

Holistic Psychopharmacology of *Fumaria indica* (Fumitory)

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ABSTRACT

Fumaria indica is a medicinal plant of the fumitory family widely growing throughout India. Classical texts of Ayurveda, *i.e.* the oldest traditionally known health care and medical system originating in Indian subcontinent, mentions diverse medicinal uses of the plant. During more recent decades broad spectrums of therapeutically interesting pharmacological properties of its extracts and secondary metabolites have also been reported. Recent observations made during efforts to define its pharmacological activity profile according to the Ayurvedic concepts of mind body medicine have revealed exceptionally broad spectrums of psychopharmacological activity profiles of diverse types of hydro alcoholic extracts of the plant. These effects of the extracts become apparent after their repeated daily doses only. Taken together with prior preclinical knowledge on the plant, these observations strongly suggest that *Fumaria indica* could be an easily available source for discovering and developing phyto-pharmaceuticals or drugs potentially useful for treatments of mental health problems commonly associated with numerous physical disorders and chronic diseases. Since several psychoactive and other phytochemical of *Fumaria indica* are also encountered in other plants commonly used in Chinese and other traditionally known medical systems, observations made and the holistic strategy used for defining its psychopharmacological activity profile could be of interest of others involved in efforts necessary for proper understanding of therapeutic potentials of many plants containing Fumaria alkaloids and other bioactive phytochemicals present in *Fumaria indica*.

Keywords: *Fumaria indica*; Fumitory Alkaloids; Ayurveda; Holistic Psychopharmacology; Comorbid Psychopathologies; Therapeutic Potential

1. Introduction

Medicinal uses of herbs and their combinations are common characteristics of Chinese as well as Indian systems of medicines. Ayurveda, *i.e.* the oldest and still the most popular health care system of India, and traditional Chinese medicine (TCM) have always been widely practiced in many Asiatic countries, and during more recent they have also been well accepted and adapted in many other parts of the economically more developed world. Such global popularity of these traditionally known medical systems, especially those of TCM [1], has increased the global demand of traditionally known herbal remedies, and has also triggered interests of numerous modern medical researchers and practitioners in properly understanding their therapeutic potentials in terms of modern medical sciences. However, despite extensive efforts and considerable progress made during past few

decades, many therapy relevant questions concerning medicinal phytochemistry and pharmacology of numerous Chinese and Ayurvedic medicinal plants cannot yet be properly answered in terms of postmodern concepts of evidence based medicine. Consequently, novel strategies and paradigms are now being conceived and tried in many laboratories for clarifying them. Hereupon, more attention is paid to the molecular mechanisms and pharmacological targets based concepts of modern medicine than to the holistic principles of traditionally known medical systems like TCM or Ayurveda. However, in numerous laboratories, especially in India, China and other Asiatic countries, the conventionally known more holistic strategies and *in vivo* animal models for evaluating therapy relevant pharmacological properties of herbs are still widely practiced.

Phytochemical and pharmacological information now available on numerous traditionally known medicinal plants strongly suggest that most, if not all, of them could have modulating effects on the essential functions of the central

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nervous system (CNS). Although several such plants have been more thoroughly explored and commercialized in the western world for combating mental health problems [2], as yet little concentrated efforts have been made to verify mental health benefits of numerous others well known as accumulators of diverse CNS-active alkaloids and other phytochemicals. Recent efforts in our laboratories to define neuro-psychopharmacological activity profiles of some Indian medicinal plants [3] led us to identify diverse psychotherapeutic potentials of several traditionally known medicinal plants, including those of *Fumaria indica* and some other currently popular Ayurvedic medicinal plants.

Fumaria indica is one such medicinal plant of the Fumitory species widely used in many other traditionally known medical systems commonly practiced in India and elsewhere. Several so-called Fumitory alkaloids and other phytochemicals encountered in *Fumaria indica* are structurally identical or similar to those of many other plants of the species, and several pharmacological properties of its extracts are also analogous or identical to those reported for extracts from other members of the family. However, potential roles of the psychoactive principles of *Fumaria indica* in therapeutically interesting pharmacological activity profiles of its diverse types of medicinally used extracts still remain speculative only. Efforts to clarify the situation are not only necessary for pharmacologically more rational standardization of its commercialized extracts, but also for identifying novel therapeutic leads potentially useful for combating comorbid mental health problems commonly encountered in chronically ill patients. In this communication our current understanding on medicinal phytochemistry of *Fumaria indica* will be summarized, and usefulness of more holistic psychopharmacological strategies for more precisely defining its therapeutically interesting pharmacological activity profile will be pointed out.

