazole as a reference drug. It showed that Asafoetida had a potent antiparasitic effect on T. vaginalis compared to metronidazole, thus, worth further investigation to study its applicability in treatment of parasitic infections.

3.10 Chemo-preventive effect

A study was conducted to ascertain the modulatory influences of Ferula asafoetida L. on the mammary epithelial tissue differentiation, hepatic drug metabolizing enzymes, antioxidant profiles and N-methyl-N-nitrosourea (MNU)-induced mammary carcinogenesis in Sprague-Dawley rats. Feeding with two doses of asafoetida (1.25 and 2.5% w/w in diet) showed a remarkable increase in the development and differentiation of ducts/ductules (p < 0.01-0.005), lobules (p < 0.005) and a decrease in terminal end buds (p < 0.05-0.005) as compared to both normal and MNU-treated control animals.

3.11 Antioxidant activities

3.11.1 The antioxidant and anticarcinogenic potential of asafoetida (Ferula narthex) in Swiss albino mice was evaluated. It was found that asafoetida is a potent antioxidant and can afford protection against free radical mediated diseases such as carcinogenesis.

3.11.2 The study was designed to examine antioxidant and antihaemolytic activities of Ferula foetida regul flower, stem and leaf extracts and it showed remarkable antioxidant and antihaemolytic activities. Biological effects may be attributed to the presence of phenols and flavonoids in the extract. It is very promising for further biochemical experiments.

3.11.3 Identification of the chemical compounds and evaluation of various antioxidant activities of Ferula-asafoetida leaves hydroalcoholic extract (FLHE) and Ferula-asafoetida leaves essential oil (FLEO) was carried out. In FLHE and FLEO, total antioxidant capacity were 1.55 ± 0.13 and 1.09 ± 0.43 nmol ascorbic acid equivalents/g, phenol content were 441.37 ± 2.50 and 76.56 ± 9.65 mg of Gallic acid equivalents (GAE)/g, and flavonoid content was 12.53 ± 3.20 and 0.015 ± 0.002 mg of quercetin equivalents/100 g respectively. This study showed that Ferula-asafoetida has good antioxidant properties.

3.12 Anti-microbial, Antioxidant, and Anti-Inflammatory Activities

Antimicrobial, antioxidant, and anti-inflammatory activities of the essential oils of 18 plant species from Tajikistan (Central Asia) were investigated. The essential oils of these aromatic plants including Ferula assa-foetida showed antimicrobial, antioxidant and anti-inflammatory activities.

3.13 Anti-haemolytic Activity

The study was designed to examine antioxidant and antihaemolytic activities of Ferula foetida flower, stem and leaf extracts and it showed remarkable antioxidant and antihaemolytic activities in Ferula foetida. Biological effects may be attributed to the presence of phenols and flavonoids in the extract. It is very promising for further biochemical experiments.

3.14 Acute and subchronic toxicity Studies

A study was performed to investigate acute and subchronic oral toxicity of Ferula assa-foetida gum (28 days) in Sprague Dawley rats. The obtained data revealed that oral administration of F. assa-foetida extract in rats for 28 successive days had no significant changes on body weight, and hematological parameters in rats all during the period of the experiment, and there were no significant increases in the activity of aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase, creatinine and urea. Liver of treated rats showed mild changes as thrombosis and sinusoidal leukocytosis. It also showed portal infiltration with inflammatory cells, while kidney of treated rat showed an atrophy of glomerular tuft, thickening of parietal layer of Bowman capsule, and focal tubular necrosis. It also showed dilatation and congestion of renal blood vessels. Therefore F. assa-foetida gum had broad safety and little toxicity for short term use in dose of 250 mg/kg.

3.15 Nephro-Protection Activity

The study validated the nephroprotective effects of Hing (Ferula foetida) extracts on gentamicin-treated rats. The subcutaneous administration of rats with Gentamicin (100 mg/kg) showed significant increase in blood urea nitrogen (BUN), serum creatinine and thiobarbituric acid reacting substances (TBARS), as an indication of renal disorder. However, co-administration of methanol soluble and insoluble fractions of Ferula foetida, to the Gentamicin- treated rats almost showed a complete reversal of the above effects, indicating nephroprotective properties of the herbal drug.

3.16 Other Biological Activities

Recent studies have shown several promising activities particularly relaxant, neuroprotective, memory enhancing, digestive enzyme, antioxidant, antispasmodic, hypotensive, hepatoprotective, antimiicrobial, anticarcinogenic, anticanecer, anticytotoxicity, antiobesity, anhelimintic and antagonistic effect.
4.0 CONCLUSION
Hing has been in use since times immemorial in Unani medicine as well as other traditional systems of medicine to treat wide range of ailments. It has been subjected to quite extensive Phytochemical, experimental and clinical investigations. Experimental studies have demonstrated diverse biological and pharmacological activities which include antioxidant, fibrinolytic, chemo preventive, anti-fungal, nephro-protective, anti-microbial, anti-convulsant, anti-parasitic, antihyperlipidemic and antidiabetic activities. The scientific studies have substantiated the claims of traditional systems of medicine. However, further detailed clinical research appears to be worthwhile to explore the full therapeutic potential of this drug.

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