Review Article
AMERICAN JOURNAL OF PHARMACY AND HEALTH RESEARCH
www.ajphr.com
2014, Volume 2, Issue 8
ISSN: 2321–3647(online)

A Review on Anxiolytic and Antiepileptic Effects of Oleo –Gum - Resin of *Ferula asafoetida*

Prabhat Kumar Upadhyay*[1],Omvir Singh[2], Amit Yadav[3], Raghvendra Sharma[3]
1. Institute of Pharmaceutical Research, GLA University, Mathura, (281406) U.P. India
2. J.K. Institute of Pharmacy and Management, Khurja, (203131), Bulandshahr,U.P. India
3. Aligarh College of Pharmacy, Aligarh, (202001) U.P. India

ABSTRACT

Asafoetida oleo-gum resin is obtained as an exudation by incising the rhizomes and roots of different Ferula species belongs to Family: Umbelliferae which are distributed from the Mediterranean region to Central Asia and contains about 40-64% resin (ester of asareninotannols, ferulic acid, pinene, vanillin and free ferulic acid), 25% endogeneous gum and 4-20 % volatile oil. Various activities of different *Ferula* species like antispasmodic and hypotensive activity, Molluscicidal activity, antioxidant activity, antinociceptive and anti-inflammatory activity, antifungal activity, antibacterial, Influenza A (H1N1) Antiviral and cytotoxic activity have been reported. The root acetone extact of Ferula gummosa is reported for its anticonvulsant property. Asafoetida is regularly consumed by the Indian population in food preparations so we decided to conduct our studies on regular available Asafoetida in India. In Ayurveda, asafoetida is considered to be one of the best spices for balancing the vata dosha. Asafoetida oleo-gum-resin is used traditionally for digestion, asthma, bronchitis, hysteria and as contraceptive/abortifacient and also has been claimed to be antiepileptic in classical Unani as well as ethnobotanical literature. So the present study was carried out to evaluate the anxiolytic and antiepileptic effect of Asafoetida.

Keywords: Asafoetida, Oleo-gum resin, *Ferula* species.

*Corresponding Author Email pharmacy2014@rediffmail.com
Received 21 July 2014, Accepted 31 July 2014

Please cite this article in press as: Upadhyay PK *et al*., A Review on Anxiolytic and Antiepileptic Effects of Oleo –Gum -Resin of *Ferula asafetida*. American Journal of Pharmacy & Health Research 2014.

INTRODUCTION

Botanical Source [1]

Asafoetida oleo-gum resin can be obtained as an exudation by incising the rhizomes and roots of *Ferula asafoetida* L., *Ferula foetida* Royel, *Ferula rubricaulis* Boiss. and some other species of Ferula belongs to Family: Umbelliferae.

Description of drug

There are two main varieties of Asafoetida i.e. Hing Kabuli Sufaid (Milky white asafoetida) and Hing Lal (Red asafoetida). Asafoetida is acrid and bitter in taste and emits a strong disagreeable pungent odour due to the presence of sulphur compounds therein. It is available in three forms i.e. 'Tears', 'Mass' and 'Paste'. 'Tears' is the purest form of resin, rounded or flattened, 5 to 30 mm in diameter and a greyish or dull yellow in colour. 'Mass' asafoetida is the common commercial form, uniform in mass. 'Paste' form contains extraneous matter. Since pure asafoetida is not preferred due to its strong flavour, it is mixed with starch and gum and sold as compounded asafoetida mostly in bricket form. It is also available in free flowing (Powder form) or in tablet forms.

Figure. 1 Bricket form of Asafoetida

Figure 2 Powder form of Asafoetida

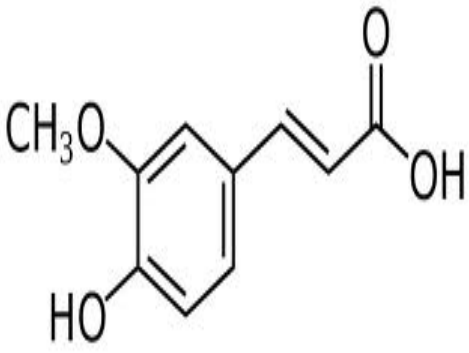
Figure. 3 Plant of Asafoetida

Origin and Distribution

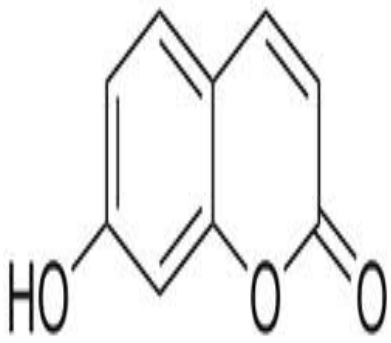
The species are distributed from the Mediterranean region to Central Asia. In India it is grown in Kashmir and in some parts of Punjab. The major supply of Asafoetida to India is from Afghanistan and Iran.