2. Historical Background

Ayurveda is one of the three major traditionally known codified systems of medicine well integrated in the modern Indian health care system. Medicinal uses of many Ayurvedic plants, including those of *Fumaria indica*, are also known to practitioners of other traditionally known medical systems in India and elsewhere. Initially, Ayurvedic codes were in Sanskrit language. However, during more recent decades extensive efforts have been made to translate, de-codify, and understand its texts in English and other modern languages. It was only through such efforts that eventually *Fumaria indica* was identified as an Ayurvedic medicinal plant. Its medicinal values are often mentioned in classical texts like Charak Samhita [4], Dhanvantari Nighantu [5] and Bhava Prakash [6]. Botanically it belongs to the *Fumaria* species,

also commonly called “fumitory”, “earth smoke”, “beggary”, “fumus”, “fumittery” or “wax dolls” in English. These are annual weeds, growing wild in plains and lower hills of India, Pakistan, Afghanistan, Turkey, Iran, Central Asia, North Dakota and Colorado [7,8]. The genus *Fumaria* (Fumariaceae/Papaveraceae) consists of many species [9], and the *Fumaria* species defined as *Fumaria indica* (Haussk) Pugsley (synonyms: *F. parviflora*, *F. vaillantii*), is now one of the most commonly used herbs in Ayurvedic, Unani and other folk medicine systems of India. In Pakistan, it is traditionally used for treatment of dermatological diseases, topical diseases, cardiovascular complaints, circulatory disease, fever and headache [10]. The plant is now commonly known as “Pitpapda” in India, and as “Shahtra papra” in Pakistan [11,12]. Its diverse currently known medicinal uses are often in agreement with, or justified by, its broad spectrum of therapeutically interesting pharmacological activity profile unraveled mainly during the 20th century [11,13]. However, many questions concerning the details of its botanical identity, chemical constituents, bioactivities, and more appropriate medicinal values still remain to be more properly answered in terms of modern sciences.

3. Pharmacognostic Features

It has recently been ascertained [12] that the genus *Fumaria* L. (Papaveraceae) consists of 60 species and that *F. parviflora*, *F. indica*, and *F. vaillantii* are closely associated species. Various vernacular names of the plant used in Indian system of medicine are given in **Table 1** [14]. The macroscopic, microscopic, and chemotaxonomic characteristics of the plant are useful tools for pharmaceutical industries for identification and authentication of its commercial samples. The HPTLC profile using rutin and protopine as marker have recently been proposed to be useful means for quality control and affirming batch to batch consistency of the plant material used by the herbal industries for manufacturing pharmaceutical products [15]. It must be noted though, that both rutin and protopine are encountered also in numerous other plants, and that they are not the only extractable bioactive constituents of the plant.

3.1. Macroscopic and Microscopic Characteristics

F. indica is a pale green colored and highly branched annual herb. Roots of the plant are cream to buff in color and comprise of tap root system with numerous rootlets and root hairs. Transverse section of root has crushed epidermis followed by thin walled, irregular shaped, parenchymatous cortex merged with endodermis and well developed vascular bundles. Its stem is smooth and

Table 1. The vernacular names of *Fumaria indica*.

Vernacular names of <i>Fumaria indica</i> [14]			
Language	Vernacular name	Language	Vernacular name
Sanskrit	Parpata/Suksmapatra	Hindi	Pitpapa
English	Fumitory	Assamese	Shahtraj
Nepalese	Kairuwa	Kashmi	Shahterah
Sinhalese	Patha padagam	Bengali	Shotara/pipapapa/bandhanian
German	Erdrach	Gujrati	Pittapapdo
Chinese	Tuysha tu chian	Marathi	Pittapapra
Unani	Shahotarah	Kannada	Parpataka/Kallu sabbasige
Arabian	Shahtraj	Tamil	Thara/Tura/Thusha
Turkish	Sahtere	Telugu	Parpatakamu

light green in color. Transverse sections of stem is quadrangular to pentagonal in shape, and consist of single layered epidermis covered with cuticle followed by two distinct layer of cortex containing closed and bicollateral vascular bundles at the ridges, without endodermis. Leaves of the *Fumaria* are compound, 5 to 7 cm long, divided into narrow segments. The lamina of leaf is made up of single layer, thin walled, rectangular to oval shaped, parenchymatous epidermis on either side; mesophyll composed of oval to polygonal thin walled parenchymatous cells; vascular bundle are scattered throughout the mesophyll; anomocytic stomata present on both the surfaces. Inflorescence has 10 to 15 flowered racemes. Flowers are 6 to 7 mm long, composed of two whitish sepals, four purplish green petals, corolla in 2 whorls, stamens 3 + 3 and 3 to 4 mm long bi-lipped stigma. Fruits are capsules, sub round to ovate, and are single seeded. The seed is spherical to ellipsoid and has an apical pore and rib [12,15-18].

