THE CHEMISTRY AND PHARMACOLOGY OF *FAGONIA* GENUS: A REVIEW

Malavika P S[1], Vachan Singh[1], Yogesh Kumar[1]

M.Pharm Research Scholars
School of pharmaceutical science, IFTM University, Moradabad, 244102
Uttar Pradesh, India.

Corresponding Author: Malavika P.S

***Abstract*: *Fagonia* is a genus of wild, flowering plants in the family *Zygophyllaceae* having about 35 species including *F.cretica, F.indica, F.arabica, F.laevis, F.californica, F.glutinosa, and F.scabra*. These species have been used ethnobotanically by traditional practitioners under different healing regimes for many maladies with whole plant or its various parts.The genus got global attention due to the presence of novel chemical constituents, covering saponins, sapogenins, alkaloids, terpenoids, sterols, flavonoids, proteins, amino acids, coumarins, vitamins and trace elements. Researchers elaborately studied the chemical composition and recent studies found some compounds for first time counting lupeol, β-amyrin, octacosonic acid, methyl triacantanoate, luteolin and triacontanoic acid. Numerous studies are winding around the *Fagonia* genus and the findings of some studies inclusive the therapeutic properties such as anti-cancer, anti-oxidant, anti-pyretic, analgesic, anti-inflammatory, wound healing, anti-tumor, anti-allergic, reno-protective, anti-diabetic and anti-bacterial. On the basis of references and well being point of view, species belong to *Fagonia* genus presents an excellent option for curing variety of ailments in human beings and it posses significant biological activities for developing a variety of new pharmaceutical products.**

Keywords*: *Fagonia* species, Chemical compositions, Pharmacological activities, *F.arabica, F.indica, F.cretica

INTRODUCTION

Since old occasions plants have been a rich wellspring of compelling and safe medicines.Due to their safe,effective and reasonable nature, indigenous cures are well known among the people worldwide and about 80% of the world's population are still dependent on traditional medicine (**Anil et al; 2012)**. *Zygophyllaceae* is a family of blooming plants that contain the bean-escapade and caltrop.The family includes around 285 species in 22 genera (**Christenhusz et al; 2016)**. One of the significant genera having a place with this family is *Fagonia*, having 35 species appropriated in different parts of Africa, the Mediterranean Basin, the Mid-East, India and parts of the America. *Fagonia* species have been used ethnobotanically by traditional practitioners under ayurvedic and other healing regimen for many maladies (**Beier; 2005)**

Fagonia species are generally minimal spiked under-hedge, sherbets or herbs, erect, more and less grandullar, branches malign, terete, triate and glabrous. Leaves inverse, 1-3 foliate; petioles entirely factor long, from 3 - 30 mm long, profoundly striate, extremely thin; stipules 2 sets of sharp thin thistles, once in a while higher than 60-100 cm, and up to about 100 cm wide (**Farheen et al, 2015; Puri et al, 2014)**. Some of the pictures of different *Fagonia* species are presented in figure 1.

Number of species like *Fagonia cretica, F. arabica, F. bruguieri, F. mysorensis, F. indica, F. schweinfurthii, F. laevis, F. longispina* and so forth have been distinguished and these species are often used as powdered form or extracted form of whole plant or its areal parts.

At the point when the powder that is comprised of the whole plant of *F. schweinfurthii* is dusted on boils and skin eruptions, it causes healing, when the whole plant is boiled in water, its shower is valuable for skin sensitivities and other skin diseases. The decoction is given orally as blood purifier. Different species like *Fagonia bruguieri* and its aqueous extract is guaranteed for anti-allergy.

Rough phytochemical extracts and isolated compounds from *F. cretica* display a different extent of scope of biological activities including anti haemorrhagic, anti tumour, anti-inflammatory, and neuro-protective effects(**Razi MT et al, 2011; Hussain A et al, 2007; Rawal AK et al, 2009; Rawal AK et al, 2004)** and methanolic extract of Fagonia cretica is guaranteed for acceptable antimicrobial potential and it showed strong free radical scavenging properties against reactive oxygen, nitrogen species and anti diabetic activity (**Puri D et al, 2014; Nazir I et al, 2017)** .