Chemical constituents [2]

Asafoetida contains about 40-64% resin, 25% endogeneous gum and 4-20 % volatile oil. The garlic like odour of the oil is due to the presence of sulphur compounds. The main constituents of the oil are isobutyl propanyl disulphide ($C_8H_{16}S_{20}$). The three sulphur compounds viz. 1-methylpropyl 1-propenyl disulphide, 1-(methylthio)-propyl 1-propenyl disulphide, and 1-methylpropyl 3-(methylthio)-2-propenyl disulphide have also been isolated from the resin. The resin portion is known to contain ester of asareninotannols, ferulic acid, pinene, vanillin and free ferulic acid. Ferulic acid on treatment with hydrochloric acid is converted into umbellic acid, which looses water to form umbelliferone.



Ferulic acid



Umbelliferone

Traditional therapeutic uses [3]

- Asafoetida is popular in India for many centuries as a flavouring agent, as an ingredient in condiments and in many spice mixtures.
- It is a valuable remedy for hysteria and nervous disorders of women and children.
- It is useful in flatulence, flatulent colic and spasmodic affections of the bowels especially when connected with hysteria, in fainting and emotional stress, nervous palpitation, hypochondriasis and other affections due to hysteria.
- It is also used in the spasmodic and the obstinate coughs of childhood remaining after attacks of inflammation and also in the advanced stages of whooping cough, pneumonia and bronchitis of children and in chronic bronchitis and asthma of adults.
- In Unani medicine system it is used in the diseases of the brain, digestive, paralysis, cholera, epilepsy, convulsion of children, flatulence, colic, caries of teeth as emmenagouge and to improve vision.
- Asafoetida is useful as an anthelmintic for round worms in children.
- It is employed as anaesthesia in hemicranias and dental caries.
- It is also used as contraceptive/abortifacient.
- In Ayurveda, asafoetida is considered to be one of the best spices for balancing the vata dosha.

Anxiety

Anxiety is a psychological and physiological state characterized by cognitive, somatic, emotional, and behavioral components. These components combine to create an unpleasant feeling that is typically associated with uneasiness, fear, or worry.

Experts say, this is an urban phenomenon and is on rapid rise. Being termed by most as celebration anxiety, the upper middle and higher strata of the society seem to be affected. Such cases have increased by 25 per cent in urban areas and if not dealt with, could lead to social disturbance.

Anxiety is a common experience in daily life and must be differentiated from anxiety disorder which causes substantial suffering in the general population. Generalized anxiety disorder, panic disorder, phobia and obsessional disorder are also now considered in the group of anxiety disorders. Considering all the anxiety disorders together, data from the western countries report prevalence estimates as high as 10 to 15% of the population. Although there are no definitive data on the prevalence of anxiety disorders in the SEA Region, indirect evidence suggests that the prevalence of these conditions is as high as in western countries and perhaps increasing due

to the changing social and cultural environment. Moreover, the easy availability of tranquillizers used widely by the common man as a remedy for anxiety is a cause of concern.

Anxiety disorders span the full range of human existence from childhood to old age, though symptoms may vary considerably owing to developmental differences and related factors. Anxiety disorders in children are often transitory phenomena, with the majority showing remission by adolescence or early adulthood. Anxiety disorders in youth appear to be a risk factor for the subsequent development of major depression in late adolescence and young adulthood. For the most part, anxiety disorders are chronic, and these persist from young adulthood into old age. But even in later life, new onset of anxiety disorders can occur, often in the context of medical illness or other sources of life stress.

Epilepsy [3]

Epilepsy is a common chronic neurological disorder characterized by recurrent unprovoked seizures. These seizures are transient signs and/or symptoms of abnormal, excessive or synchronous neuronal activity in the brain. About 50 million people worldwide have epilepsy, with almost 90% of these people being in developing countries. Epilepsy is more likely to occur in young children or people over the age of 65 years; however it can occur at any time. Epilepsy is usually controlled, but not cured, with medication, although surgery may be considered in difficult cases. However, over 30% of people with epilepsy do not have seizure control even with the best available medications.