3.2. Phytochemicals

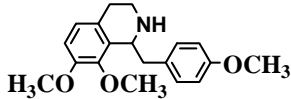
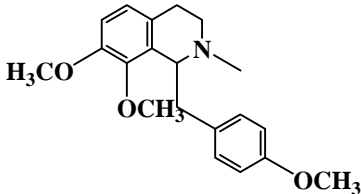
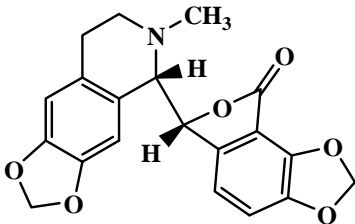
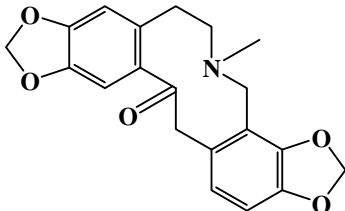
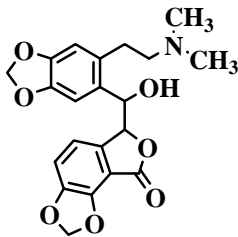
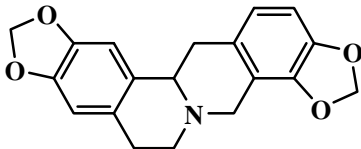
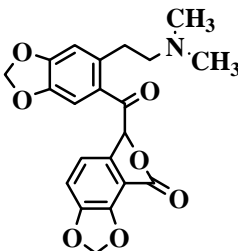
Extensive efforts made during the latter half to the 20th century in several Indian and other laboratories have led to the identification and characterization of numerous phytochemicals from the leaves, stem, root and seed of the *Fumaria indica*. The very first report on isolation, structure elucidation, and pharmacology of protopine and a few other alkaloids isolated from *Fumaria indica* appeared during 1971 [19]. Since then presence of numerous others alkaloids (often referred to as Fumitory alkaloids), flavonoids, glycosides, tannins, saponins, anthraquinones, steroids and triterpenoids in diverse parts of the plant have been reported [11,13,20]. Structures of the phytochemical isolated from different parts of *Fumaria indica* are given in **Table 2** [21-33]. Amongst them, a group of benzyloquinoline alkaloids commonly known

as “protopine alkaloids” are encountered in all parts of the plant. It must be noted though that depending on the acidic environments protopine alkaloids can exist in two isomeric forms [34], which theoretically must not possess the same biological activities. Such characteristics of these and other alkaloids are often neglected by modern medicinal chemists and pharmacologists. Moreover, quantitatively as well as qualitatively the alkaloid contents of *Fumaria indica* extracts depend not only on the extraction procedure used, but also on the harvesting period of the plant itself [35], possible influences of such variations, and of drying and extraction procedures, on the pharmaceutical quality of *Fumaria indica* extracts have not yet been carefully examined. In view of the recent report [12] that drying induced morphological changes do occur in *Fumaria* species, such characteristics of a plant can not necessarily be used for acquiring its authentic samples for medicinal purposes. More detailed phytochemical analysis might be a better alternative for medicinal purposes. For such purposes, a simple, fast and efficient method based on the use of GC-MS technique for proper chemotaxonomic identification of plants of *Fumaria* species [9] has recently been published.

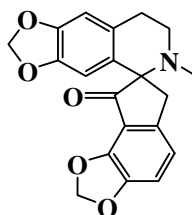
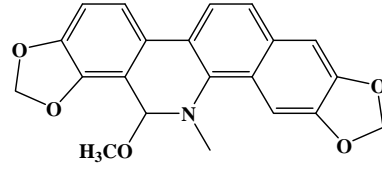
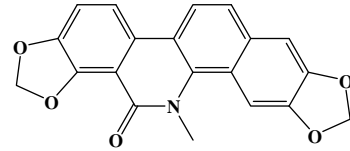
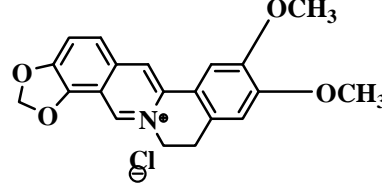
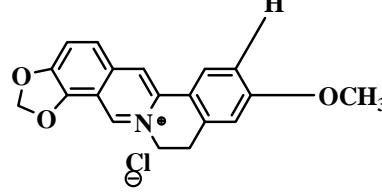
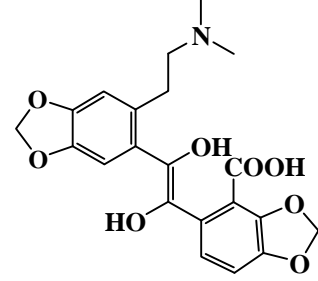
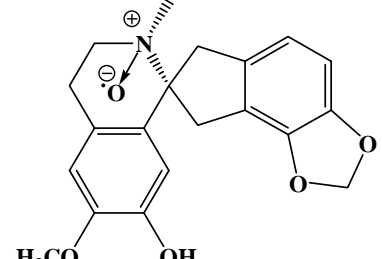
4. Medicinal Uses

Like for other traditionally known medical systems, the theories, principles, and practices of Ayurveda have little in common with those of the so called “western” medical systems. Details of Ayurvedic principles and medicinal recommendations for *Fumaria indica* are now available in authoritative publications in English [14,36]. Traditionally, the plant has been used as anthelmintic, anti-dyspeptic, blood purifier, anti periodic, cholagogue, diaphoretic, diuretic, laxative, stomachic, sedative, tonic [37], and has also been considered to be useful for treatment

