

REVIEW ON MEDICINAL AND BIOACTIVE ROLE OF GENUS FAGONIA

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Abstract

The plants of genus *Fagonia* are used commonly as home remedy and their aqueous and alcoholic extracts as medicines for treatment of conditions like diabetes, fever, asthma, toothache, stomach pain and kidney problems. This genus is a rich source of triterpenes and saponins. Various researches have undertaken studies on the chemistry and biological activities of *Fagonia* species. Pharmacological studies of their aqueous extracts on animals have also shown cytotoxic, anti-cancer and some other important activities. To facilitate further studies on this genus, we highlight the comprehensive account of the medicinal and biological activities of various extracts obtained from different species.

Introduction

The genus *Fagonia* belongs to the family Zygophyllaceae in the major group Angiosperms (flowering plants) (Pullaiah 2006). The genus includes thirty five species which are confined to warm and arid areas of India and all continents including eastward to Pakistan (NWFP, Punjab, Balochistan and Sindh) except Australia. *Fagonia* species have medicinal and bioactive properties (Chopra *et al.*, 1982).

All species of *Fagonia* are shrub, shrublets or herbs, rarely higher than (60 to 100 cm), and up to about 100 cm wide. It has spine scent or pointed stipules, pink or purple petals and an obconical, more or less pubescent, loculicidal capsule. The circumscription of species in *Fagonia* is known for being notoriously difficult (Manjunath, 1956; Beier 2005). It is annual to perennial, covered with whitish pruinose or sessile glands or glabrous shrublets. Stem basally somewhat woody, branches procumbent or erect cylindrical, striate, internodes 2.5-5 cm long. Leaves mostly unifoliolate or basal ones trifoliolate and upper unifoliolate, leaflets linear-oblong or lanceolate, 6-35 mm long, 3-4 mm broad, mucronate, short to long petioled or sessile; stipular spines shaped, patent to ascending, equal to shorter than leaves, occasionally deficient or minute (Shinwari and Shah, 2003).

In Unani system of medicine, plants of this genus are considered bitter, antiseptic, astringent, febrifuge, stimulant, alternative, analgesic, antipyretic, tonic, antiemetic, diuretic and deobstruent; used in the treatment of fever, asthma, vomiting, dysentery, urinary discharge, leucoderma, biliousness and typhoid. Leaves and twigs are used in snake bite (Shinwari and Shah, 2003). Sometimes whole plants and its ash have been used as home remedy whilst, mostly their aqueous and alcoholic extracts are used as medicines prescribed by physicians.

Medicinal Importance

Whole plant of *Fagonia indica* is used as a blood purifier and plant ash is given to children suffering from anemia. The fruit of this plant is rich in ascorbic acid. The twigs are commonly applied as tooth brushes and bark in the scabies (Shinwari and Shah, 2003). It has also been used in the treatment of dropsy (Ansari, 1983). Leaves, twigs and juice of this plant are used in the form of decoction or infusion as gargle in sore mouth and stomatitis. In irritability of the skin and intense scratching, decoction of the plant is used as a medicated bath with benefit (Nadkarins, 1954). Extracts of the aerial parts of *Fagonia indica*, stem and leaves of *Aloe vera* and fresh branches of *Tylophora hirsute* L are mixed together and given a teaspoon three times a day. According to the rural inhabitants of the area this mixture is very useful and 100 % effective to control the blood glucose level of diabetics (Ahmad *et al.*, 2009).

Its aqueous extract has been claimed by some physicians of "Unani Tibb" as being useful in the treatment of certain types of cancer. Since preliminary pharmacological tests of aqueous extracts on mice have shown some anti-cancer activity ((Ansari, 1983). Aerial parts of *Fagonia indica* is used as a remedy for tumors and leaf and twigs exhibit anticancer activity (Graham *et al.*, 2000).

To assist further studies on this genus we hereby present a review on the biological activities on *Fagonia* genus.

