CODEN [USA]: IAJPBB ISSN: 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES

http://doi.org/10.5281/zenodo.1210515

Available online at: http://www.iajps.com Review Article

FUMARIA PARVIFLORA- A REVIEW

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Abstract:
The preliminary phytochemical analysis of Fumaria parviflora revealed the presence of flavonoids, glycosides, tannins, saponins, steroids, triterpenoids, phenols, alkaloids and anthraquinones. The pharmacological studies showed that Fumaria parviflora possess hepatoprotective, antidiabetic, antiinflammatory, antipyretic, analgesic, prokinetic, laxative, dermatological, antimicrobial, antiparasitic, reproductive, anticholinesterase and smooth muscle relaxant effects. This review will highlight the chemical constituents and the pharmacological effects of Fumaria parviflora.

Keywords: *chemical constituents, pharmacology, Fumaria parviflora*

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QR code

Please cite this article in press Ali Esmail Al-Snafi., Fumaria Parviflora- A Review, Indo Am. J. P. Sci, 2018; 05(03).

INTRODUCTION:

Two thirds of the new chemicals identified yearly were extracted from higher plants. 75% of the world's population used plants for therapy and prevention. In the US, where chemical synthesis dominates the pharmaceutical industry, 25% of the pharmaceuticals are based on plant-derived chemicals [1-35]. The preliminary phytochemical analysis of *Fumaria parviflora* revealed the presence of flavonoids, glycosides, tannins, saponins, steroids, triterpenoids, phenols, alkaloids and anthraquinones. The pharmacological studies showed that *Fumaria parviflora* possess hepatoprotective, antidiabetic, antiinflammatory, antipyretic, analgesic, prokinetic, laxative, dermatological, antimicrobial, antiparasitic, reproductive, anticholinesterase and smooth muscle relaxant effects. This review was designed to highlight the chemical constituents and the pharmacological effects of *Fumaria parviflora*.

Plant profile:

Synonyms:

Fumaria affinis Griff., *Fumaria caespitosa* Loscos ex Willk. & Lange, *Fumaria diffusa* Moench, *Fumaria glauca* Jord., *Fumaria leucantha* Viv., *Fumaria minima* Pugsley, *Fumaria officinalis var. parviflora [Lam.]* Ewart, *Fumaria parviflora var. latisecta* Hausskn., *Fumaria parviflora var. sinaitica* Hausskn., *Fumaria sicula* Biv., *Fumaria tenuifolia* Symons, *Fumaria tenuisecta* Syme [36].

Taxonomic classification:

Kingdom: Plantae, **Subkingdom**: Viridiplantae, **Infrakingdom**: Streptophyta, **Superdivision**: Embryophyta, **Division**: Tracheophyta, **Subdivision**: Spermatophytina, **Class**: Magnoliopsida, **Superorder**: Ranunculanae, **Order**: Ranunculales, **Family**: Papaveraceae, **Genus**: *Fumaria*, **Species**: *Fumaria parviflora* [37].

Common names:

Arabic: Shahitreg, homaira**; Bengali**: Vanshulpha, Bansulpha; **English**: fine-leaf fumitory**, Indian** fumitory, small-flower fumitory; **Hindi:** Pittapapada, Dhamgajra, Pittapapara; **Punjabi**: Shahtara, Pittapapara; **Sanskrit**: Varatikta, Sukshmapatra**; Tamil**: Tura, Tusa; **Unani**: Shaahtaraa; **Urdu**: Parpata [38-39].

Distribution:

Fumaria parviflora was found in Europe, Africa and Asia especially Middle East. The plant was distributed in **Africa**: **[**Algeria**;** Egypt**,** Libya**,** Morocco**,** Tunisia];**Asia**: [Armenia**,** Azerbaijan**,** Tajikistan**,** Turkmenistan, Afghanistan**,** Iran, Iraq, Palestine, Jordan**,** Lebanon**,** Syria**,** Turkey**]**; **Europe**: **[**Ukraine, Belgium**,** Germany**,** Hungary, United Kingdom, Bosnia, Herzegovina, Bulgaria, Croatia, Greece, Italy, Romania, Slovenia, France, Portugal, Spain] [38, 40].