Fagonia indica has been a rich wellspring of viable and safe medicines. It is astringent, antiseptic, blood-purifier, febrifuge and prophylactic against smallpox. The plant is bitter and utilized for the treatment of fever, thirst, vomiting, dysentery, asthma, urinary discharge, liver inconvenience, typhoid, toothache, stomach troubles and skin diseases (**Anil P et al, 2012; Rahman A et al, 1984; Shehab NG et al, 2011)** and ethanolic extract of the aerial parts and whole plant of F.indica indicated against diabetic, tumor, inflammatory, microbial and analgesic properties (**Rahman A et al, 2019).**

Fagonia species were broadly concentrated by numerous specialists with respect to their therapeutic utilizes, since these plants were anti-tumor, antioxidant, analgesic, astringent, febrifuge and prophylactic against small-pox agents. Types of *Fagonia* were additionally utilized for the treatment of cancer in the indigenous system, fever, asthma, urinary discharges, toothache, stomach troubles and kidney diseases. Types of *Fagonia* have been found to contain saponins , sapogenins, alkaloids , terpenoids , sterols , flavonoids , proteins and amino acids, coumarins , vitamins and trace elements.

Fig 1: *Fagonia arabica* photographs (A,B) *Fagonia indica* photographs (C,D,E) *Fagonia cretica* photographs (F).

CHEMICAL COMPOSITION

In a long time period by various studies conducted, numerous types of plant metabolites were isolated from different Fagonia species with some important groups like saponins, sapogenins, alkaloids, glycosides, vitamins, terpenoids, tannins, flavanoids, steroids, proteins, amino acids, coumarins, and trace elements. A comprehensive list of some known and selected *Fagonia* species and it constituents, including plant part(s) were isolated are depicted in **Table 2**

Preliminary phytochemical screening on shoot system of *F.indica* shows it contain three sapogenins named nahagenin-**1**, hederagenin-**2** and ursolic acid-**3 (Rahman A et al ,1984; Rahman A et al , 1982)** and these have been isolated from aerial part[1]. And several saponins or triterpenoid glycosides have been isolated, they were characterized as pinatol-**4,** 23,28-di-O-β-D-glucopyranosyltaraxer-20-en-28-oicacid20,3β,28-di-O-β-D-glucopyracid20,21,22αepoxy-23-O-β-D-glucopyranosyl nahagenin, 3-O-{[β-d-glucopyr-anosyl-(1→2)] [α-l-arabinopyrano syl-(1→3)]-α-l-arabinopyranosyl}ursolicacid-28-O-[β-d-glucopyranosyl] ester (indicasaponinA)-**5,** and 3-O-{[β-d-glucopyranosyl (1→2)] -[α-l-arabinopyranosyl -(1-3)]-α-l-arabinopyranosyl} oleanol -icacid-28-O-[β-d-glucopyranosyl]ester(indicasaponinB)-**6 (Anil P et al, 2012; Shehab NG et al,2011)**. Four flavonoidal compunds identified as quercetin-**7,** isorhamnetin -α - 3-Orhamnoside **-8,** Quercetin3-O-β-D-glucopyranosyl(1"-6"')-β-D-glucopyranoside and quercetin 3-O - β-D galactopyr anosyl-(6"--1"')-α-L-2"'acetylrhamnose (3"'-1"")β-D-glucode were isolated from thealcoholic extract and also oleanolic acid-**9,**β-sitosterol-3-O-β-D-glucoside-**10,** and stigmasterol-3-O-β-Dglucoside-**11** **(Shehab NG et al ,2011).** Indicacin-**12** and fagonicin-**13** are the two new compounds and also β-amyrin-**14** and lupeol-**15** were isolated from aerial parts of *F.indica (***Farheen R et al, 2015; Shaker KH et al ,1999)**.

Iqbal Hussain et al reported the presence of alkaloid, phenol**,** flavonoid, saponin ,protein and pectin in *F.cretica* (**Rahman A et al,1984)**. Three triterpenoid saponins including two new ones pyranosiwere identified from aerial parts of *F.cretica*, the new saponins were characterized as 3-O [β-D-xylopyranosyl(1-->2)α-L-arabinopyranosyl]27-hydroxyoleanolic acid 28-O-[β-D-glucopyran
osyl (1-->6) β D glycopyranosyl] ester and 3β-O-[β-D-xylopyranosyl(1-->2)α-L- arabinopyranosyl]
olean-12-en-27aloic acid28-O[β-D-glucopyranosyl(1-->6)βD-glycopyranosyl] ester (**Abdel-Khalik SM et al 2001)**. Further the bioactivity of *F.cretica* was guided with compounds such as quinovic acid-**16,** quinovic acid-3βOβD-glycopyranoside-**17,** quinovic acid- 3β O-βDglycopyranosyl(28-->1)
β-D-glucopyranosylester-**18** and stigmasterol-**19 (Saleem S et al, 2014)**. Anjum et al isolated 11 new compounds from the n-hexane extract of *F.cretica* including linoleic acid-**20,** octacosanoic acid-**21,** methyl triadecanoate-**22,** β-amyrin acetate-**23,** taraxerol-**24,** oleanolic aldehydeacetate-**25** and triacontanoic acid-**26 (Anjum M I et al, 2007)**. Hamid A et al isolated docosyl docosanoate-**27** from its plant etract (**Hamid A et al, 1989)**. C R Khare wrotes that *F.cretica* contains the phyto constituents Diosgenin-**28**, cryptogenin -**29**, lanosterol-**30,** harmine-**31,** oleanolic acid, chinovic acid
-**32,** fagogenin, betulin-**33**, campesterol -**34** in the book of Indian herbal remedies (**Khare C.P, 2004).**