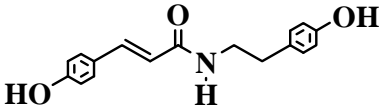
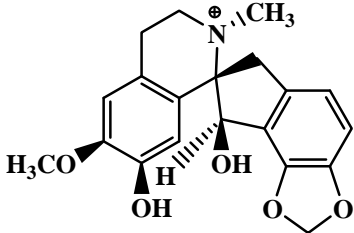
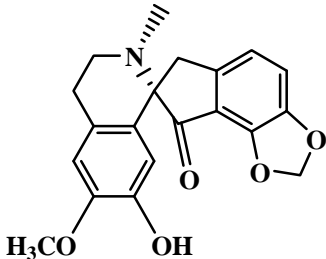
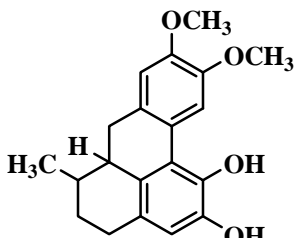
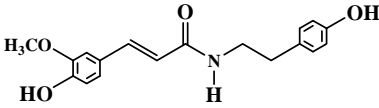
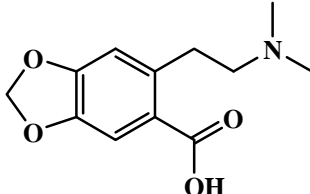
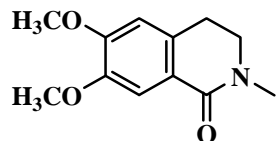
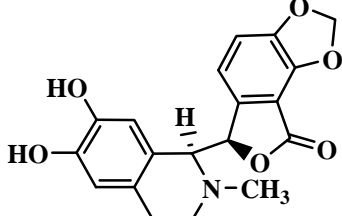
Table 2. Structures of some bioactive phytochemicals of *Fumaria indica*.

S. No.	Chemical constituent	Plant part	Structure	Reference
Alkaloids				
1.	Fuyuzipine	Whole plant		[21,22]
2.	(±)- α -Hydrastine	Whole plant		[22]
3.	Bicuculine	Whole plant		[22]
4.	Protopine	Whole plant, stem, leaves and seed		[19,23]
5.	Narlumicine	Stem		[23]
6.	Stylophine/ DL-Tetrahydrocoptisine	Whole plant, stem and seeds		[23]
7.	Narlumidine	Whole plant and stem		[23]

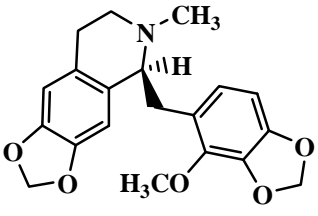
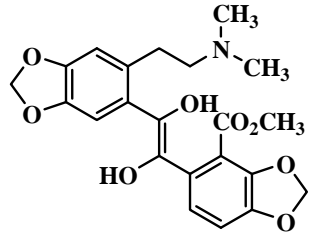
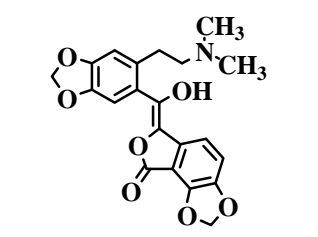
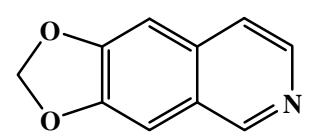
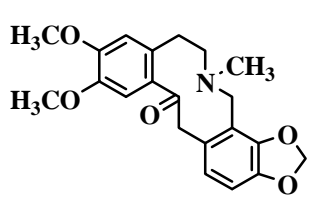
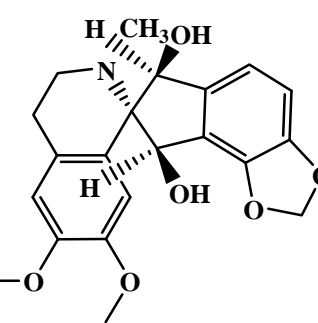
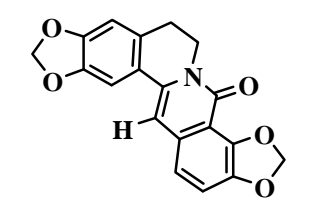
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8.	Fumariline	Whole plant and seed		[24]
9.	(-)-8-methoxydihydroanguinarine	Seed		[24]
10.	Oxysanguinarine	Seed		[24]
11.	Coptisine chloride	Whole plant		[25]
12.	Dehydrocheilanthifoline	Whole plant		[25]
13.	Narceimicine	Seed		[26,27]
14.	Papracinine	Aerial parts		[28]