Description:

Annual herb, erect or somewhat prostrate. Stem glabrous, up to 60 cm tall, with cylindrical, tapering root measuring about 10 to 15 cm in length and 0.4 to 0.8 mm in diameter, bearing lateral wiry rootlets; erect, longitudinally wrinkled, often branched 20-30 cm long stem with 4 to 5 winged projections; alternate, exstipulate leaf that is finely divided into narrow flat segments, each segment being broad oblong or linear lanceolate, 2 to 3 cm in length and 1 to 2 mm in width with acute or sub-acute apex, 2 to 4 cm long twisted petiole, sheathing at base; small white or pink flowers with purplish tips, in terminal inflorescence; indehiscent, tiny, sub-globose and externally faintly rugose fruits and globose minute seeds[41-42].

Traditional uses:

Entire herb was used traditionally in leprosy, fever, for detoxification, and as laxative, diuretic and diaphoretic [43-44]. The extract of the plant was used as bitter tonic, astringent, for the treatment of dyspepsia and scrofulous skin infections [45]. *Fumaria parviflora* was also used traditionally in dermatological diseases, in stimulation of liver function and gall bladder and also as antiscabies, antiscorbite, antibronchite, diuretic, expectorant, antipyretic, diaphoretic, appetizer and laxative [46]. In folk medicine of Turkey it was used against hepato‑biliary dysfunction, while, in the Unani traditional system it was prescribed to treat gut and respiratory disorders, abdominal cramps, indigestion and asthma [47].

Physicochemical characteristics:

Physicochemical parameters [% w/w]: Loss on drying: 78.3 ± 0.12, total ash: 25.63 ± 0.75, water soluble ash: 8.63 ± 0.44, acid insoluble ash: 4.75 ± 0.26, water soluble extractive value: 34.0 ± 0.19 and alcohol soluble extractive value: 7.5 ± 0.35[42].

Chemical constituents:

The preliminary phytochemical analysis of *Fumaria parviflora* revealed the presence of flavonoids, glycosides, tannins, saponins, steroids, triterpenoids, phenols, alkaloids and anthraquinones [47-48].

Fumaria parviflora contained [%w/w] alkaloids: 6.21 ± 0.13, phenolics: 6.15 ± 0.28 and flavanoids: 3.64 ± 0.35 [42].

The plant contained wide range of alkaloids, the methanolic extraction of 10.5 kg of the plant yielded 0.39% of total alkaloids, the following alkaloids have been identified parfumine, norjusiphine, N-methyladlumine, d-fumaricine, adlumiceine, adlumidiceine, [+]-adlumidine, [+]-adlumine, [-]-adlumine, [+]- bicuculline, [±]-bicuculline, bicucullinine [narceimine], [-]-cheilanthifoline, coclaurine, coptisine, [-]-corlumine, cryptopine, dehydrocheilanthifoline, dihy drohmariline, dihydrosanguinarine, fumaramidine, fumaramine, fumaridine, fumariflorine ethyl ester, fumarilicine, [+]-fumariline, fumaritine, [+]-α- hydrastine, [+]-isoboldine, izimirine, lahoramine, lahorine, 8-methoxydihy drosanguinarine, methylhydrastinium, N-methyladlumine, N-methylhydrasteine, N-methylhydrastine, N-methyloxohydrasteine, narlumidine, norjuziphine, noroxy- hydrastinine, 8-oxocoptisine, oxysanguinarine, [+] - pahidine, [+]-parfurnine, [+]-parviflorine, protopine, thequaternarysalt of protopine, sanguinarine, [-]-scoulerine, [-]-stylopine, and [±]-stylopine [48-53]. Phthalide isoquinoline alkaloid [[-]-corlumine] and rhoeadines-like alkaloid [rhoeagenine] were isolated from Fumaria parviflora [52, 54].