Quercetin,kaempferol**,**23,38-di-o-β-d-glucopyranosyl-taraxer-20-en-28 oicacid and vitamins such as riboflavin-**35,** niacin-**36,** and ascorbic acid-**37** are identified from leaves and flowers of *F.arabica*, and also it contain carbohydrates, or glycosides, sterols, triterpenoids-**38**, alkaloids, flava
noids, minerals such as sulphate and chlorides , anthraquinone **39,** cyanogenins, and coumarin - **40.**
Docosyl docosanoate**,** cerylalcohol-**41,** β-setosterol-**42,** n-tricontanol chenovic acid**,** 4,5-dicaffeoyl quinic acid-**43,** 3,5dicaffeoylquinic acid-**44,** syringaresinol hd glucoside-**45,** scopoletin-**46**, rutin-**47,**
and kaempferol (**Ibrahim LF et al, 2008)** were identified from hydrolysed plant extract of *F.arabica* **(Anil D, 2006; Khare CP, 2007; Shoeb H A et al, 1994)**. F.Khattak wrotes that fagonone, nahagenin, sapogenin, oleanolic acid, diterpenes are present in *F.arabica* (**K.F.Khattak, 2012)**. Eman A El-Wakil fractioned two flavanoid glycosides kaempferol-7-*O*-rhamnoside and acacetin-7-*O*-rhamnoside, Four triterpenoidal glycosides 3-*O*-β-d glucopyranosyl(1->3) *α*-L arabino
Pyranoside oleanolic acid-**48**, 3-*O*-*α*-Larabinopyranosyl quinovic acid 28Oβ-d-glucopyranoside-**49**,
O-[βd-glucopyranosyl-(1->2)]-β-d-glucopyranosyl(1->3)-αL arabinosyl oleanolic acid-**50** and 3*O*βd
glucopyranosyl-(1->3)*α*L-arabinopyranosyl quinovic acid 28-*O*-β-d glucopyranoside-**51 (El wakil E A et al, 2007)**.

Lamyaa F Ibrahim isolated apigenin-**52**, apigenin 7O glucoside-**53**, kaemferol-**54,** kaemferol
3-OGlucoside, quercetin from methanolic extract of *F.taeckhomiana* (**Ibrahim L F et al, 2008).**