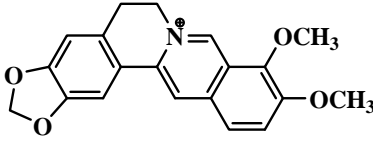
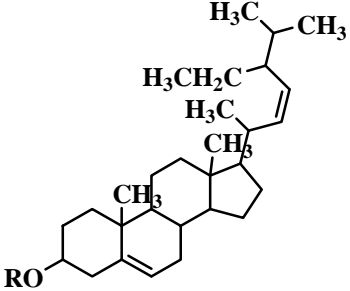
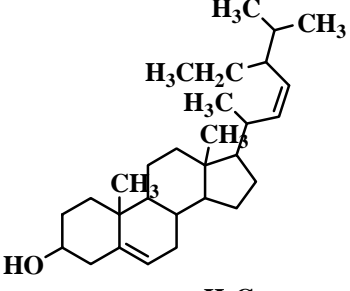
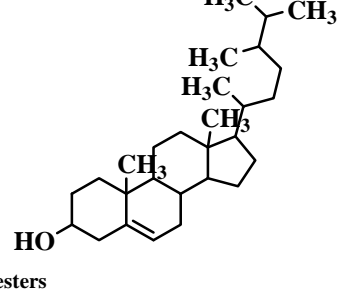
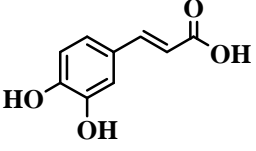
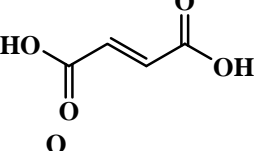
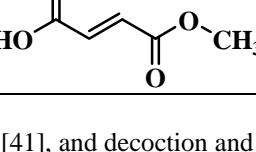
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15.	Paprazine	Aerial parts		[28]
16.	Fumaritine N-oxide	Whole plant and aerial parts		[28]
17.	Parfumine	Aerial parts		[28]
18.	Lastourvilline	Aerial parts		[28]
19.	Feruloyl tyramine	Aerial parts		[28]
20.	Fumariflorine	Aerial parts		[28]
21.	N-methyl corydaldine	Aerial parts		[28]
22.	Papraine	Aerial parts		[29]

Continued

23.	Fumarizine	Whole plant and aerial parts		[30]
24.	Paprafumine	Aerial parts		[31]
25.	Paprarine	Aerial parts		[31]
26.	Papraline	Aerial parts		[31]
27.	Cryptopine	Aerial parts		[31]
28.	Raddeanine	Aerial parts		[31]
29.	8-oxocoptisine	Aerial parts		[31]

Continued

30.	Berberine	Stem and leaves		[32]
Steroids				
1.	β -sitosterol	Whole plant, stem, leaves and aerial parts		[11,13]
2.	Stigmasterol	Whole plant and aerial parts		[11,13]
3.	Campesterol	Whole plant and aerial parts		[11,13]
Organic acid and their esters				
1.	Caffeic acid	Whole plant and aerial parts		[11,13]
2.	Fumaric acid	Whole plant and aerial parts		[11,13]
3.	Monomethyl fumarate	Whole plant and aerial parts		[33]

of abdominal cramps [38], diarrhea, fever [39], jaundice, leprosy and syphilis [18], blood disorders and tuberculosis [40]. The leaf paste has been used to treat headache

and fever [41], and decoction and infusion of the herb are indicated for treatments of goiter, leprosy, constipation, jaundice, chronic fevers and dyspepsia [42]. Fresh juice

of the plant are administered orally for common fever, removing worms from the abdomen, blood purification and as liver tonic for hepatic ailment, and also used for the treatment of simple goitre, diabetes and bladder infection by taking its extraction early morning [43,44]. Whole plant of *F. indica* is an important ingredient of many common household, Ayurvedic, Unani medicinal preparations like *Ayurveda capsule*, *Parpatadi-kwath*, *parpatadya arista*, *Parpatadi-arka*, *trifala shahtara*, *Sharab-pittapapada* [15,33], and other marketed polyherbal formulations such as *Livokriti syrup*, *Esno capsule* [45]. Examples of some such marketed formulations are given in **Table 3**. Furthermore, in Unani system of medicine, paste of fine powder of whole plant of *Fumaria indica* along with *Azadirachta indica* leaves, *Swertia chirata*, *Sphaeranthus indicus* flowers and *Rosa damascene* leaves in sufficient quantity of curd, has been used against pimples as routine home remedy [46].

5. Biological Activities and Safety

The very first reports on pharmacology of *Fumaria indica* concentrated mainly on the bioactivities of the alkaloids of the plant. Many of these alkaloids and other bioactive constituents of the plant are also encountered in other plants, and during more recent years the list of

therapeutically interesting bioactivities constituents of *Fumaria indica* has enlarged considerably. Diverse reported pharmacological properties of such secondary metabolites of *Fumaria indica* are summarized in **Table 4** [47-64]. The doses and routes of administrations used in these studies are also mentioned in this table. Other reports on therapeutically interesting pharmacological properties of different types of extracts obtained from the whole plant or from its areal parts and seeds have appeared also. **Table 5** [65-81] gives an overview of these reports which also includes the type of extracts and their doses used in the study. More detailed or critical analysis of available information on bioactivities and safety of *Fumaria indica* extracts and their bioactive constituents is beyond the scope of this communication. For such purposes a recent review [13] and several monographs now available on the plant can be consulted.

6. Psychopharmacological Aspects

Initial reports on psychopharmacology of *Fumaria indica* dealt mainly with the CNS function modulating effects of its alkaloids. Amongst them the so called benzylisoquinoline alkaloid protopine is one of the more well studied one, and it is also one of the quantitatively major alkaloid of *Fumaria indica*. Protopine was first

Table 3. Marketed formulations containing *Fumaria indica* extracts.