The Total alkaloids mg/ 100g dry weight of the aerial parts of plants was 521, the quantities of different alkaloids isolated from *Fumaria parviflora* were: protopine [protopine: 57 mg/100g dry weight, cryptopine: 5 mg/100g dry weight], tetrahydroprotoberine [sinactine: 2 mg/100g dry weight], [adlumine: 3 mg/100g dry weight] spirobenzyl isoquinoline [parfumine: 14 mg/100g dry weight, fumariline: 10 mg/100g dry weight, parfumidine: 7 mg/100g dry weight] and benzophenanthridine [dihyrosanguinarine: 2 mg/100g dry weight] [55].
The unsaponifiable matter as well as the total fatty acids fractions of the lipoidal matter of *Fumaria parviflora* were investigated. β-sitosterol, stigmasterol, campesterol as well as C30H62 hydrocarbon were isolated. GLC of fatty acids methyl esters revealed the presence of: capric [1%], lauric [1.9%], myristic [1.16%], myristoleic [4.55%], palmitic [3.9%], stearic [29%], linoleic [10.5%], and arachidonic [7.23%] acids, in addition to unidentified peaks. The flavonoids identified in the plant were 3, 5, 3', 4' tetrahydroxy flavone-3-arabinoside; 3'-4'-dihydroxy flavone and 3,7,4'-trihydroxy flavone [56].

N-octacosan 7β ol, [5αH,11α H]-8-oxo-homoiridolide; *n*-docosanyl-2-*O* -β-*D*-glucopyranosyl salicylate; 2-methyl-6- hydroxy methylene dodecan -10-oyl-12, 15-olide14-*O*-β -*D*-xylopyranoside; 4-oxo- stigmast-5-en-3 β -ol-*D*-glucopyran oside; salicylic acid-*O*-β-*D*-xylopyranoside; α-*D*- glucopyranosyl hexadecanoate; α-*D*- gluco-pyranosyl- [2 → 1′]-α -*D*- glucopyranoside; *n*-propyl-3,4-dioxymethylene benzene; 5β, 6, 7, 8, 9, 10β-hexahydrocoumarin; 2,6-dimethyl dodecan-10-oyl-12,15-olide; *n*-tetradecanyl *n*-octadec-9-enoate, propanyl triol- 3, 2- *n*-di-octadecanoyl-1-*n*-octadeca-9′,12′-dienoate and *n*-tetradecanyl *n*-octadec-9,12-dienoate were isolated from the aerial parts of *Fumaria parviflora*. While, nonacosane-10-ol and 23α-homostigmast-5-en-3β-ol were isolated from the roots of *Fumaria parviflora* [47, 57-59].

Pharmacological effects:
Protective effect:
The hepatoprotective effect of the ethanol extract of the aerial part of *Fumaria parviflora* [250 mg/kg daily 5 days prior to the experiments till 2 days after injection of CCl4] was evaluated in carbon tetrachloride induced liver injury in rats. The extract possessed hepatoprotective effects based on serum glutamate oxaloacetate transaminase, serum glutamate pyruvate transaminase, alkaline phosphatase and total bilirubin. The normal histological appearance of hepatocytes indicated a good protection of the extract against carbon tetrachloride hepatotoxicity [60].

The protective effect of *Fumaria parviflora* on nimesulide induced cell death was investigated in primary rat hepatocyte cultures. *Fumaria parviflora* extract treated cells showed increased viability as compared to nimesulide stressed cells as assessed by MTT assay. LDH leakage increased significantly at 500microM nimesulide, and the data suggested that apoptosis was the predominant mechanism responsible for cell death. Nimesulide induced apoptosis was further confirmed by DNA fragmentation and chromatin condensation. Nimesulide exposure increased intracellular ROS, translocation of Bax and Bcl2 followed by mitochondrial depolarization and cytochrome c [Cyt c] release along with caspase-9/-3 activity confirming involvement of mitochondria in nimesulide induced apoptosis. Events like membrane depolarization of mitochondria, expression of Bax, Bcl2, and externalization of phosphatidyl serine were substantially reversed by the pre-treatment of of *Fumaria parviflora* extract. These results indicated that of *Fumaria parviflora* extract modulates critical events regulating pro and anti-apoptotic proteins in mitochondria dependent apoptosis induced by nimesulide [61].

