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A review on ethnobotany, phytochemistry and pharmacology of *Fumaria indica* (Fumitory)

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ABSTRACT

Fumaria indica (Hausskn.) Pugsley (Fumariaceae), known as "Fumitory", is an annual herb found as a common weed all over the plains of India and Pakistan. The whole plant is widely used in traditional and folkloric systems of medicine. In traditional systems of medicine, the plant is reputed for its anthelmintic, diuretic, diaphoretic, laxative, cholagogue, stomachic and sedative activities and is used to purify blood and in liver obstruction in ethnopharmacology. The whole plant is ascribed to possess medicinal virtues in Ayurvedic and Unani systems of medicine and is also used in preparation of important Ayurvedic medicinal preparations and polyherbal liver formulations. The review reveals that phytochemical constituents of wide range have been separated from the plants and it possesses important pharmacological activities like smooth muscle relaxant, spasmogenic and spasmolytic, analgesic, anti-inflammatory, neuropharmacological and antibacterial activities. The separation of hepatoprotective and antifungal constituents from this plant was also reported newly. This review highlights the traditional, ethnobotanical, phytochemical, pharmacological information available on *Fumaria indica*, which might be helpful for scientists and researchers to find out new chemical entities responsible for its claimed traditional uses.

1. Introduction

The genus *Fumaria* (Fumariaceae) consists of 46 species in the world and *Fumaria* species are known as "fumitory, earth smoke, beggary, fumus, vapor, fumittery or wax dolls" in English[1]. *Fumaria indica* (Hausskn.) Pugsley (*F. indica*) (Fumariaceae) is a small, scandent, branched, annual herb growing wild in plains and lower hills. It is locally known as ''Pitpapra'' or ''Shahtrah'' in India[2], and its vernacular names are "Common fumitory" in English, "Pitpapra" in Hindi, "Shotara, pipapapra" in Bengali, "Pittapapra" in Marathi, "Pittapapdo" in Gujrati, "Parpataka" in Kannad, "Shahterah" in Kashmiri, "Turu'' or ''thusha" in Tamil, and "Chata-rashi" in Telgu.

Ayurvedic description:

Sanskrit: Parpata, Parpataka (Charaka, Sushruta).

Synonyms: Varatikta, pittahara, renu, kavacha, charmaahvya, rajorenu, charmakantaka, sooksmapatra, yavakantaka.

Properties: Rasa-Tikta; Guna-Laghu; Veerya-Sheeta; Vipaaka-Katu.

Action/Uses: Sangraahi, raktavikaarashamana, raktapitiahara, madhura, bhramaghna, aruchihara, daahahara, pitajwaraghna, kaphajwaraghna, pipaasashamani, chardighna[3].

2. Geographical distribution

The *Fumaria* is a genus of herbs distributed in Asia, Europe and Africa. The *F. indica* plants are distributed over the greater part of India upto 2 438 m on the Himalayas, Baluchistan, Afganistan, Persia, and Mongolia[4]. According to wealth of India, Indian plant bearing the name "Shahtrah" or "Pitpapra" has been wrongly referred as *Fumaria officinalis* Linn. or *Fumaria paviflora* lam. by many authors, which are common fumitory in Europe but not found in India[5]. The identification of *Fumaria* species is difficult due to the occurrence of inter-specific hybridisation[6] and the best condition to identify a *Fumaria* species is to study fresh material, as many changes occur in the herbarium specimens during drying[7].

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3. Botanical description

F. indica is a much-branched, suberect or diffuse, pale-green, annual herb that is up to 61 cm in height. Leaves are multifid and more or less glaucous; leaflets are 2-4 in number and pinnatisect; segment is long, linear or linear-oblong, flat, and acute. Recemes have 10-12 flowers that are rather dense; bracts lanceolate-subulate and slightly acuminate, and pedicels (2.0-2.5 in number) are rarely 4.5 mm long, erect and thickened at the apex. Sepals are about 1.5 mm long, 0.5-1.0 mm broad, lanceolate or ovate, acuminate, more or less inciso-dentate, rose colored and often persistent in the young fruit. Corrola is 5-6 mm long and rose colored. Fruit is about 2.5 mm broad, subrotund, quadrate, subtruncate and sometimes obscurely retuse. Stem is light green, smooth, hollow, about 3-4 mm thick, with root brown color and branches that are about 2-3 mm thick, and cylindrical[4,8,9].

