

PHARMACOGNOSTICAL, PHYTOCHEMICAL AND PHARMACOLOGICAL REVIEW OF FAGONIA CRETICA FOR ANTI-ASTHMATIC ACTIVITY

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ABSTRACT: *In recent times, focus on plant research has increased all over the world and a large body of evidence has collected to show immense potential of medicinal plants used in various traditional systems. Use of plant based drugs and chemicals for curing various ailments and personal adornment is as old as human civilization. Fagonia cretica is used for curing various diseases and symptoms. Fagonia cretica is useful in asthma, emmanagogue, lever trouble, chronic bronchitis, ophthalmia, toothache, and stomatitis.*



Introduction

A small spiny undershrub with stiffy branches often more or less prostrate. Twigs Slender, terete, striate, glabrous, and glandular. Leaves opposite, 1-3 foliate, about 12 by 2.5 mm., entire, linear or elliptic, mucronate; petiole very variable, 0-3 cm, long sometimes leaflike; stipules transformed into sharp slender spines upto 1.2 cm. long, persistent and continuing growth long after the fall of the leaves. Flowers solitary, rose-coloured, on peduncles 5-12mm. long, arising from between the stipules sepals 5, deciduous, imbricate, half as long as the petals. Petals 6mm. long, spatulate with a marked claw. Disk short, inconspicuous. Stamens 10, inserted on the disk; filaments filiform, naked; anthers oblong. Ovary hairy, sessile, 5-angled, 5-celled, tapering into a 5 angled style; stigma simple. Fruit 5 mm. long, of 5 1 seeded cocci dehiscing along the ventral suture and separating from a horny endocarp.[1]

Distributional range:

Found in deserts and dry areas from India to Tropical Africa and in Chile as well as USA. In UAE it is widespread, found in shallow sands over gravels or limestone, hillsides and wadis

- **AFRICA**
Northern Africa: Algeria; Egypt; Morocco; Tunisia
Northeast Tropical Africa: Yemen - Socotra
- **ASIA-TEMPERATE**
Arabian Peninsula: Saudi Arabia
Western Asia: Cyprus

- EUROPE

Southeastern Europe: Greece [incl. Crete]; Italy - Sicily; Malta

Southwestern Europe: Spain [incl. Balears]

Deccan, catch, Sind, Baluchistan, Waziristan, w.rajputana, upper gangatic plain, westward to Afghanistan-Persia, Arabia and Mediterranean. [1]

Macroscopy:

Perennial, minutely and densely glandular, very much branched desert herb up to 80cm. Stem with woody base, finely striate but terete; only the highest internodes sulcate. Leaves unifoliate, elliptical to linear- lanceolate, acute, mucronate, 8-15 mm long; petioles variable, 1-3 mm long. Stipular spines on swollen nodes, 5- 20 mm long, shorter or exceeding the leaves. Flowers solitary in the axils, fragrant, to 12mm in diameter, pedicels 3-8 mm long, with pink to purple petals. Fruit a capsule 3-5 mm long, 2-5 mm wide, short pubescent with persistent style. Seeds flat rounded and brown in color.

Root - Tap root externally brownish green, rough, with longitudinal striations, core yellowish-green; fracture, fibrous. [4]

Stem - Stem pieces 0.5 to 1.5 cm thick, of variable lengths; young green, mature brown; spiny, two pairs of spines present at each node, spines sharp, slender, 1.5 to 2 cm in length; external surface of stem green, whitish brown when dry, striated; transversely smoothed surface showing a thin bark and prominent wood bark peeling from stem; fracture, short. [4]

Leaf - Small, sessile, linear, oblong, leaflets entire, green or blackish brown, 0.5 to 1.5 cm in length and 0.05 to 0.1 cm in width, without any prominent midrib region projected above the level of lamina.[4]

Flower - Flowers small, pale rose or purple, pedicels slender, 6 to 12 mm long; sepals 3 to 4 mm long, ovate, aristate; petals twice as long as the sepals, spatulate, claw long; ovary hairy, style tapering.[4]

Fruit - Pentagonal schizocarp, composed of five compressed, two valved cocci. [4]