The hepatoprotective potential of *Fumaria parviflora* extract was evaluated against nimesulide

induced oxidative stress in rats, and regulation of critical events in mitochondria mediated apoptosis. Pre-treatment with *Fumaria parviflora* extract for 5 days significantly reduced the impact of nimesulide induced toxicity as evident from the serum biomarkers of liver damage and histopathology. It also modulated mRNA expression and antioxidant enzymes [SOD, glutathione peroxidase, glutathione reductase] and reduced lipid peroxidation during nimesulide toxicity. Nimesulide exposure decreased GSH content [92.9%] and increased reactive oxygen species [9.29 fold] which was attenuated in *Fumaria parviflora* extract treated rats. *Fumaria parviflora* extract pre-treatment significantly altered key apoptotic events like Bcl2 and Bax translocation, inhibited mitochondrial depolarization, prevented cytochrome c release, caspase-9/caspase-3 activation and DNA damage [62].

The hepatoprotective activity of an aqueous-methanolic extract of *Fumaria parviflora* was investigated against paracetamol- and CCI4-induced hepatic damage. Pretreatment of animals with the plant extract [500 mg/kg; orally] reduced the death rate from 100 to 50%. Pretreatment of rats with plant extract [500 mg/kg, orally twice daily for 2 days] prevented [P < 0.001] the paracetamol [640 mg/kg]-induced rise in serum enzymes alkaline phosphatase and transaminases [GOT and GPT], whereas the same dose of the extract was unable to prevent [P > 0.05] the CCI4-induced rise in serum enzyme levels. Posttreatment with 3 successive doses of the extract [500 mg/kg, 6 hourly] also restricted the paracetamol-induced hepatic damage [63].

The protective effect of ethanolic extract of *F. parviflora* was investigated against lead-induced testicular oxidative stress in rats. Adult Wistar rats were treated with 0.1% lead acetate in drinking water with or without 200 mg kg/ day *F. parviflora* extract via gavage for 70 days. Lead acetate treatment resulted in significant reduction in testis weight, seminiferous tubules diameter, epididymal sperm count, serum testosterone level, testicular content of superoxide dismutase [SOD] and glutathione peroxidase [GPx]. Moreover, significant elevation was observed in content of malondialdehyde [MDA] in lead-treated rats. Co-administration of *Fumaria parviflora* extract showed a significant increase the reproductive parameters in lead-treated rats [64].

Antidiabetic effect:

The hypoglycaemic effects of methanolic extract of *Fumaria parviflora* [125 mg and 250 mg/ kg/ day, ip for seven days] was evaluated in normal and streptozotocin-induced diabetic rats. Administration of methanolic extract of *Fumaria parviflora* extract showed potent glucose lowering effect only on streptozotocin induced diabetic rats below 100 mg/dl [P<0.001]. However, no significant differences in the blood glucose levels were recorded between diabetic rats received 125 or 250 mg/kg of plant extracts [46].

The effect of oral consumption of *Fumaria parviflora* [6.25%, orally after injection of streptozocin for five weeks] was assessed on serum glucose and lipid levels in streptozocin diabetic rats. Serum levels of glucose, triglyceride, total cholesterol, HDL and LDL were evaluated before and three and six weeks after the treatment. The results revealed that there was no significant difference in the glucose level between diabetic rats treated with *Fumaria parviflora* and untreated diabetic rats at third and sixth weeks. However there was a significant decrease in triglyceride level in *Fumaria parviflora* treated group as compared to untreated diabetic rats at third and sixth weeks. In *Fumaria parviflora* treated group, serum total cholesterol, showed a significant decrease and HDL cholesterol showed a significant increase at sixth week [65].