4. Pharmacognostic studies

Microsopically, the lamina of leaf has single layer epidermis on either side, consisting of thin walled, rectangular, oval shaped, parenchymatous cells; mesophyll is composed of thin walled, oval to polygonal, parenchymatous cells; vascular bundles are scattered throughout the mesophyll; anomocytic stomata are present on both the surfaces. Microscopically, the stem of *F. indica* is quadrangular to pentagonal in shape. The outer most single layered epidermis is covered with cuticle. The cortex is divided into two regions and endodermis is absent. Closed and bicollateral vascular bundles are either single or in group of two and arranged at the ridges. Each vascular bundle is capped with sclerenchyma. In root, epidermis is obliterated or crushed and cortex consists of thin walled, irregular shaped, parenchymatous cells; endodermis is not distinct; secondary phloem is well developed and consists of sieve tube, companion cells and phloem parenchyma[9].

5. Medicinal uses

5.1. Classical uses

In Charaka and Sushruta, parpata is recommended for treatment of fevers and blood disorders. In Sushruta, the plant has also been recommended in case of chronic skin diseases, urinary diseases and cough. *F. indica* alone or combined with *Tinospra cardifolia*, *Emblica officinalis*, *Santalum album* or *Zingiber officinale* was prescribed for alleviating fever. *F. indica* is an important ingredient in Amrtaarishta (*Bhaishajya Ratnaavali*, an ancient indian medical book), prescribed as an antipyretic and antiperiodic compound; Arvindaasava, prescribed as a carminative and restorative; Chandanaasava, prescribed for urinary and urogenital disorders; Mahaatikta Ghrita (*Ashtaanga Hridaya*, an ancient indian medical book), prescribed as ablood purifier, antiinfective, appetizer and restorative.

In Unani medicine, *Fumaria* plant imported from Persia is used as "shaahtara" and is an important ingredient in a number of blood purifying compounds. Itrifal-e-Shaahtara is prescribed for putrefaction of blood, syphilis, skin diseases. Majoon-e-Musaffi-e-Khoon are reputed blood purifying compounds in Unani medicine[10].

5.2. Uses in pharmacopeias and traditional system of medicine

Plants have been used as a source of medicine by humankind since ancient times. The indigenous knowledge of many traditional communities has been formulated, been documented, and eventually become organized system of medicine, such as Ayurveda, Siddha, Unani, and other systems outside India. According to wealth of India, *F. indica* is used to treat fever and influenza[5]. In the indigenous system of medicine, the plant is regarded as a laxative, diuretic and diaphoretic and is said to be beneficial in dyspepsia, liver complaints and scrofulus skin affections[4]. Decoction of *F. indica* stem and leaves is given as a tonic, anthelmintic and aperient. It is also used in syphilis, scrofula, leprosy, and constipation and given in ague and jaundice[11]. In traditional system of medicine, the plant is reputed for its anthelmintic, antidyspeptic, cholagogue, diaphoretic, diuretic, laxative, stomachic, tonic properties and claimed to possess various curative properties for ailments of the blood, skin, gastrointestinal systems and central nervous system[12]. It is also used as a component of various herbal products such as Livokriti syrup, Esno capsule and Ayurveda capsule, available in Indian market. The whole plant forms a constituent of many common households, Ayurvedic, Unani medicinal prepartions and marketed polyherbal liver formulations[13]. The plant is used to purify blood in cutaneous disease and liver obstruction. The plant is reported to be slight diaphoretic, aperient, alterative and anthelmentic[3].

5.3. Uses described in folk medicines, supported by experimental animal studies

In recent years, ethno-medicinal studies have received much attention, bringing to light the numerous little known and unknown medicinal uses especially of plant origin. They obviously deserve evaluation by modern scientific methods such as phytochemical analysis, biological screenings and clinical trials[14]. Whole plant *F. indica* is documented to possess medicinal benefits in ethnobotanical surveys conducted by researchers. *F. indica* is used as a blood purifier in skin diseases, styptic and febrifuge and is also used in the disorder of liver in folk medicine[10]. The plant is considered useful and scientifically supported to treat abdominal cramps, diarrhea, fever, jaundice, leprosy and syphilis[8].

6. Phytochemistry/major chemical constituents

Extensive chemical work has been done to separate and

characterize a number of compounds from the leaf, stem, root and seed of the plant. The major chemical constituents of the plant include narceimine, (−)−tetrahydrocoptisine, narlumidine, methyl fumarate, protopine, bicuculine, and fumariline.