S. No.	Name of formulation	Indication(s)	Manufacturer
1.	Phytoliv tablets	Liver disorders	Tomer Laboratories 350 Campus Drive Somerset, New Jersey 08873 http://www.tomerlabs.com/
2.	Esno capsule	Chronic eosinophilla, cough and cold	Vita Health Private Limited Plot No. 753, At Rakanpur, Ta. Kalol, Gandhinagar-382721, Gujarat, India http://vitahealth.in/
3.	Livokriti syrup	Liver disorders	Elson Llc Wz-49h, 01st Floor, Budella, Vikas Puri, New Delhi-110018, India http://elsonusa.com/
4.	Valiliv forte tablets	Liver disorders	Unijules Life Sciences Limited Universal Square, 1505-1 Shantinagar Nagpur-440001, Maharashtra India http://www.unijules.com/
5.	Raktashodhak syrup	Blood purification	D.G. Ayurvedic Sangrah #14, J. P. Road, Opp. Ram Hanuman Mandir, Andheri West, Mumbai-400058, Maharashtra, India http://www.healthbyayurveda.in/
6.	Redliv DS caps	Liver disorders	Altis Life Sciences A-1/40, IIIrd floor, Sector-7, Rohini, Near M2K. Delhi-110085, India http://www.altislifesciences.com/

Table 4. Reported pharmacological activities of secondary plant metabolites isolated from *Fumaria indica*.

S. No.	Chemical Constituents	Pharmacological activities	Dose, duration and route of administration	References
1.	Fumariline	CNS depressant Anticonvulsant Analgesic Antifungal	10 - 50 mg/kg, single dose, i.p.	[47,48]
2.	Protopine	CNS stimulant Antidepressant Hepatoprotective Smooth muscle relaxation Choleretic Anti-thrombotic Anti-platelet aggregation Anti-inflammatory Anti-inflammatory Analgesic Anti-acetylcholinesterase Antifungal Antibacterial Antiviral	10 mg/kg, single dose, i.p. 5 - 20 mg/kg, single dose, p.o. 25 - 50 mg/kg, 7 days, p.o. 0.5 - 5 µg/ml <i>in vitro</i> 5 mg/kg, single dose, i.v. 50 - 100 mg/kg, single dose, i.p. 50 - 100 mg/kg, single dose, i.p. 50 - 100 mg/kg, single dose, i.p. 5 mg/kg, single dose, i.v. 10 - 40 mg/kg, single dose, s.c. 1.8 µM <i>in vitro</i> 8 - 64 µg/ml <i>in vitro</i>	[19,48-56]
3.	Narceimine, adlumidine and narlumidine	Anti-inflammatory Antifungal	10 mg/kg, single dose, i.p.	[48,49]
4.	<i>L</i> -tetrahydrocoptisine	Neuroleptic Antifungal	50, 100 mg/kg, 7 days, p.o.	[48,57]
5.	Monomethyl fumarate	Hepatoprotective Anti-inflammatory Anti-psoriatic Neuroprotective activity	50 mg/kg, 3 days, p.o. and 10 - 100 µg/ml <i>in vitro</i> 200 µM <i>in vitro</i>	[33,58-60]
6.	Fumaric acid	Neuroprotective Anti-psoriatic Immunomodulatory Anti-inflammatory	200 µM <i>in vitro</i> 95 mg, three times a day, p.o.	[58,59,61,62]
7.	Fuyuziphine	Antifungal	1250 ppm <i>in vitro</i>	[21]
8.	Berberine iodide	Antifungal Antibacterial Antiviral	1.5 g/L <i>in vitro</i> 8 - 64 µg/ml <i>in vitro</i>	[32,56]
9.	N-octacosanol	Hepatoprotective	100 µg/ml <i>in vitro</i>	[63]
10.	Fatty acids	Antioxidant		[64]
11.	Caffeic acid	Anti-inflammatory Antinociceptive		[11]
12.	β -sitosterol	Anti-inflammatory Antinociceptive Antipyretic agent		[11]

isolated from opium during 1875, and since then it has been detected in numerous other medicinal plants, including several of them commonly used in TCM (Table 6 [82-120]). During more recent decades diverse therapeutically interesting pharmacological properties of protopine have been identified, and many analogous activities have also been reported for extracts of diverse other protopine producing plants. One such report dealing with antidepressant like properties of the alkaloid revealed that it is a potent inhibitor of neuronal serotonin and noradrenaline transporter, and does not have any effects on dopamine or GABA transporters [50]. Despite exten-

sive efforts though, no antidepressant like activity of a hydro alcoholic *Fumaria indica* extract could be detected in rodent behavioural models commonly used for detecting such activities of synaptic serotonin and noradrenaline reuptake inhibitors [74]. Since protopine content of the tested extract is not known, no definitive statements on the role of protopine in psychotherapeutic potentially of *Fumaria indica* extracts can yet be made.

However, more recent efforts in our laboratories have revealed diverse therapeutically interesting psychopharmacological activities of hydro alcoholic extracts of *Fumaria indica*. They include their mental stress alleviating

Table 5. Reported pharmacological activities of *Fumaria indica* extracts.