The antidiabetic effect of various doses of the powdered *Euphorbia prostrata* was investigated on blood glucose levels of the normal and alloxan-diabetic male albino rabbits. *Fumaria parviflora* produced significant hypoglycaemic effects in the normal rabbits only. Moreover, acute toxicity studies and records of behavioural patterns carried out in rabbits and rats, respectively showed no adverse effects in the dosages tested. It was conceivable that the plant contained some hypoglycaemic principles which act probably by initiating the release of insulin from the pancreatic beta cells of normal rabbits [66].

Antiinflammatory, antipyretic and analgesic effects:

The anti-inflammatory activity of leaves extract of *Fumaria parviflora* and underlying mechanisms was studied in rats by using *in vivo* models of inflammation. The anti-inflammatory activity was studied using carrageenan-induced paw edema method and cotton pellet granuloma method. Levels of cytokines such as TNF-α, IL-6 and IL-1 and activity of antioxidant enzymes including catalase [CAT] and glutathione peroxidase [GPx] were estimated. Leaves extract of *Fumaria parviflora* possessed significant [P<0.001] decrease in paw edema in carrageenan-induced paw edema method. It diminished the serum tumour necrosis factor-α [TNF-α], IL-6 and IL-1 levels and also significantly attenuated the malondialdehyde [MDA] levels. The activity of CAT and GPx was increased in paw tissue. It also demonstrated significant decrease in

granuloma formation in cotton pellet-induced granuloma method [67].

The anti-inflammatory effect of hydro alcoholic extract of *Fumaria parviflora* was investigated in rats at doses of 200, 400, 600, 800 or 1000 mg/kg using carageenan model. 200 and 400 mg/kg doses of extract had less effect on the paw's edema in comparison with animal group received aspirin [P<0.05]. However, 600, 800 and 1000 mg/kg of the extract possessed more antiinflammatory effects, and the difference between groups was not statistically significant [p>0.05] [68].

The antipyretic activity of *Fumaria parviflora* was studied in rabbits. Pyresis was induced by subcutaneous yeast injections. Significant oral antipyretic activity in rabbits was exhibited by hexane-, chloroform- and water-soluble extracts of *Fumaria parviflora* comparable with aspirin. The antipyretic activity was more prominent in the hexane-soluble extract [69].

The antinociceptive effects of the methanolic extract of *Fumaria parviflora* were evaluated in mice subjected to acute thermal [hot-plate] and persistent chemical [formalin] pain stimuli. Intra-peritoneal injection of the percolated extract evoked significant antinociceptive effects at a dose of 100 mg/kg in the second phase of formalin test. The maximum antinociceptive effect was induced by the dose of 300 mg/kg that was significant in both phases of formalin test. The results showed that only percolated extract had significant antinociceptive effect in hot-plate. Pretreatment of mice with naloxane, an opioid antagonist did not change antinociceptive effect of percolated extract in formalin test, but in hot-plate it increased extract's effect after the first 15 minutes [70].

Prokinetic and laxative effects:

The effects of *Fumaria parviflora* were evaluated in gut motility disorders in experimental animals. The *in vivo* prokinetic and laxative assays were conducted in mice. The effects on contraction of the smooth muscles were investigated using isolated intestinal preparations [ileum and jejunum] from different animal species [mouse, guinea-pig and rabbit]. The aqueous-methanol extract of *Fumaria parviflora*, showed partially atropine-sensitive prokinetic and laxative activities in the *in vivo* in mice at 30 and 100 mg/kg. In the *in vitro* studies, the aqueous-methanol extract of *Fumaria parviflora* [0.01-1 mg/ml] caused a concentration dependent atropine-sensitive stimulatory effect both in mouse tissues [jejunum and ileum], and rabbit jejunum but had no effect on rabbit ileum. In guinea-pig tissues [ileum and jejunum], the crude extract showed a concentration dependent stimulatory effect with higher efficacy on ileum and the effect was partially blocked by atropine, indicating the involvement of more than one types of gut-stimulant components [atropine-sensitive and insensitive] [71].

Dermatological effects:

In a randomized double-blind, placebo-controlled study, 44 patients with hand eczema were randomly assigned to apply 4% cream of *Fumaria parviflora* or vehicle cream to hand twice daily for 4 weeks. The reduction of eczema area and severity index score before and two weeks after therapy was statistically significant between vehicles treated and 4% cream *Fumaria parviflora* treated patients. Only one patient showed side effect [erythema and population] [72].