Epilepsy affects 2-10 per 1,000 populations. Studies from different parts of India reveal that the problem varies from 9 per 1,000 in Bangalore, 5 per 1,000 in Mumbai, 4 per 1,000 in New Delhi and 3 per 1,000 in Calcutta. In a survey conducted in Kandy district of Sri Lanka, it was observed that 9 out of 1,000 people had epilepsy. Though there are no national statistics from Bangladesh, it is estimated that there are at least 1.5-2.0 million people with epilepsy. About 70-80% of people with epilepsy can lead normal lives if properly treated. However, 80-90% of people with epilepsy are not being treated at all.

Pharmacotherapeutic approaches for the management of these ‘‘modernization-borne diseases’’ include psychotropic drugs such as barbiturates, benzodiazepines, azapirones, nor-epinephrine and serotonin-reuptake inhibitors, monoamine oxidase inhibitors, and phenothiazines. Among these, benzodiazepines are the most widely prescribed synthetic chemical drugs for the treatment of anxiety, insomnia, epilepsy, and stress. Regular use of benzodiazepines causes deterioration of cognitive functioning, addiction, physical dependence, and tolerance. In the light of adverse effects associated with the synthetic drugs, researchers of today are exploring natural resources

to discover safer and cost effective drugs. Investigating plants, based on their use in traditional systems of medicine, is a sound, viable, and cost-effective strategy to develop new drugs.

Reported pharmacological activities of some *Ferula* species

Mohammad Fatehi et al reported the antispasmodic and hypotensive effects of *Ferula asafoetida* gum extract. Exposure of the precontracted ileum by acetylcholine (10µM) to *Ferula asafoetida* gum extract caused relaxation in a concentration-dependent manner. Similar relaxatory effect of the extract was observed on the pre-contracted ileum by histamine (10µM) and KCl (28 mM). However, when the preparations were pre-incubated with indomethacin (100 nM) and different antagonists such as propranolol (1µM), atropine (100 nM), 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/100 g body weight) significantly reduced the mean arterial blood pressure in anaesthetised rats. [4]

Pradeep Kumar et al reported Molluscicidal activity of *Ferula asafoetida*, *Syzygium aromaticum* and *Carum carvi* and their active components against the snail *Lymnaea acuminate*. Ethanol extract was more toxic than other organic extracts. The ethanol extract of *S. aromaticum* (24 h LC_{50}:83.53 mg/l) was more effective than that of *F. asafoetida* (24 h LC_{50}:132.31 mg/l) and *C. carvi* (24 h LC_{50}:130.61 mg/l) in killing the test animals. [5]

Abbas Ali Dehpour et al determined the antioxidant activity of the methanol extract of *Ferula asafoetida* and its essential oil composition by employing Gas Chromatography–MassSpectrometry, DPPH, Radical-scavenging activity, Reducing power determination, Assay of nitric oxide-scavenging activity, Metal chelating activity, Determination of Antioxidant Activity by the FTC Method and concluded that the aerial parts of the extract of F. assafoetida exhibited good but different levels of antioxidant activity in all the models studied. The extracts had good Fe^{2+} chelating ability, DPPH radical and nitric oxide scavenging activity. [6]

Mohammad Sayyah et al reported that the root acetone extract of *Ferula gummosa* exhibited dose-dependent prevention of tonic seizures induced by pentylenetetrazole (ED50 = 154.4 mg/kg). However, the extract produced sedation and motor impairment with TD50 value of 546 mg/kg. Preliminary phytochemical analysis showed the presence of terpenoids, alkaloids and a little amount of cardenolids in the extract. [7]

Uzma Sitara et al evaluated the antifungal effect of essential oils from *Ferula assafoetida* on in-vitro growth of pathogenic fungi. Asafoetida oil @ 0.1% and 0.15% significantly inhibited the growth of *Aspergillus niger, Fusarium oxysporum, F. moniliforme, F. nivale, F. semitectum, Drechslera hawiinesis* and *Alternaria alternate* . [8]

Ali Mandegary et al conducted antinociceptive and anti-inflammatory activity of the aqueous, methanolic and acetone extracts of the seed and root of *Ferula gummosa* Boiss in Mice and Rats. None of the extracts had anti-inflammatory effect in Cotton pellet granuloma. Preliminary phytochemical analysis of methanol and acetone extracts showed presence of terpenoids and alkaloids and small amounts of cardenolids. [9]

Venugopal Amrita et al reported antibacterial Effect of Asafoetida on Escherichia coli by conducting Turbidometric Method, Paper Disc Method and Agar Ditch Method. Asafoetida significantly inhibited the growth of *E.coli*. [10]

Types of anxiety disorders [11]

Anxiety disorders as recognized clinically include:

- Generalized anxiety disorder
- Panic disorder
- Phobias
- Post-traumatic stress disorder
- Obsessive compulsive disorder

Generalized Anxiety Disorder (GAD) [12,13,14]

GAD is an anxiety disorder characterized by chronic anxiety, exaggerated worry and tension, even when there is little or nothing to provoke it. It is an ongoing state of excessive anxiety lacking any clear reason or focus.