Biological Activities

Cytotoxic Activity

Two new compounds indicacin and fagonicin isolated from the methanolic extract of *Fagonia indica* were examined for their cytotoxicity against human colorectal cancer cell line H-29. Indicacin exhibited 51.40% cytotoxicity at 6.25 mM/mL dose whereas fagonicin demonstrated 39.3% cytotoxicity at the above dose (Farheen *et al.*, 2015).

Furthermore, an aqueous extract of the aerial parts of the *Fagonia cretica* can activate cell cycle arrest and apoptosis via p53-dependent and independent mechanisms, with initiating of the DNA damage response. It indicates that *Fagonia cretica* aqueous extract can be used as anti-cancer agents acting singly or with breast cancer cell proliferation via DNA damage-induced FOXO3a and p53 expression (Mattlam *et al.*, 2012).

Significant cytotoxic activity of *Fagonia cretica* was reported against brine shrimps at LD₅₀ 118.89 ppm, while antitumor test indicated that the extract showed tumor induction on potato discs. The overall results indicate that this plant has strong anti-cancerous potential (Hussain *et al.*, 2007). It is also reported that aqueous infusion of the whole plant extract showed different tumor statics effect which is more significant in the female rats as compare to male rats (Soomro and Jafarey, 2003).

The earlier work on *Fagonia taekholmiana* disclosed that alcohol and aqueous extracts of the aerial parts exhibited cytotoxic activity against MCF7 human breast tumor cells in culture indicated an IC₅₀ of 8.72 and 9.80 µg/ml, respectively (Manjunath, 1956).

Clotlytic Activity

Therothrombic diseases (myocardial or cerebral infections) are serious consequences of the clump formed in blood vessels. Thrombolytic agents are used to fuse the already formed clots in the blood vessels. Using a vitro thrombolytic procedure, aqueous extract of the whole plant of *Fagonia arabica* exhibited appreciable percentage of clot lysis (75.6%) with reference to streptokinase as a positive control and water as a negative control (Parasad *et al.*, 2007). Clot lytic ability of *Fagonia arabica* was also determined clearly by means of the tube method developed in the laboratory (Chourasia *et al.*, 2011).

Antimicrobial Activity

Whole plant extracts (aqueous, methanolic and ethanolic) of *Fagonia cretica* in various concentrations were also experienced against *Staphylococcus aureus*, *Bacillus subtilis*, *Escherichia coli* and *Pseudomonas aeruginosa* by disc diffusion method. MIC of plant extract was also determined against *Staphylococcus aureus*, *Pseudomonas aeruginosa* and *Bacillus subtilis*. Aqueous and methanolic extract indicated more activity against all the tested bacteria as compared to ethanolic extract (Sajid *et al.*, 2011).

Antimicrobial study of ethanol extract of *Fagonia indica* leaves extracts (25, 50 and 100 mg/ml) was recorded against Gram-negative and Gram-positive bacterial strains (*E.coli*, *S. aureus*, *P. aeruginosa* and *B.cereus*) by observing zone of inhibition. Comparatively ethanol extract showed significant inhibitory effect against *Bacillus cereus* and minimum for *P. aeruginosa* (Sharma *et al.*, 2009).

β -sitosterol-O- β -D-(6'-hexadecanoyl)-glucopyranoside, taraxerol, taraxerone, arjunolic acid and 23-hydroxy ursolic acid isolated from *Fagonia cretica*. These isolated compounds showed significant antimicrobial activity against *Bacillus subtilis*, *Sheigella flexneri*, *Staphylococcus aureus*, *Escherichia coli*, *Pseudomonas aeruginosa*, *Salmonella typhi*, *Trichophyton longifusus*, *Candida albicans*, *Aspergillus flavus*, *Microsporium canis*, *Fusarium solani* and *Candida glabrata*, while linoleic acid (C₁₈H₃₂O₂), methyltriacontanoate (C₃₁H₆₂O₂), β -amyryn acetate (C₃₂H₅₂O₃), oleanolic aldehyde acetate (C₃₂H₅₂O₃), triacontanoic acid (C₃₀H₆₀O₂) and octacosanoic acid (C₂₈H₅₈O₂) showed weak to moderate activity (Anjum *et al.*, 2007).