The efficacy of *Fumaria parviflora* for reducing uremic pruritus severity among hemodialysis patients was investigated by randomized, double-blind, placebo-controlled trial. A total of 79 hemodialysis patients with pruritus were randomly assigned to receive either *Fumaria parviflora* [2 X 500-mg plant powder capsules/ day] or a placebo [2X 500 mg Wheat flour capsule/ day] for eight weeks. The visual analogue scale [VAS], the Duo score for calculating pruritus score, serum interferon- [IFN-α] level, interleukin-4 [IL-4], and high-sensitivity C-reactive protein were measured before and after treatment. At the end of the treatment phase, the pruritus score decreased in both groups [P < 0.001]; however, the mean reduction in pruritus scores was significantly higher in the *Fumaria parviflora* group than the placebo group according to VAS [-6.15±2.12 vs. -2.25±2.46, P <0.001] and Duo scores [-22.03±9.64 vs. -8.38±6.28, P < 0.001]. The mean serum IFN-α levels in the *Fumaria parviflora* group were significantly decreased [P< 0.001], but there was no significant change in these levels in the placebo group [P = 0.604]. The mean serum IL-4 level was significantly elevated in the *Fumaria parviflora* group [P = 0.028] but not in the placebo group [p = 0.100]. The authors concluded that ***Fumaria*** *parviflora* can significantly decrease the severity of uremic pruritus in hemodialysis patients [73].

Smooth muscle effects:

In the *in vitro* studies, the aqueous-methanol extract of *Fumaria parviflora* relaxed CCh and isotonic high K+ physiological salts solutions-induced contractions in jejunum, ileum and tracheal preparations of rat, guinea-pig and rabbit. The aqueous-methanol extract of *Fumaria parviflora* was predominately more potent against CCh than isotonic high K+ solutions-induced contractions, similar to dicyclomine, suggesting the presence of anticholinergic and calcium channel blocking [CCB] activities, which were confirmed when the aqueous-methanol extract

of *Fumaria parviflora* shifted the CCh and Ca2+ concentration-response curves in rat ileum and trachea, towards right. Among intestinal preparations from various species, both anticholinergic and CCB effects of the aqueous-methanol extract of *Fumaria parviflora* were exhibited at lower concentrations in rat than the other species. In tracheal preparations, the aqueous-methanol extract of *Fumaria parviflora* was the most potent in its CCB effect in rabbit [74].

Antiparasitic effect:

The anthelmintic activity of *Fumaria parviflora* was evaluated against the gastrointestinal nematodes of sheep [*H. contortus* , *O. circumcincta*, *Trichostrongylus Spp.*, *S. papillosus*, *Oe. columbianum* and *Chabertia ovina*] through egg hatch and larval development tests *in vitro* and faecal egg counts reduction test *in vivo*. *In vitro* studies revealed that aqueous and ethanolic extracts at the concentration of 3.12, 6.3, 12.5, 25.0 and 50.0 mg/ml exhibited ovicidal and larvicidal effects [P<0.05] against the eggs and larvae of gastrointestinal nematodes. The highest effective dose [ED50] value of *Fumaria parviflora* extract was recorded on the eggs of *Chabertia ovina* [14.45 mg/ml] with aqueous extract; whereas, the higher LC50 value of *Fumaria parviflora* extracts was recorded against the larvae of *Strongyloides papillosus* [16.60]. *In vivo* studies revealed that experimental animal groups treated with the doses of 200 mg/kg of either aqueous or ethanolic extracts of *Fumaria parviflora* exhibited higher [P<0.05] reduction rate on faecal egg counts [FEC]. The highest reduction rate on FEC of treated animal groups recorded was 77.6 and 70.05% with ethanolic and aqueous extracts, respectively at the dose of 200 mg/kg on the day 14 post treatment [75].