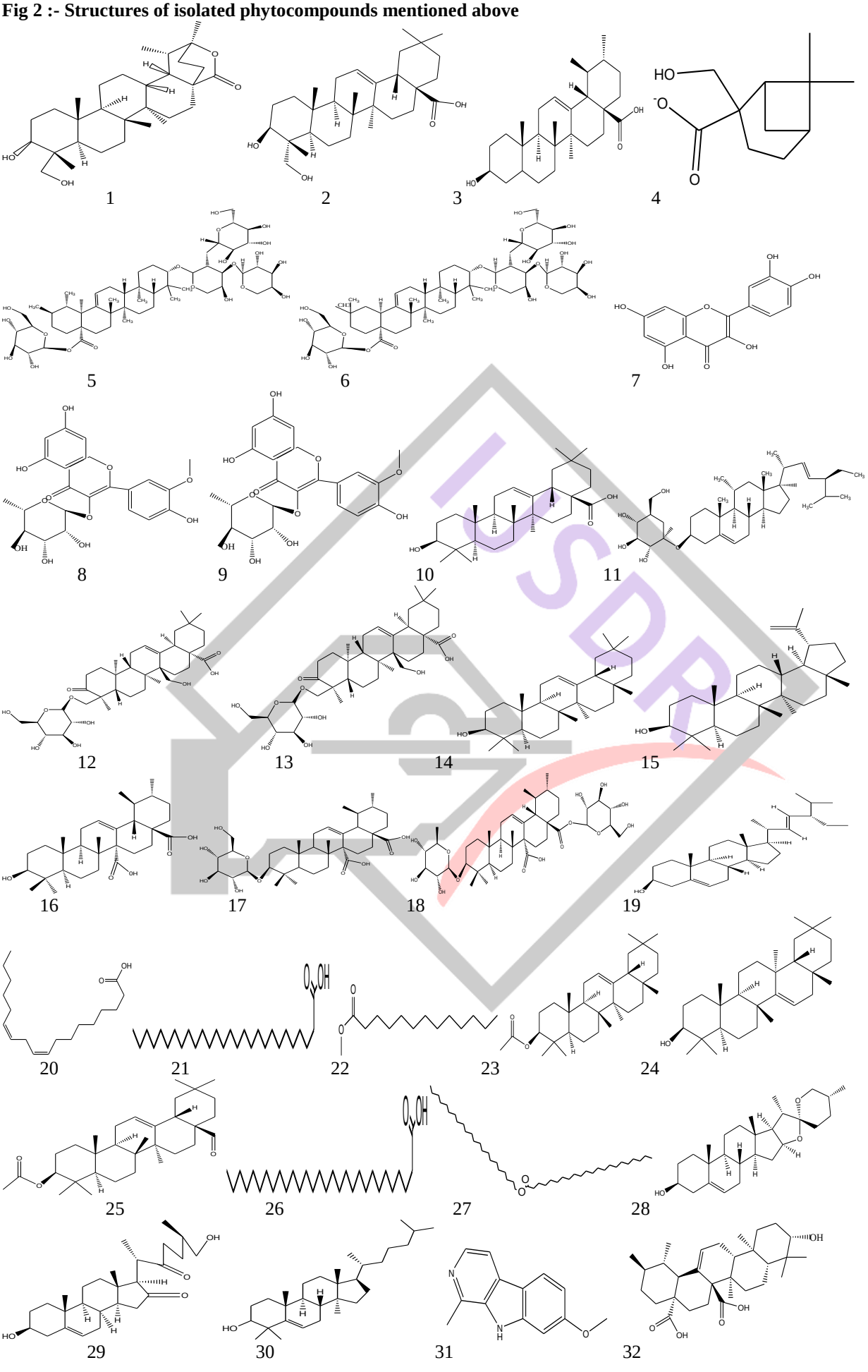
F R Melek et al were isolatedtwelve triterpinoids saponins, including six new from the aerial parts of *F.glutinosa*. The new saponins includes 3-O-[β-D-glucopyranosyl (1-->2)] [β-D glucopyran
osyl (1-->3)]-α-L-arabinopyranosyl-27-hydroxy oleanolicacid-28-O-β-D-glucopyranosyl ester 3-O-[β-D-glucopyranosyl (1-->3)]-α-L-arabinopyranosyl ursolic acid, 3-O-α-L-arabinopyranosyl ursolic
Acid 28-O-β-D-glucopyranosyl ester and 3-O-[β-D-glucopyranosyl(1-->2)] [β-D-glucopyranosyl (1-->3)] -α-L-arabinopyranosyl-27-hydroxy ursolic acid 28-O-β-D-glucopyranosyl ester **(Melek FR et al, 2000).**

Hamidi N et al characterized 12 phytochemical constituents in ethyl acetate extract from the aerial parts of *F.longispina* by gas chromatography-mass spectrometry (GC-MS) such as Cis-4-(4-T
butylcyclohexyl)-4-methyl-2-pentanone, 4β-(tert-butyl)1 α-(1 methyl vinyl) cyclohexane methanol**,**
cyclohexyl-2-methylenebutanylketone**,** trans-4-(t-butylcyclohexyl)-4-methyl2-pentanone-**55,** 2,6,10
-trimetyl,14-ethylne-14pentadecene-**56,** 2-butyl-decen-1-ol-**57,** 3,7,11,15- tetramethyl-2 hexadecen-
ol-**58,** 2-nonen-1-ol-**59,** citronellyl acetate-**60,** tetratetracontane-**61,** hexatriacontane-**62,** and phytol-
acetate-6**3 (Hamidi N et al,2012; Hamidi N et al 2016)** .