Analgesic and anti-inflammatory Activity

Analgesic activity of ethanol and aqueous extract (200 and 400 mg/kg) of *Fagonia indica* was studied by tail flick method in rats. The results were analyzed statistically by regression method showed that the ethanol extract has considerable inhibitory effect against *Bacillus cereus* and less inhibitory effect against *Pseudomonas aeruginosa*. In this experiment both extracts (ethanol and water) were exposed significant (p < 0.05) analgesic activity (Sharma *et al.*, 2009). Acute and sub-acute anti-inflammatory activities of the 10% ethanolic extract of *Fagonia indica* were also assessed in rats (Liu *et al.*, 2001).

Antioxidant Activity

Antioxidant potential of *Fagonia arabica* and the associated mechanism of antioxidant defense in rat pheochromocytoma (PC12) cells subjected to chemical ischemia were studied. Alternation in the activities of cellular antioxidant enzymes (SOD, CAT, GSH-Px and gsh-r) were measured. Antioxidant potential of herb (ABTS), extent of lipid peroxidation (MDA and 4-HAE), total antioxidant status (TAS) and total glutathione

(reduced, oxidized and their ratio) were evaluated from *Fagonia arabica* scavenges the free radicals (ABTS) and showed a concentration dependent antioxidant activity, highest being at 1000 µg/ml. Its treatment with ischemic cells ameliorates the GSH and TAS level and also helps the cells to restore the activities of the cellular antioxidant enzymes and also reduced the degree of lipid peroxidation. *Fagonia arabica* scavenges the free radicals and attenuates oxidative stress mediated cell injury during ischemia (Satpute *et al.*, 2009).

Hepatoprotective Activity

The methanolic extract of *Fagonia indica* on CCl₄ induced hepatotoxicity in albino rats was examined. The results suggested that MEFI in different doses have significant hepatoprotective activity against CCl₄ induced hepatotoxicity and this might be linked with the presence of flavonoids and tannins in this plant (Bagban *et al.*, 2012).

Antihemorrhagic potential

The methanolic extract from the aerial parts (leaves and twigs) of *Fagonia cretica* has antihemorrhagic potential. The hemorrhagic response of poison of black snake was dose dependent from 0.1 to 4.0 µg per 1.5 µL PBS (phosphate buffer) saline tested on fertilised hens' eggs in their shells. This extract efficiently removed and neutralised the hemorrhagic effect of snake poison. The extract has proved as hemorrhagic inhibitor against snake and can be used for the treatment of snake bite on the scientific basis (Razi *et al.*, 2011).