S. No.	Type of extract	Plant part used	Pharmacological activity	Dose, duration and route of administration	References
1.	Aqueous-ethanolic	Whole plant	Anthelmintic	183 mg/kg, 13 days, p.o. 50 - 200 mg/kg, 14 days, p.o. 3.12 - 50 mg/ml <i>in vitro</i>	[65,66]
2.	Hydro-alcoholic	Whole plant	Spasmogenic Spasmolytic	1.0 - 5.0 mg/ml <i>in vitro</i> 0.1 - 1.0 mg/ml <i>in vitro</i>	[67]
3.	Aqueous-ethanolic	Whole plant	Anti-inflammatory and anti-nociceptive	100, 200 and 400 mg/kg, single dose, p.o.	[11]
4.	Aqueous, methanolic, petro- leum ether	Whole plant	Hepatoprotective		[68]
5.	Hydro-ethanolic	Whole plant	Hepatoprotective	100 and 400 mg/kg, 7 days, p.o.	[51]
6.	Aqueous-methanolic	Whole plant	Hepatoprotective	500 mg/kg, twice daily for 2 days, p.o.	[69]
7.	Aqueous-methanolic	Whole plant	Potentialiation of pentobarbital sleeping	500 mg/kg, single dose, p.o.	[69]
8.	Hydro-ethanolic	Seed	Antibacterial	100 µl <i>in vitro</i>	[70]
9.	Aqueous	Whole plant	Anti-hypochlorhydric	20 mg/kg, 14 days, p.o.	[8]
10.	Chloroform-methanolic	Whole plant	Anti-acetylcholinesterase Anti-butyrylcholinesterase	1 mg/ml <i>in vitro</i>	[71]
11.	Hydro-alcoholic	Whole plant	Antipyretic		[72]
12.	Aqueous-ethanolic	Whole plant	Hepatoprotective Antioxidant Anti-apoptotic	200 mg/kg, 5 days, p.o.	[73]
13.	Hydro-alcoholic	Whole plant	CNS depressant	100, 200 and 400 mg/kg, 7 days, p.o.	[74]
14.	Hydro-alcoholic	Whole plant	Safety profile: Acute toxicity Sub-chronic toxicity Chronic toxicity Cytotoxicity	1 - 5 g/kg, p.o. 100 - 400 mg/kg, 30 days, p.o. 100 - 400 mg/kg, 30 days, p.o. 50 - 100 µg/ml <i>in vitro</i>	[45,75]
15.	Hydro-alcoholic	Whole plant	Anti-stress	100, 200 and 400 mg/kg, 7 days, p.o.	[76]
16.	Hydro-alcoholic	Whole plant	Anti-aggressive	100, 200 and 400 mg/kg, 7 days, p.o.	[77]
17.	Hydro-alcoholic	Whole plant	Anti-anxiety	100, 200 and 400 mg/kg, 7 days, p.o.	[78]
18.	Aqueous-methanolic	Aerial parts	Prokinetic and laxative	30 - 100 mg/kg, single dose, p.o. 0.1 - 5 mg/ml <i>in vitro</i>	[20]
19.	Aqueous	Aerial parts	Gastroprotective Cytoprotective Anti-secretory Anti-ulcer Anti- <i>H. pylori</i>	100, 200 and 300 mg/kg, single dose, i.g. 100, 200 and 300 mg/kg, single dose, i.p. 0.25 - 1.0 mg/disc <i>in vitro</i>	[79]
20.	Aqueous	Whole plant	Dysentery		[80]
21.	Aqueous-ethanolic	Whole plant	Spermatogenesis	250 mg/kg, 5 days, p.o. 750 and 1050 mg/kg, 3 days, p.o.	[81]

[76], anti-aggressive [77], and anxiolytic [74,78] activities. During the course of these studies it became apparent also that the psychopharmacological activity profile

of a given *Fumaria indica* extract depends largely on the functional state of the central nervous system. Thus for example, although no antidepressant like effects of a

Table 6. Some plants known to contain protopine and other *Fumaria* alkaloids.