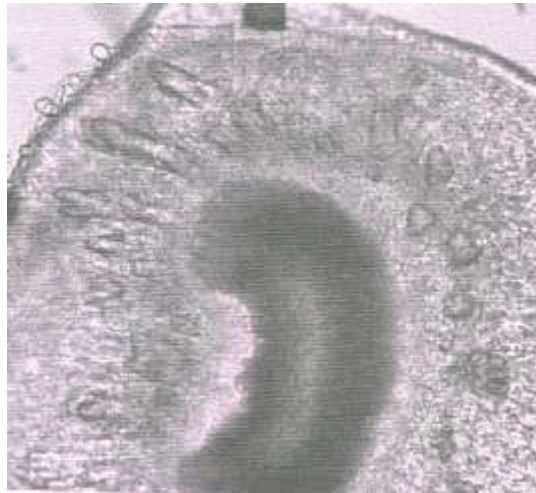
Microscopic

Root - T.S. shows outermost cork represented by 4 or 5 layers of small, narrow, tangentially elongated cells; phelloderm composed of 6 to 10 layers of somewhat tangentially elongated, thin walled parenchymatous cells, some cells having rhomboid crystals of calcium oxalate measuring 10 to 15 μ in length and 8 to 10 μ in width; outer part of secondary phloem characterized by the presence of abundant, but small patches of 2 or 3 thick walled phloem fibres; wood composed of vessels, xylem fibres and traversed by 1 to 3 seriate medullary rays; vessels arranged in singles or doubles; fibres long, thick walled with tapering ends and measuring upto 500 μ in length and about 25 μ in width. [4]

Stem - T.S. shows more or less circular outline; single layered epidermis with thick cuticle; unicellular trichomes occasionally present; cortex consisting of 7 to 10 layers of parenchymatous cells showing large patches of fibres; sclereids with narrow lumen occurring singly or in groups in the cortex, measuring upto 50 μ in diam.; several cortical cells contain tannins; secondary phloem consisting of thin walled cells; vascular cambium composed of 3 to 4 layers of thin walled tangentially elongated cells;secondary xylem composed of fibres, tracheids, vessels, xylem parenchyma; fibres long,thick walled with tapering ends and measuring 260 to 950 μ in length and upto 20 μ in width; medullary rays mostly uniseriate or sometimes biseriate; pith composed of large thin walled parenchymatous cells, some cells containing tannins; rhomboid crystals measuring 18 to 30 μ in length and 12 to 20 μ in width present in cortex and pith.[4]

Leaf - Isobilateral; single layered epidermis consisting of mostly tangentially elongated cells covered with thick cuticle. In surface view both upper and lower epidermii show anomocytic type of stomata, epidermal cells polygonal in shape; 2 or 3 layered palisade cells present on both the sides, adjacent to the epidermis; vascular bundles show xylem towards lower side and phloem towards upper side; sclerenchyma tissue occur as a bundle cap just above the phloem; small lateral vascular bundles also present in lamina; vein-islet number 11 to 14; stomatal index 16 to 17 on lower epidermis and 5 to 7 on upper epidermis; palisade ratio 2 or 3 on upper epidermis and 2 to 4 on lower epidermis.[4]

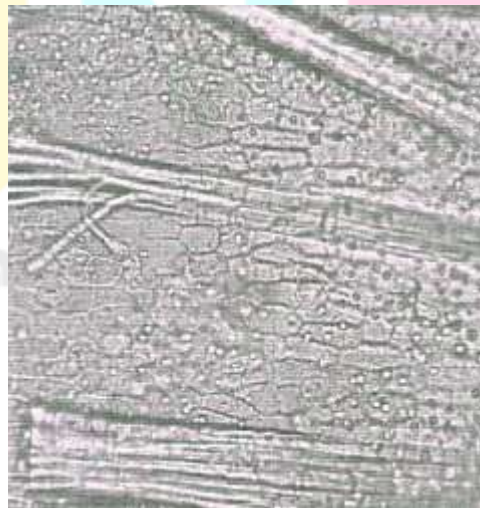
Powder Yellowish-white, bitter taste, showing groups of fibres, bordered pitted vessels, fragments of palisade tissue, sclereids, rhomboid crystals of calcium oxalate, cork cells, and unicellular glandular and nonglandular trichomes (both from fruit epicarp) epidermal cells (cubical, rectangular or polygonal) with slightly wavy walls and anomocytic stomata. [4]



TS of a branch showing the epidermis with thick cuticle followed by cortex parenchyma (embedding zones of bundles of fibres), the endodermis, and then crescent-shaped vascular tissues (dark-colored) and pith (less dark).



Detailed TS of a branch showing the outer small rectangular epidermal cells followed by oblong cortical parenchyma cells, a zone enclosing bundles of fibres, inner layers of cortex, endodermis, a circle of vascular tissues (dark) and hexagonal pith cells. The epidermis is covered with a thick cuticle.



Surface view of the inner part of the leaf epidermis polygonal cells showing the granular contents of the cells, stomata and groups of fibre bundles encircled by cortical parenchyma cells.