Firstly, seven isoquinoline alkaloids have been separated from alcoholic extract of whole plant *F. indica*, and these alkaloids include protopine, tetrahydro coptisine, tautomeric form of fumariline (a homogenous gum), a racemic mixture of bicuculine and its optical antipode, bicuculine, fumarilicine and narceimine[15]. Later on, protopine, quanternary salt of protopine, nona cosanol and sitosterol were separated from the stem and leaves of *F. indica*[16]. The protopine content in the seeds is about double of that in the whole plant, and the yield of tetrahydro coptisine is 50 times more in the seeds than in the whole plant. More importantly, the latter is present as an optically active form in seeds rather than as a racemic mixture[17]. Then, three new alkaloids, *i.e.*, fumariline, 8−methoxy dihydro sanguinarine and oxysanguinarine, were separated from *F. indica*[18]. A secopthalide isoquinoline alkaloid narceimine has also been isolated from *F. indica* seeds and its structure was established by spectroscopic method[19]. By further chemical analysis, a new isoquinoline base, which is papracine along with six known bases, *i.e.*, oxyhydrastinine, noroxyhydrastinine, fumaramine, stylopine, bisnorargemonine and fumaritine, has been separated from *F. indica* for the first time[20].

Two new spirobenzyl isoquinoline (tyramine base) alkaloids papracinine and paprazine together with six other known alkaloids, which include fumaritine N−oxide, parfumine, lastourvilline, feruloyl tyramine, fumariflorine and N−methyl corydaldine, were identified from aerial parts of *F. indica*[21]. A new seco−phthalide isoquinoline alkaloid narlumicine have been identified from stem of *F. indica* together with protopine nitrate, protopine, *DL*−tetrahydrocoptisine and narlumidine[22]. Similarly, three new seco−pthalide isoquinoline alkaloids peprafumine, peprarine and papraline along with three other known alkaloids, which include cryptopine, raddeanine and oxocoptisine, has been identified from aerial part of *F. indica*[23]. Recently, a new alkaloid fuyuziphine together with (+/−)−alpha−hydrastine has been separated from the whole plant *F. indica*[24]. Phytoconstituents present in different parts of *F. indica* are summarized in Table 1.

Table 1

Phytoconstituents present in different parts of *F. indica*.

Plant part	Phytoconstituent
Aerial part	Papracine, paprazine, sitosterol, stigmasterol, campesterol
Root	Protopine, octacosanol, narceimine, narlumidine, adlumidine
Leaf & stem	Narlumicine, protopine, narlumidine, nona cosanol
Seed	Fumariline, tetrahydrocoptisine, bicuculine, oxysanguinarine

6.1. Alkaloidal content

The concentrations of alkaloidal constituents present in *F. indica* have been determined at different stages of its life span and the detection results showed that *F. indica* bears a maximum concentration during the middle of its life span. Among the pure individual alkaloids, the major constituent protopine was found to maintain at the highest concentration in the first 20 d, then gradually declined and almost disappeared after 60 d[25].

7. Pharmacological activities

The total tertiary alkaloid of *F. indica* has smooth muscle relaxant and hydrocholerretic activities. Pharmacological studies were conducted to study the major alkaloid protopine, present in *F. indica*.

7.1. Smooth muscle relaxant activity

Protopine at concentrations of 0.5−5.0 μg/mL was found to produce a moderate to marked relaxation of the separated ileum of guinea−pig, rabbit and albino rat *in vitro* and its relaxation activity was approximately equipotent to that of papaverine[15].

7.2. Hepatoprotective activity

F. indica showed hepatoprotective activity against carbon tetrachloride, paracetamol and rifampicin induced heptatotoxicity in albino rats. The petroleum ether extract against carbontetrachloride, total aqueous extract against paracetamol, and methanolic extract against rifampicine induced hepatotoxicities showed similar reductions in the elevated levels of some of the serum biochemical indicators in a manner similar to that of silymarin, indicating its potential as a hepatoprotective agent[26].

Further investigation reveals that an active compound monomethyl fumarate has been separated from methanolic extract of whole plant *F. indica* and the compound showed no hepatocytotoxicity up to the dose of 1 mg/mL *in vitro* and up to 50 mg/kg (p.o.) *in vivo* in albino rats. *In vivo*, monomethyl fumerate showed significant antihepatotoxic activity against carbon tetrachloride, paracetamol and rifampicine induced hepatotoxicities to an extent almost similar to that of silymarine, a known antihepatotoxic agent[27]. Nimbkar have also reported that *F. indica* have good hepatoprotective activity against hepatotoxicity caused by anti−tubercular drug[28]. Recently, protopine present in *F. indica* at doses of 10−20 mg/kg (p.o.) also proved to be equally effective hepatoprotectants as standard drug silymarine (single dose of 25 mg/kg, p.o.)[29].