S. No.	Botanical name	Medicinal uses in Chinese medicine	Reference
1.	<i>Arctomecon alifornica</i>	-	[82]
2.	<i>Argemone Mexicana</i>	-	[83]
3.	<i>Aristolotelia chilensis</i>	-	[84]
4.	<i>Aristolochia constricta</i>	-	[85]
5.	<i>Chelidonium majus</i>	Yes	[86,87]
6.	<i>Corydalis adunca</i>	Yes	[88]
7.	<i>Corydalis bungeana</i>	Yes	[89]
8.	<i>Corydalis calliantha</i>	-	[90]
9.	<i>Corydalis cava</i> (<i>C. tuberosa</i>)	-	[91]
10.	<i>Corydalis crispa</i>	-	[92]
11.	<i>Corydalis decumbens</i>	Yes	[93]
12.	<i>Corydalis intermedia</i>	-	[94]
13.	<i>Corydalis marschalliana</i>	-	[95]
14.	<i>Corydalis meifolia</i>	-	[96]
15.	<i>Corydalis pumilis</i>	-	[94]
16.	<i>Corydalis racemose</i>	Yes	[97]
17.	<i>Corydalis solida</i>	-	[94]
18.	<i>Corydalis speciosa</i>	-	[98]
19.	<i>Corydalis tashiroi</i>	-	[99]
20.	<i>Corydalis ternate</i>	-	[100]
21.	<i>Corydalis thyrsoflora</i>	-	[101]
22.	<i>Corydalis yanhusuo</i>	Yes	[102]
23.	<i>Dactylicapnos scandens</i>	Yes	[103]
24.	<i>Eomecon chionantha</i>	Yes	[104]
25.	<i>Eschscholtzia californica</i>	-	[105]
26.	<i>Fumaria agrarian</i>	-	[9]
27.	<i>Fumaria bastardii</i>	-	[9]
28.	<i>Fumaria capreolata</i>	-	[9]
29.	<i>Fumaria densiflora</i>	-	[9]
30.	<i>Fumaria faurei</i>	-	[9]
31.	<i>Fumaria indica</i>	-	[19]
32.	<i>Fumaria macrosepala</i>	-	[9]
33.	<i>Fumaria officinalis</i>	-	[106]
34.	<i>Fumaria parviflora</i>	-	[107]
35.	<i>Fumaria petteri</i>	-	[9]
36.	<i>Fumaria schrammii</i>	-	[106]

Continued

37.	<i>Glaucium flavum</i>	-	[108]
38.	<i>Glaucium grandiflorum</i>	-	[109]
39.	<i>Glaucium oxylobum</i>	-	[110]
40.	<i>Glaucium pulchrum</i>	-	[111]
41.	<i>Glaucium vitellinum</i>	-	[111]
42.	<i>Hypocoum erectum</i>	Yes	[112]
43.	<i>Hypocoum lactiflorum</i>	Yes	[113]
44.	<i>Hypocoum leptocarpum</i>	Yes	[114]
45.	<i>Macleaya cordata</i>	Yes	[115]
46.	<i>Macleaya microcarpa</i>	Yes	[116]
47.	<i>Papaver bracteatum</i>	Yes	[117]
48.	<i>Papaver coreanum</i>	-	[118]
49.	<i>Papaver somniferum</i>	-	[117]
50.	<i>Sanguinaria canadensis</i>	-	[119]
51.	<i>Thalictrum rugosum</i>	-	[120]

hydro alcoholic *Fumaria indica* extract were detectable in non-stressed animals [74], such effects of the same extract was apparent in the same tests using mentally stressed animals [76]. It must be mentioned also that anxiolytics like and diverse other psychopharmacological activities of *Fumaria indica* extracts can be observed after their repeated daily doses only, and that their efficacies increase with the number of their daily oral doses administered. These and many other observations made to date with diverse types of *Fumaria indica* extracts and their bioactive constituents clearly reveal that their pharmacological targets and modes of actions are not like those of any known psychoactive drugs and other bioactive agents studied to date. It was only by the use of appropriate holistic psychopharmacological strategy, and proper choices of plant materials and extraction procedures, that these conclusions could be reached with certainty.

7. Concluding Remarks

It cannot be overemphasized that like many other medicinal plants *Fumaria indica* also produces structurally and functionally diverse bioactive secondary plant metabolites, not all of which can be extracted by a single solvent or extraction procedure. Moreover, therapeutically interesting bio-activity profile of a given plant extract is not only a resultant of the combined effects of all bioactive ingredients present in it, but also depends on its treatment regimen used to define its activity profile. Complexities arising from these facts clearly indicate that

translation of traditional knowledge on medicinal uses of *Fumaria indica*, or of any other medicinal plant, in terms of modern medical sciences is possible only when the plant is considered as a whole, and its diverse types of extracts are tested in a battery of therapy relevant animal models. Hereupon, due attention has to be paid to the psychopharmacological activity profiles of the extracts.

It is now well established that all chronic diseases, or illnesses, always causes mental health problems, and that bi-directional interactions between mental health problems and physical health is a common feature of almost all socioeconomically important health problems. Unfortunately, even today, modern medicinal phyto-chemists and pharmacologists pay little attention to these facts and continue to explore traditionally known medicinal plants as sources for structurally and functionally novel therapeutic lead molecules only. Lessons learned and experiences gained from extensive efforts made since decades in our laboratories and elsewhere strongly suggest that *Fumaria indica* could be a valuable tool for identifying novel pharmacological targets and mechanisms potentially useful for achieving better and reproducible successes with phyto-pharmaceuticals containing its extracts as active ingredients. Since *Fumaria indica* is a weed, and holistic pharmacological strategies can easily be practiced in many developing and underdeveloped countries, efforts to better understand and more precisely define its therapeutic potentials can be strongly recommended. Moreover, since the lists of plants producing the same or structurally analogous bioactive secondary metabolites of *Fumaria indica* are long (for example see **Table 6**),

know how gained from the efforts to properly decode its pharmacology will certainly be useful for decoding medicinal values of many other as yet underexplored ones. In any case, experiences gained with *Fumaria indica* strongly suggest that repeated oral dose studies with psychoactive alkaloid containing plants could be the more appropriate ones for properly evaluating their psychotherapeutic potentials.

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