Naima Boutaghane et al were isolated eight compounds from *F.scabra* for the first time including luteolin-**64** and different triterpinoidsaponins (**Rathi S S et al, 2013; Boutaghane N et al, 2016).**

The structures of the isolated phytocompounds from *Fagonia* species are given in **Table 1**

Fig 2 :- Structures of isolated phytocompounds mentioned above



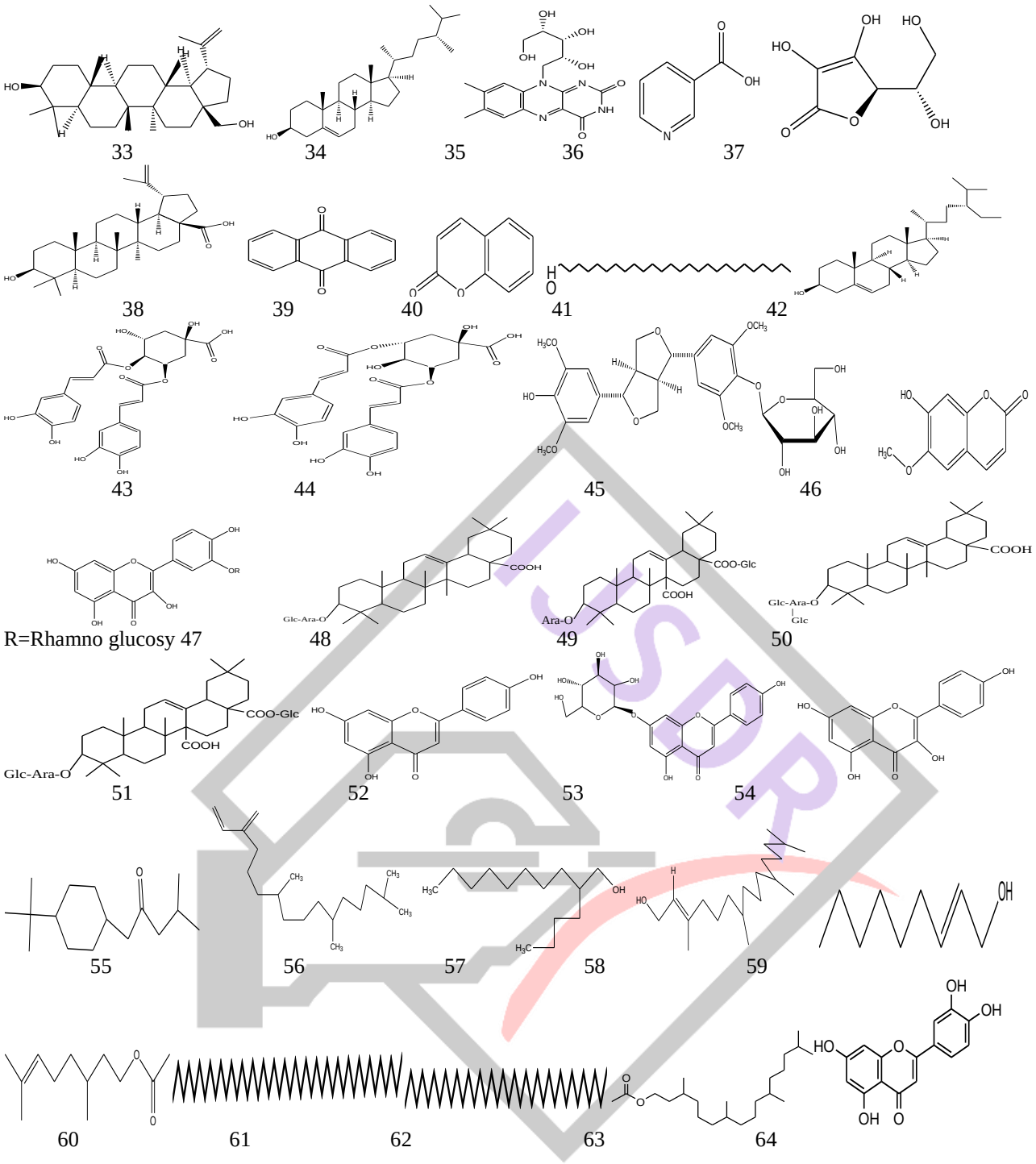


Table 1: Phytochemicals extracted from different species of *fagonia* genus and its plant part