Signs & Symptoms

People with generalized anxiety disorder can't seem to shake their concerns. Their worries are accompanied by physical symptoms, especially fatigue, headaches, muscle tension, muscle aches, difficulty in swallowing, trembling, twitching, irritability, sweating, and hot flashes.

Panic Disorder

It is characterized by unexpected and repeated episodes of intense fear accompanied by physical symptoms that may include chest pain, heart palpitations, shortness of breath, dizziness, or abdominal distress. Such attacks can be induced even in normal individuals by infusion of sodium lactate, and the condition appears to have a genetic component.

Signs & Symptoms

People with panic disorder have feelings of terror that strike suddenly and repeatedly with no warning. During a panic attack, most likely heart pounds and person may feel sweaty, weak, faint, or dizzy. Hands may tingle or feel numb, and person might feel flushed or chilled. Person may have nausea, chest pain or smothering sensations, a sense of unreality or loss of control.

Phobias

These include strong fears of specific objects or situations. e.g. snakes, open spaces, flying, social interactions. Social Phobia or Social Anxiety Disorder is an anxiety disorder characterized by overwhelming anxiety and excessive self-consciousness in everyday social situations. Social phobia can be limited to only one type of situation such as a fear of speaking in formal or informal situations, or eating or drinking in front of others or in its most severe form, may be so broad that a person experiences symptoms almost anytime they are around other people.

Signs & Symptoms

People with social phobia have a persistent, intense, and chronic fear of being watched and judged by others and being embarrassed or humiliated by their own actions. Their fear may be so severe that it interferes with work or school and other ordinary activities. Physical symptoms often accompany the intense anxiety of social phobia and include blushing, profuse sweating, trembling, nausea, and difficulty in talking.

Post-Traumatic Stress Disorder (PTSD) [15,16]

PTSD is an anxiety disorder that can develop after exposure to a terrifying event or ordeal in which physical harm occurred or was threatened. Traumatic events that may trigger PTSD include recall of past stressful experiences like violent personal assaults, natural or human-caused disasters, accidents or military combat.

Signs & Symptoms

People with PTSD have persistent frightening thoughts and memories of their ordeal and feel emotionally numb, especially with people they were once close to. They may experience sleep problems, feel detached or numb.

Obsessive-Compulsive Disorder (OCD) [17]

OCD is an anxiety disorder and is characterized by recurrent, unwanted thoughts (obsessions) and/or repetitive behaviours (compulsions). Repetitive behaviours such as hand washing, counting, checking, or cleaning are often performed with the hope of preventing obsessive thoughts or making them go away. Performing these so-called "rituals" however provides only temporary relief and not performing them markedly increases anxiety.

Signs and Symptoms

Common obsessive thoughts in obsessive-compulsive disorder (OCD) include: Fear of being contaminated by germs or dirt or contaminating others, Fear of causing harm to yourself or thers, Intrusive sexually explicit or violent thoughts and images, Excessive focus on religious or moral ideas, Fear of losing or not having things you might need, Order and symmetry: the idea that

everything must line up just right, Superstitions; excessive attention to something considered lucky or unlucky.

While the onset of obsessive-compulsive disorder usually occurs during adolescence or young adulthood, younger children sometimes have symptoms that look like OCD. However, the symptoms of other disorders, such as ADD, autism, and Tourette's syndrome, can also look like obsessive-compulsive disorder, so a thorough medical and psychological exam is essential before any diagnosis is made.

Neuroanatomic circuits supporting fear and anxiety [18,19,20]

Fear and anxiety normally comprise adaptive responses to threat or stress. These emotional-behavioral sets may arise in response to exteroceptive visual, auditory, olfactory, somatosensory stimuli or to interoceptive input through the viscera and the endocrine and autonomic nervous systems. Anxiety may also be produced by cognitive processes mediating the anticipation, interpretation or recollection of perceived stressors and threats.