7.3. Spasmogenic and spasmolytic effect

In vitro, the crude extract of *F. indica* and its fractions showed spasmogenic and spasmolytic effects due to the presence of cholinergic and calcium channel blockade constituents, which may explain the respective traditional use of the *F. indica* in constipation and diarrhea[30].

7.4. Anti-inflamatory and anti-nociceptive activity

F. indica showed significant and dose dependent anti-inflamatory activity in acute and chronic cotton models of inflammation in experimental animals. The extract also showed anti-nociceptive activity and medicated both centrally and peripherally[31].

7.5. Neuropharmacological activity

Using various behavioural models, 50% (v/v) ethanolic extract of *F. indica* at doses of 100, 200 and 400 mg/kg was investigated for its neuropharmacological activity, antidepressant activity and general effects on central nervous system. The results showed that *F. indica* had a significant and dose dependent increase in pentobarbital-induced sleeping time, a marked decrease in onset of sleeping time in rats and a significant decrease in locomotor activity and anticonvulsant activity. However, *F. indica* did not show any muscle relaxant effect and antidepressant activity. Studies indicated that *F. indica* has significant depressant activity towards central nervous system and lacks antidepressant activity in rodents[32].

7.6. Antibacterial activity

F. indica plant was evaluated for its potential anti-bacterial activity against six bacterial strains belonging to Enterobacteriaceae, *viz. Enterobacter aerogenes*, *Escherichia coli*, *Klebsiella pneumonia*, *Proteusmirabilis*, *Proteus vulgaris*, and *Salmonella typhimurium*). The results showed that *Klebsiella pneumonia* was the most susceptible bacterium, while *Salmonella typhimurium and Escherichia coli* were the most resistant bacteria[33].

7.7. Antifungal activity

Fuyuziphine, an alkaloid separated from *F. indica,* showed antifungal activity against spore germination of some plant pathogenic fungi (*Collectotrichum* sp., *Collectotrichum gloeosporioides*, *Collectotrichum falcatum*, *Curvularia maculans*, *Curvularia lunata*, *Erysiphe cichoracearum*, *Helminthosporium pennisetti*, *Oidium erysiphoides*, *Ustilago cynodontis*, *Alternaria chieranthi*, *Alternaria melongenae*, *Alternaria brassicicola* and *Alternaria solani*. The results showed that germination of most fungi was significantly inhibited by fuyuziphine at 100-750 ppm[34].

Further, berberine iodide, an isoquinoline alkaloid separated from *F. indica* significantly inhibited the spore germination of *Curvularia lunata*, *Erysiphe cichoracearum*, *Erysiphe pisi*, *Fusarium udum* and *Penicillium* species. Complete inhibition (100%) of spore germination was observed in *Erysiphe cichoracearum* and *Penicillium* species at 1.5 g/L[35].

7.8. Antioxidant activity

Fumaria species contain some kinds of fatty acids with antioxidant effects. A part of these lipids are phospholipids. Antioxidant activity of ethanolic extracts of *F. indica* was determined using the DPPH (1,1-diphenyl-2-picrylhydrazyl) method. Free radical scavenging activity was recorded from *F. indica*, which showed 61.8% activity[36,37].

7.9. Chemopreventive effect

F. indica showed chemopreventive effects by suppressing the tumour burden and restoring the activities of hepatic cancer marker enzymes on *n*-nitrosodiethylamine and carbon tetrachloride-induced hepatocarcinogenesis in wistar rats[38].

8. Toxicity studies

Recently, it have been reported that *F. indica* is safe during an acute and subchronic oral toxicity study in rodents[39]. In preclinical study, *F. indica* was found to be safe in cytotoxic test and devoid of toxic manifestations during chronic administration[40].

9. Conclusions

F. indica plant has been explored exhaustively for their phytochemical and pharmacological activities. From the foregoing accounts, it is evident that *F. indica* plant has been used ethno-medicinally as a valuable therapeutic agent for a variety of diseases, as we have illustrated in this article. Moreover, numerous research works have proven its uses beyond the ethno-medicinal ones in experimental animals. Various compounds which were separated from this plant may be responsible for its pharmacological activities.

Conflict of interest statement

We declare that we have no conflict of interest.

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