Str No	Compound	Plant part(s)	Species	Reference
1	Nehagenin	Aerial parts	*F.indica*	Rahman A et al ,1984; Rahman A et al , 1982
2	Hedaragenin	Aerial parts	*F.indica*	Rahman A et al ,1984; Rahman A et al , 1982
3	Ursolic acis	Aerial parts	*F.indica*	Rahman A et al ,1984; Rahman A et al , 1982
4	Pinatol	Aerial parts	*F.indica*	Anil P et al, 2012; Shehab NG et al,2011
5	Indicasaponin A	Aerial parts	*F.indica*	Anil P et al, 2012; Shehab NG et

				al,2011
6	Indicasaponin B	Aerial parts	*F.indica*	Anil P et al, 2012; Shehab NG et al, 2011
7	Quercetin	Whole plant	*F.indica*	Shehab NG et al, 2011
8	isorhamnetin-α-3-O-rhamnoside	Whole plant	*F.indica*	Shehab NG et al, 2011
9	oleanolic acid	Whole plant	*F.indica*	Shehab NG et al, 2011
10	β-sitosterol-3-O-β-D-glucoside	Whole plant	*F.indica*	Shehab NG et al, 2011
11	stigmasterol-3-O-β-D- glucoside	Whole plant	*F.indica*	Shehab NG et al, 2011
12	Indicacin	Aerial parts	*F.indica*	Farheen R et al, 2015; Shaker KH et al,1999
13	fagonicin	Aerial parts	*F.indica*	Farheen R et al, 2015; Shaker KH et al,1999
14	β-amyrin	Aerial parts	*F.indica*	Farheen R et al, 2015; Shaker KH et al,1999
15	lupeol	Aerial parts	*F.indica*	Farheen R et al, 2015; Shaker KH et al,1999
16	Quinovic acid	Aerial parts	*F.cretica*	Saleem S et al, 2014
17	Quinovicacid-3β-O-β-D-glycopyranoside	Aerial parts	*F.cretica*	Saleem S et al, 2014
18	Quinovic acid-3β -O-βD-glucocpyranosyl-(28-->1)-β-D-glucopyranosylester	Aerial parts	*F.cretica*	Saleem S et al, 2014
19	stigmasterol	Aerial parts	*F.cretica*	Saleem S et al, 2014
20	linoleic acid	Aerial parts	*F.cretica*	Anjum M I et al, 2007
21	octacosanoic acid	Aerial parts	*F.cretica*	Anjum M I et al, 2007
22	methyl triadecanoate	Aerial parts	*F.cretica*	Anjum M I et al, 2007
23	β-amyrin acetate	Aerial parts	*F.cretica*	Anjum M I et al, 2007
24	taraxerol	Aerial parts	*F.cretica*	Anjum M I et al, 2007
25	oleanolic aldehyde acetate	Aerial parts	*F.cretica*	Anjum M I et al, 2007
26	triacontanoic acid	Aerial parts	*F.cretica*	Anjum M I et al, 2007
27	Docosyl docosanoate	Whole plant	*F.cretica*	Hamid A et al, 1989
28	Diosgenin	Whole plant	*F.cretica*	Khare C.P, 2004
29	cryptogenin	Whole plant	*F.cretica*	Khare C.P, 2004
30	lanosterol	Whole plant	*F.cretica*	Khare C.P, 2004
31	harmine	Whole plant	*F.cretica*	Khare C.P, 2004
32	chinovic acid	Whole plant	*F.cretica*	Khare C.P, 2004
33	Betulin	Whole plant	*F.cretica*	Khare C.P, 2004
34	campesterol	Whole plant	*F.cretica*	Khare C.P, 2004
35	riboflavin	Whole plant	*F.arabica*	Ibrahim LF et al, 2008
36	niacin	Whole plant	*F.arabica*	Ibrahim LF et al, 2008
37	Ascorbic acid	Whole plant	*F.arabica*	Ibrahim LF et al, 2008
48	3-O-β-Dglucopyranosyl(1->3α	Aerial parts	*F.arabica*	El wakil E A et al,