The Amygdala (amygdalae; plural) are a pair of small organs within the medial temporal lobes of the brain. The amygdala is a part of the limbic system which performs important roles in the formation and storage of memories associated with emotions including anxiety.

The structures that function in concert with the amygdala during fear learning include other mesiotemporal cortical structures, the sensory thalamus and cortices, the orbital, medial prefrontal cortex (mPFC), the anterior insula, the hypothalamus and multiple brainstem nuclei. Much of this network appears to participate in the general process of associating a conditioned stimulus (CS) or operant behavior with an emotionally salient unconditioned stimulus (US).

REFERENCES

1. Mohammad Ali. Text Book of Pharmacognosy. 2nd ed. New Delhi: CBS Publishers and Distributers; 2007. pp. 242-243.
2. Spices board India. Ministry of commerce and industry. Govt. of india. [cited 2009 Nov 19] Available from: URL: http://www.indianspices.com/html/s062hasf.htm
3. Kokate CK, Purohit AP, Gokhale SB. Pharmacognosy. 37th ed. Pune: Nirali Prakashan; 2007. p. 402-404.
4. Mohammad Fatehi, Freshteh Farifteh and Zahra Fatehi-Hassanabad. Antispasmodic and hypotensive effects of Ferula asafoetida gum extract. J Ethnopharmacol, 2004; 91(2-3):321-324.

5. Pradeep Kumar and D.K. Singh, Molluscicidal activity of Ferula asafoetida, Syzygium aromaticum and Carum carvi and their active components against the snail Lymnaea acuminate. Chemospher 2006; 63:1568-1574.
6. Abbas Ali Dehpour, Mohammad Ali Ebrahimzadeh, Nabavi Seyed Fazel, and Nabavi Seyed Mohammad. Antioxidant activity of the methanol extract of Ferula assafoetida and its essential oil composition. Grasas Y Aceites 2009; 60(4):405-412.
7. Mohammad Sayyah, Ali Mandgary. Anticonvulsant effect of Ferula Gummosa root extract against experimental seizures. Iran Biomed J 2003; 7(3): 139-143.
8. Uzma Sitara, Ishrat Niaz, Jawed Naseem, Nasreen Sultana. Antifungal effect of essential oils on in- vitro growth of pathogenic fungi. Pakistan J Bot 2008; 40(1):409-414.
9. Ali Mandegary, Mohammad Sayyah, Mahmood Reza, Heidari Ali. Antinociceptive and Anti-inflammatory activity of the seed and root extracts of Ferula gummosa Boiss in Mice and Rats. 2004; 12(2) 2004.
10. Venugopal Amrita, Dasani Sonal, Rai Shalini. Antibacterial Effect of Herbs and Spices Extract on Escherichia coli. Electronic J Biol 2009; 5(2): 40-44.
11. Amadea Morningstar, Urmila Desai. The Ayurvedic Cookbook: Lotus Light; 1991. p. 74.
12. Srinivasan K. Role of Spices beyond Food Flavoring: Nutraceuticals with Multiple Health Effects: Food Reviews International; 2005:21(2):167 — 188.
13. Nadkarni KM. Indian Materia Medica Bombay: Popular Prakashan;2000.p.537-540
14. Riddle John M. Contraception and abortion from the ancient world to the Renaissance: Harvard University Press; 1992:28.
15. Vishwnath GL, Nandakumar K. Anxiolytic and anticonvulsant activity of alcoholic extract of heartwood of Cedrus deodara roxb in rodents. J Pharmaceut Res *Health Care* 2009; 1(2):217-239.
16. Yadav AB, Kawale LA, Nade VS. Effect of Morus alba L. (mulberry) leaves on anxiety in mice. Ind J Pharmacol 2008; 40(1):32-36.
17. Vyawahare NS, Pujari RR. Neurobehavioural effects of Phoenix dactylifera in mice. J Young Pharmacists 2009; 1(3):225-232.
18. Thirupathykumaresan P, Saravanan A. Anticonvulsant activity of Morinda tinctoria-Roxb. Afr J Pharm Pharacol 2009; 3(2):063-065.
19. Dhayabaran D, Jeyaseeli Florance E, Nandakumar K, Puratchikody A. Anxiolytic and anticonvulsant activity of alcoholic extract of heart wood of *Cedrus deodara roxb.* in rodents. *J Med Plants* Res 2010; 4(14):1374-1381.

20. Adnaik RS, Pai PT et al. Anxiolytic activity of Vitex negundo Linn. in experimental models of anxiety in mice. Int J Green Pharm 2009; 3(3): 243-247.