References

- Ahmad, M., Qureshi, R., Arshad, M., Khan, M. and Zafar, M. (2009). Traditional herbal remedies used for the treatment of diabetes from district Attock (Pakistan). *Pak. J. Bot.*, 41(6): 2777-2782.
- Anjum, M., Ahmed, E., Jabbar, A., Malik, A., Ashraf, M., Moazzam, M. and Rasool, M. (2007). Antimicrobial constituents from *Fagonia cretica*. *J. of Chem. Soc. Pakistan*, 29: 634-639.
- Ansari, A. (1983). *Isolation and characterization of chemical constituents of Berberis aristata, Fagonia indica and Daucus carota*. Ph. D Thesis, University of Karachi, Pakistan, p.76.
- Bagban, I., Roy, S., Choudhary, A., Das, S., Gohil, K. and Bhandari, K. (2012). Hepatoprotective activity of the methanolic extract of *Fagonia indica* B. in carbon tetra chloride induced hepatotoxicity in albino rats. *Asian Pacific Journal of Tropical Biomedicine*, 1457-1460.
- Beier, A. B. (2005). A revision of the desert shrub *Fagonia* (Zygophyllaceae). *Systematics and Biodiversity* 3: 221-263.
- Chopra, R.M., Handa, K. L., Kapur, L. D. and Chopra, I. C. (1982). *Indigenous drugs of India*. 2nd ed. New Delhi, India. Academic Press, p 507.
- Chourasia, S.R., Kashyap, R.S., Purohit, H.J., Deopujari, I.Y., Taori, G.M. and Dagainawala, H.F. (2011). In vitro clot lytic potential of *Fagonia arabica*, a comparative study of two methods. *Blood Coagulation & Fibrinolysis*, 22(4): 288-294.
- Farheen, R., Siddiqui, B.S., Mahmood, I., Simjee, S.U. and Majeed, S., (2015). Triterpenoids and triterpenoid saponins from the aerial parts of *Fagonia indica*. *Phytochemistry letters*, 13: 256-261.
- Graham, J. G., Quinn, M. L., Fabricant, D. S. and Farnsworth, N. R. (2000). Plants used against cancer- an extension of the work of Jonathan Hartwell. *Journal of Ethnopharmacology* 73: 347-377.
- Hussain, A., Zia, M. and Bushra, M. (2007). Cytotoxic and antitumor potential of *Fagonia cretica*. *Turk J Biol.* 31: 19-24.
- Liu X. M., Islam, M. W. and H. B. Ismail. (2001). Evaluation of anti-inflammatory activity of *Fagonia indica* in rats. *International Congress and 49th Annual Meeting of the society for Medicinal Plant Research*, September 2-6. Erlangen, Germany.
- Manjunath, B. L. (1956). *The Wealth of India*, Council of Scientific and Industrial Research, New Delhi, 4: 01.
- Mattlam, A., Carmichael and R. Griffiths. (2012). An aqueous extract of *Fagonia cretica* induces DNA damage and apoptosis in breast cancer cells via FOXO3 and p 53 expression. *PLOS ONE*, 7: 40152.
- Nadkarins, K. M. (1954). *Indian Materia Medica*, 1:533.
- Parasad, S., Kashyab, R., Deopujari, J., Purohit, H., Taori, G. and Dagainawala, H. (2007). Effect of *Fagonia arabica* on in vitro thrombolysis. *BMC Complement Altern Medicine*, 7: 36-40.
- Pullaiah, T. (2006). *Encyclopedia of the World Medicinal Plants*. Regency Publication, New Delhi, India. 2: 934-935.
- Razi, M.T., Asad, M.H.H.B., Khan, T., Choudhary, M.Z., Ansari, M.T., Arshad, M.A. and Saqib, Q.N. (2011). Antihemorrhagic potential of *Fagonia cretica* against naja naja karachiensis (cobra) venom. *Nat. Prod Res*, 25: (20), 1902-1907.
- Sajid, Alia, Rizwana, Uzma, Alamgeer. and Hafiz, M. (2011). Phytochemical screening and antimicrobial activity of *Fagonia cretica* plant extracts against selected microbes. *Journal of Pharmacy Research*, 4: 4-8.

- Satpute, R., Kashyab, R., Deopujrai, J., Purohit, H., Taori, G. and Daginawala, H. (2009). Protection of PC 12 cells from chemical ischemia induced oxidative stress by *Fagonia arabica*. *Food and Chemical Toxicology*, 47: 2689-2695.
- Sharma, S., Joseph, L., George, M. and Gupta, V. (2009). Analgesic and anti-microbial activity of *Fagonia indica*. *Pharmacology online*, 3: 623-632.
- Shinwari, M. I. and Shah, M. (2003). *Medicinal Plants of Margalla Hills*. National Park Islamabad, vol. 1. Pakistan Museum of Natural History, Islamabad., p.72.
- Soomro, A. and Jafarey., N. (2003). Effect of *Fagonia indica* on experimentally produced tumors in rats. *Journal of Pakistan Medical Association*, 53: (6), 100.