	L-arabinopyranoside oleanolic acid			2007
49	3-O-αL-arabinopyranosyl-quinovic acid 28-O-βD gluco pyranoside	Aerial parts	*F.arabica*	El wakil E A et al, 2007
50	3-0-[βD-gluco pyranosyl(1->2)] βD glucopyranosyl(1->3)αL ar-Binosyl oleanolic acid	Aerial parts	*F.arabica*	El wakil E A et al, 2007
51	3OβD glucopyranosyl (1->3)α L arabino pyranosyl quinovic acid 28-O-β Dglucopyranoside	Aerial parts	*F.arabica*	El wakil E A et al, 2007
52	Apigenin	Whole plant	*F.taeckholmiana*	Ibrahim L F et al, 2008
53	Apigenin 7-O-glucoside	Whole plant	*F.taeckholmiana*	Ibrahim L F et al, 2008
54	Kaempferol	Whole plant	*F.taeckholmiana*	Ibrahim L F et al, 2008
55	trans-4-(t-butylcyclohexyl)-4-methyl2-pentanone	Aerial parts	*F.longispina*	Hamidi N et al,2012; Hamidi N et al 2016
56	2,6,10 -trimetyl,14-ethylne-14pentadecene	Aerial parts	*F.longispina*	Hamidi N et al,2012; Hamidi N et al 2016
57	2-butyl-decen-1-ol	Aerial parts	*F.longispina*	Hamidi N et al,2012; Hamidi N et al 2016
58	3,7,11,15-tetramethyl-2-hexadecen-1-ol	Aerial parts	*F.longispina*	Hamidi N et al,2012; Hamidi N et al 2016
59	2-nonen-1-ol	Aerial parts	*F.longispina*	Hamidi N et al,2012; Hamidi N et al 2016
60	citronellyl acetate	Aerial parts	*F.longispina*	Hamidi N et al,2012; Hamidi N et al 2016
61	tetratetracontane	Aerial parts	*F.longispina*	Hamidi N et al,2012; Hamidi N et al 2016
62	hexatriacontane	Aerial parts	*F.longispina*	Hamidi N et al,2012; Hamidi N et al 2016
63	phytol acetate	Aerial parts	*F.longispina*	Hamidi N et al,2012; Hamidi N et al 2016
64	Lutin	Aerial parts	*F.scabra*	Rathi S S et al, 2013; Boutaghane N et al, 2016

PHARMACOLOGY

- Analgesics activity :

Shehab NG et al. Investigated on the alcoholic extract of *Fagonia indica Burm F.* on analgesic activity and it was tested by the writhing and the hot-plate tests using acetyl salicylic acid (200 mg kg-1, i.p.,) and morphine (10 mg kg-1, i.p.,) as reference drugs. The alcoholic extract of the whole plant possesses analgesic action which is likely intervened through both central and peripheral mechanisms. **(Anil P et al,2012; Shehab NG et al, 2011).**

Sharma S et al. evaluated the anti-microbial and analgesic activity of the ethanol and aqueous extract of *Fagonia indica* leaves extracts.Both solvent extracts (ethanol and water) of *Fagonia indica* was studied by tail flick method in rats to check the analgesic activity and were shown significant ($p< 0.05$) analgesic activity (**Sharma S et al, 2009; Puri D et al, 2014).**

- Anti inflammatory and wound healing property :

Alqasoumi S I et al. conducted a study on 90% alcoholic extract of *Fagonia schweinfurthii* formulated gel on carrageenan actuated rodents paw edema and excision wound model to investigate the anti-inflammatory and wound healing influence respectively. The impact were compared with the anti-inflammatory ointment diclofenac sodium (Diclomax®) and the wound healing povidone-iodine (Betadine®) drugs. The formulated gels and diclofenac sodium ointment were topically applied (0.5 g) to the grower surface of the left rear paw, as result of it anti-inflammatory effect was observed within 3 h. The wound healing effect was explored by use of 0.5 g/wound of the *F. schweinfurthii* gel and Betadine® in the direction of once per day used for 19 days to the excision wound of albino rodents and results observed at 4 days intervals. It was observed that gel formulations have dynamic anti-inflammatory impact and quicken the wound healing time. *F. schweinfurthii* plant extract gel formulation showed anti-inflammatory and wound healing effects (**Puri D et al, 2014; Alqasoumil S I et al, 2012).**

- Anti oxidant property :

Amier YAE et al Examined the antioxidant activity of *F. arabica, F. criticus* and *F. mollis* extracts by using the free radical scavenging method (DPPH) described by Miguel (2010). All the tested extracts have considerable antioxidant scavenging activities but with values lower than that of catechol. Catechol was employed as standard compound in this assay (**Amier YAE et al, 2019).**

Satpute R et al examined the anti oxidant property of alcoholic and acetone extract of *Fagonia arabica,* tested by measuring the entire polyphenolic content (TPC) and antioxidant potential of the herb by using DPPH and ABTS scavenging and ferric ion reducing antioxidant potential (FRAP) assays; its impact on neuroprotection and energy metabolism was additionally studied **(Satpute R et al, 2012)**.