Extracts or ingredients of six different plant species were tested against exsheathed infective larvae of *Haemonchus contortus* using a modified methyl-thiazolyl-tetrazolium [MTT] reduction assay. Pyrantel tartrate was used as reference anthelmintic. The ethanolic extracts of the whole plant of *Fumaria parviflora* showed an anthelmintic efficacy of up to 93%, relative to pyrantel tartrate [76].

Helminth-free lambs were infected artificially with 10.000 third stage larvae of *Haemonchus contortus* or 20,000 third stage larvae of *Trichostrongylus colubriformis*. Thirty days post-infection the lambs were treated orally with a single dosage of 3 mg/kg body weight of aqueous ethanol extract of the whole plants of *Fumaria parviflora*. Of many medicinal plant treatments, only the ethanol extract of *Fumaria parviflora* caused a strong reduction of the faecal egg counts [100%] and a 78.2 and 88.8% reduction of adult *H. contortus* and *T. colubriformis* on day 13 post-treatment. The extract was as effective as the reference compound, pyrantel tartrate [77].

The antifasciolic effect of powdered plant drugs including *Nigella sativa* seeds, *Fumaria parviflora* aerial parts and *Caesulpinia crista* seeds was investigated in buffaloes. The trial results showed that *Fumaria parviflora* possessed significant efficacy against fascioliasis. Its highest doses produced highly significant [P<0.001] decrease in EPG counts on 15th days. Among the 3 plants used in the trial, the maximum antifasciolic efficacy, judged on the basis of % EPG count reduction was shown by *Fumaria parviflora* [93.2 ±0.5%]. No visible side effects were produced by any of these plant drugs. Single oral treatment with 25 mg/kg of *Nigella sativa* seeds or 60 mg/kg of *Fumaria parviflora* aerial parts and 40 mg/kg of *Caesulpinia crista* seeds exerted highly significant antifasciolic efficacies on the day 15 after treatment [78].

The nematicidal activity of nonacosane-10-ol and 23a-homostigmast-5-en-3β-ol, isolated from the n-hexane fraction of the roots of *Fumaria parviflora* was investigated against eggs and juveniles of Meloidogyne incognita *in vitro* at the concentrations of 50, 100, 150, and 200 µg/ml. Over 120 h of incubation, the cumulative percent mortality and hatch inhibition of both ranged from 20 to 100% and from 15 to 95.0%, respectively [59].

The antiprotozoal effect of the ethanol extracts of five Fumaria species [*Fumaria densiflora*, F*umaria cilicica*, *Fumaria rostellata*, *Fumaria kralikii*, and *Fumaria parviflora*] was investigated against *Plasmodium falciparum* [malaria] and *Trypanosoma brucei rhodesiense* [human African trypanosomiasis] at 0.81 and 4.85 µg/ml concentrations. The results revealed that anti -*Plasmodium falciparum* effect of *Fumaria parviflora* was 18.70% at concentration of 4.85 µg/ml and anti- *T. brucei rhodesiense* was 5.60 at concentration of 0.81 µg/ml and 11.25 at concentration of 4.85µg/ml [79].

N-octacosan 7β ol was isolated from the methanolic extract of whole plant of *Fumaria parviflora*. The *in vitro* antileishmanial evaluation of isolated compound against *Leishmania donovani* promastigotes was investigated by growth kinetics assay, reversibility assay, analysis of cellular morphology, adverse toxicity and determination of 50% growth inhibitory concentration [GI50]. N-octacosan-7β-ol [OC], possessed significant anti-*Leishmania donovani* promastigotes activity with GI50 = 5.35 [57].

Reproductive effect:

The effects of *Fumaria parviflora* ethanolic leaves extract on reproductive parameters were studied in adult male rats. Healthy adult male rats were treated

with 100, 200 and 400 mg/kg/day of *Fumaria parviflora* leaves extract via gavage for 70 days. The body weight was not affected, while the weights of testis and epididymis were significantly enhanced in rats treated with 200 and 400 mg/kg/day *Fumaria parviflora* extract. No significant changes were observed in seminal vesicle and ventral prostate weight. Significant increase was found in epididymal sperm density and percent of morphologically normal sperm in extract-treated rats. Serum testosterone levels were significantly higher in rats received 200 and 400 mg/kg/day [80].