IDENTITY, PURITY AND STRENGTH

- | | | |
|-------------------------------|-----------------------------|--------------------|
| 1. Foreign matter | Not more than 2 per cent, | Appendix 2.2.2. |
| 2. Total Ash | Not more than 10 per cent, | Appendix 2.2.3. |
| 3. Acid-insoluble ash | Not more than 0.4 per cent, | Appendix 2.2.4. |
| 4. Alcohol-soluble extractive | Not less than 5 per cent, | Appendix 2.2.6. |
| 5. Water-soluble extractive | Not less than 10 per cent, | Appendix 2.2.7.[4] |

Phytochemistry

Triterpenoid, saponins, alkaloids, coumarins, flavonoids and tannins. The aerial parts contain several triterpenoid saponins which gave sapogenin, nahagenin, oleanolic acid. Aerial parts also gave diterpenes, fagonone, 16-o-acetylfagonone, ternatin, Herbacetin-3, 8-dimethyl ethyl, herbacetin-3, 7, 8-trimethyl ether, gossepetin-3, 8, 3', 4'- tetramethyl ether and its derivatives, besides flavonoids. The flavonoids, quercetin and kaempferol, isolated from the leaves.

Fruit are rich in ascorbic acid.[1,2]

Alkaloids (Harmine); amino acids (alanine, glycine, leucine, arginine isoleucine, lysine, phenylalanine, proline, tyrosine and valline); terpenoids of oleanane group.[4]

Preliminary phytochemical screening on callus of *F. arabica* leaf explants

Preliminary phytochemical screening (Table: 4) was carried out on calli of different plant parts explants of *Fagonia arabica*, *Fagonia indica* and *Fagonia bruguieri* and intact plant parts of them revealed that, callus of *Fagonia arabica* leaf explants that selected quantitatively before (% of calli induction and weight of the obtained callus) was also the best callus regarding active constituents under investigation. Callus was found to contain saponins, alkaloids, coumarins, chlorides more than the intact leaf.

Concentration of different active ingredients (mg/g fresh weight)			
Total phenols	Total alkaloids	Total flavonoids	Total saponins
1.95	113.40	0.78	10.00

Pharmacological and Toxicological studies:

Effects of powdered *Fagonia cretica* plant and triterpenoid from its ethanolic extract showed that the saponins had highly significant decreasing effects on the amount of total leukocyte count of rabbit's blood (Asif et. al., 2003). The plant leaf extracts were found most effective against *Salmonella typhi*. (Geholt et. al., 2000).

The plant extract showed molluscicidal activity (Shoeb et. al., 1987). New erythropane-type diterpenoids from *Fagonia* showed cancer-preventing agent (Gedara et. al., 2003).

The pharmacological and toxicological studies carried out in laboratory and the results in brief, on *Fagonia cretica* (10% ethanolic extract) have been given below.

ACTIVITY RESULTS

Anti-inflammatory activity-Rat paw oedema	Significant anti-inflammatory activity (Liu et al., 2001).
Anti-inflammatory activity-Cotton pellet	Significant anti-inflammatory activity (Liu et al., 2001).
Antinociceptive activity-Writhing	Showed no analgesic activity (Liu et al., 2001).
Anti-hypertensive activity-Anesthetic rats	No effect on BP & HR observed. (Liu et al., 2001).
Vasorelaxant activity-Isolated aortic strip	No relaxation produced in Na contracted strip. (Liu et al., 2001).

Cardiotonic activity & HR Isolated rat atria	Increase in force of contraction, very significantly reduced the rate observed.
Effect on GIT smooth Muscle-	No change in resting tension noted.
Isolated guinea pig ileum	No effect of amplitude or frequency of contraction reported.
Effect on GIT smooth Muscle- Isolated rabbit jejunum	No toxicity observed. (Liu et al., 2001).
Gross behavioral studies- Writhing	No toxicity observed. (Liu et al., 2001).
Gross behavioral studies- Diarrhea, Urination	No abnormal signs recorded (Liu et al., 2001).
Mortality	No death recorded. (Liu et al., 2001).
Motor co-ordination (String & Platform test)	Motor coordination not affected. (Liu et al., 2001).
Anti-asthmatic activity- Tracheal Chain	No relaxation in histamine- contracted chain reported (Liu et al., 2001).
Acute toxicity studies	No toxicity observed. (Liu et al., 2001).
LD50 evaluation (i.p.)	987.4 mg/kg. (Liu et al., 2001).