The effect of *Fumaria parviflora* alcoholic extract on spermatogenesis was studied in rats. *Fumaria parviflora* was administered orally at doses of 750 and 1050 mg/kg bw for 3 days and 250 mg/kg bw for 5 days through oral gavage. Rats were sacrificed on day fifteenth after the first gavage. The weight and volume of the testes was increased in experimental groups but these increases were not significant. Histopathological analysis showed that *Fumaria parviflora* significantly increased the number of spermatogonium, spermatocytes, spermatozoids and Leydig cells [P<0.001] [81].

Co-administration of ethanol *Fumaria parviflora* extract [200 mg kg/ day via gavage for 70 days] with 0.1% lead acetate in drinking water showed a significant increase in testis weight, seminiferous tubules diameter, epididymal sperm count, serum testosterone level, testicular content of superoxide dismutase [SOD] and glutathione peroxidase [GPx], the parameters which decreased in lead-treated rats [64].

The ethanolic extract of the plant as well as the isolated alkaloid protopine exhibited a stimulatory effect on rat's uterus at various stages of sex cycle *in vitro*. The extract shows *in vivo* oestrogen-like effects as evidenced by vaginal smear and uterine weight tests. In contrast, it failed to produce progesterone or testosterone-like activities [56].

Anticholinesterase activity:

The chloroform: methanol [1:1] extracts of a number of the plant species belonging to eight families, including *Fumaria parviflora*, were screened for their anticholinesterase activity on acetyl cholinesterase [AChE] and butyrylcholinesterase [BChE] enzymes by *in vitro* at 10 microg/ml and 1 mg/ml concentrations. Among the screened extracts, all of the Fumaria extracts displayed highly potent inhibition against both of the enzymes at 1 mg/ml concentration compared to the standard [82].

Antimicrobial effect:

Disc diffusion and broth micro dilution methods were used to study the antibacterial [Gram positive, *Staphylococcus epidermidis* and *Bacillus subtilis*; Gram negative, *Escherichia coli* and *Salmonella typhimurium*] and antifungal [*Candida albicans* and *Aspergillus niger*] activity of N-octacosan 7β ol isolated from the methanolic extract of whole plant of *Fumaria parviflora*. N-octacosan-7β-ol , possessed significant antibacterial and antifungal activity against *Staphylococcus epidermidis*, *Escherichia coli*, *Candida albicans* and *Aspergillus niger in vitro* with MIC of 250, 250, 500 and 250 µg/ml respectively [57].

Side effects and toxicity:

The effects of long term use of *Fumaria parviflora* on serum concentrations of total protein, glucose, cholesterol, triglyceride, aspartate aminotransferase [AST], alanine aminotransferase [ALT] and blood urea nitrogen [BUN] were investigated in rats. Blood samples were taken after 15 and 30 days of oral administration of 100, 200 and 300 mg/kg of hydroalcoholic extract of the plant. The results revealed no significant difference between treatment and control groups at day 15. At day 30, administration of 300 mg/kg of the extract caused significantly higher serum concentration of AST than other groups [P<0.05]. This group also had higher serum ALT than the group received 100 mg/kg of the extract [p = 0.043]. The rats received 300 mg/kg of the extract had significantly higher serum total protein than the group received 100 mg/kg of the extract [p = 0.04] and had a marginally higher total protein than the control group [p = 0.08] [83].

Dose of 400 mg/kg of the percolated extract in mice induced acute adverse effects such as diarrhea, polyurea, malasia and hyperventilation. In histopathological evaluation of liver, toxic dose of percolated extract [400 mg/kg] caused degeneration and necrosis of hepatic cells. The study of ulcerogenic effects of oral percolated extract on stomach in rats showed that this adverse effect was significantly lower in comparison with the same dose of indomethacin [70].

CONCLUSION:

The review highlighted the chemical constituent, pharmacological and therapeutic effects of *Fumaria parviflora* as promising source of drugs because of its safety and effectiveness.

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