Uses

The plant is acrid and bitter; cooling; removes “vatta”, asthma, fever, thirst, vomiting, cures fevers, dysentery, urinary discharges, erysipelas, typhoid; alexipharmic; reduces tumor; purifies the blood (ayurveda). [1]

The plant is acrid and bitter; cooling; removes “vatta”, asthma, emmenagogue; good for liver trouble, in chronic bronchitis, spitting of blood, ophthalmia, toothache, stomatitis (unani). [1]

Bark

Used for dermatosis. The bark is used in scabies.[1]

Leaves

Leaves are useful in fever, thirst, vomiting, boils, leucoderma, and biliousness.[1]

Extract of aerial parts—antiviral, antiamphetamine, spasmogenic[1]

Plant ash—given to children suffering from anaemia[1]

The herb is prophylactic against small pox. [2]

An aqueous decoction of the plant is a popular remedy for cancer in the indigenous

system of medicine [7]

Several saponin glycosides have been separated and characterized .Other constituents, such as docosyl docosanoate from hexane extract and water soluble proteins from aqueous extract of air-dried *F. cretica* plants, have been isolated; furthermore, nahagenin , hederagenin, ursolic acid and pinitol from other *Fagonia* species have also been separated and characterized [10]

Effect of saponin I & II on Prolactin

Saponins exhibited more marked effects on the serum prolactin. Both saponins further showed significant decrease in prolactin levels after 16 days, as compared to the crude drug treatment group and the control group [10]

Effects of saponin I & II on Thyrotropin (TSH)

Both saponins in 30 mg doses were associated with much greater decreases in the serum TSH level than occurred in the control and crude drug treatment groups. Furthermore, as far as the serum TSH is concerned, there seemed to be a pronounced effect of the dose of both saponins. 30 mg

dose of both the saponins was more effective than 20 mg dose. Over all, the saponin-II was more effectual than saponin-I in this regard, during the whole of the study period [10]

Effects of saponin I & II on Thyroxine (T4)

Both the crude drug (in 1g and 2g doses) and saponin-I (in both 20 and 30 mg doses) have equal effects and there is no significant difference between the two materials as regards the activity of the serum thyroxine level in the blood is concerned, when compared with the controlled group of animals. On the other hand, saponin-II in a 30mg dose has a significant effect in reducing the quantity of thyroxine in the blood serum [10]

Effects of saponin I & II on Cortisol

30 mg doses of triterpenoid saponin-I and saponin-II, isolated from *F. cretica*, had greater decreasing effects on prolactin and serum TSH levels of the blood of rabbits than 1 and 2g doses of crude powdered *F. cretica* and with the same parameters in controlled animal's groups. The serum thyroxine level was also significantly reduced by a 30mg dose of saponin-II, while the crude powdered *F. cretica* drug and saponin-I had no significant effects on the serum thyroxine level, Furthermore saponin-II seemed to have a greater influence on this parameter of serum than the other saponin. A maximum increase in the serum cortisol level of the blood of rabbits was noticed with saponin-II[10]

Effects of saponin I & II on red blood cells

Effects of powdered *Fagonia cretica* plant and its two major triterpenoid saponins (saponin-I and saponin-II), isolated from its ethanolic extract, on red blood cells (RBC) count, haemoglobin concentration (HC), mean corpuscular haemoglobin (MCH) and on total leucocyte (WBC) count of normal male rabbits were investigated. Saponins treated three dose groups of animals indicated significant decrease in RBC count during the experimental period of 16 days. This effect was more pronounced in animals treated with saponin-II than saponin-I. The 0.50 and 1.0 g crude drug treated animals and 10 and 20 mg of both the saponins treated animals, indicated a decreasing tendency of HC up to the 4th day, which increased afterwards up to the 16th day. The third dose of these materials (1.50 g of crude drug and 30 mg of both saponins) exhibited a highly significant decreasing pattern, up the 16 days. The decreasing effect of haemoglobin concentration was more distinct in the saponin-II treated animals than saponin-I and the crude drug. The MCH followed a reverse pattern than RBC and HC. A continued decreasing trend was found in total WBC during the 16 days treatment. An amount of 1.50 g of the crude drug and 30 mg of both the saponins had highly significant decreasing effects on the amount of total leukocyte count of rabbit's blood. [10]

In vitro thrombolysis

Dhamasa possesses thrombolytic properties that could lyse blood clots in vitro; however, in vivo clot dissolving properties and active component(s) of *Dhamasa* for clot lysis are yet to be discovered. Once found *Dhamasa* could be incorporated as a thrombolytic agent for the improvement of patients suffering from a thrombotic diseases. [9]

Conclusion

Fagonia cretica belonging to family Zygophyllaceae is an indigenous herb which was chosen for further study of antiasthmatic activity as folk claims shows that they possess treatment for chronic bronchitis and asthma. The scanty availability of information on this plant facilitates the study on it since ages various part of this part is being used for their medicinal use.

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