Eman AA examined powdered sample of sprout of Fagonia indica was calculated for antioxidant activity with Electron Spin Resonance (ESR) instrument [Eman AA, 2011]. The extract of F.indica effectively reduced free radical levels by mechanisms involving overdoned expression of Cu-ZnSOD, diminished expression of iNOS and coincidental scavenging of the free radicals such as O2-, OH., NO and ONOO **(Ali SS et al,2008)**.

- Anti microbial activity

Sharma S et al. evaluated the anti-microbial activity of the ethanolic and aqueous extract of Fagonia indica leaves. Ethanolic extract of Fagonia indica leaves (25, 50 and 100 mg/ml) were tested against gram negative and gram positive bacterial strains by observing zone of inhibition. The bacterias used in this study *were Escherichia coli, Staphylococcus aureus, Pseudomonas aeruginosa* and *Bacillus cereus*. The result was shown that the ethanolic extract showed significant inhibitory effect against all bacterial strains and it showed maximum inhibitory effect against *Bacillus cereus* and minimum inhibitory effect against *Pseudomonas aeruginosa (***Sharma S et al, 2009).**

Anjum et al. worked on Fagonia cretica and investigate the antimicrobial activity of its constituents. In the study eleven compounds have been isolated from methanolic extract of whole plant of F. cretica. The methanolic extract was fractionated in to n-hexane, EtOAc, n-BuOH, and H2O soluble fractions. The repeated silica gel column chromatography and preparative TLC of n-hexane and EtOAc soluble fractions resulted in eleven compounds including linoleic acid, β-sitosteryl-3-O- β -D- (6-hexadecanoyl)-glucopyranoside), methyltriacontanoate, teraxerol, β amyrin acetate, oleanolic acid, octacosanoic acid, tetraxerone, arjulonic acid, and 23-hydrixy ursolic acid. The isolated compound were tested for their antimicrobial activity. The compounds showed significant antimicrobial activity against *Bacillus subtilis, Shigella flexneri, Staphylococcus aureus, Escherichia coli, Pseudomonas aeruginosa, Salmonella typhi, Trichophyton longifusus, Candida albicans, Aspergillus flavus* and *Candida glabrata* **(Anjum et al,2007)**.

Kouser R et al evaluate the antibacterial activity of different extract (n-hexane, chloroform, acetone, ethyl acetate, butanol, ethanol and methanol) of F.indica was tested against four gram positive (S.aureus,S.epidemidis,L.bulgaricus,and M.luteus) and four gram negative strain (E.coli, K.pneumonia, P.aeruginosa and S.typhi).Zone of inhibition for all tested samples for gram -ve and gram +ve bacteria strains were compared to standard antibiotic chloramphenicol. All the extracts have shown activity against the tested bacteria strains (**Kouser R et al,2013)**.

Sajid B et al evaluated the antimicrobial activity of aqueous and methanolic extracts of *Fagonia cretica*. The antimicrobial assay of plants extract(s) against different bacterial strains was conducted by disk diffusion method, In vitro antimicrobial activity was screened by using Mueller Hinton Agar plates. 0.1ml of inoculum having turbidity adjusted according to Mc Farland, S1 as standard was spreaded uniformly on plates. The different concentrations of plant extracts (1mg, 2mg) were loaded on 6mm discs of whatsman No.1 filter paper.Phytochemical analysis of *F.cretica* showed strong antimicrobial activity **(Sajid B et al, 2011)**.

- Cytotoxic and anti tumor activity

Hussain A et al observed the cytotoxic and antitumor activity of Fagonia cretica. In the investigation, this information was analyzed at laboratory level by performing cytotoxic, antitumor (potato disc) and DNA damage assay. Critical cytotoxic activity was found against brine shrimps at LD50 118.89 ppm, while antitumor assay indicated that the extract inhibited tumor induction on potato discs. Critical antitumor activity was found against every tumor-inducing Agrobacterium strains tried such as At6, At10 and At77 and extreme tumor inhibition with 77.04% was found against At10. Nevertheless, the extract did not display any lethal activity against Agrobacterium tumefaciens strains, and moreover, no DNA damaging activity was observed. The gross results indicate a strong anti-cancerous potential of this plant **(Hussain A et al, 2007)**.

Lam M et al shows that the cell cycle arrest and apoptosis via p53-dependent and independent mechanisms are elicited by an aqueous extract of Fagonia cretica with stimulation of the DNA damage response. They also show that FOXO3a is a requisite for the action in the absence of p53. Their discoveries demonstrates that Fagonia cretica aqueous extract contains potential hostiles to cancer agents acting either singly or together against breast carcinoma cell proliferation through DNA damage-induced FOXO3a and p53 articulation (**Lam M et al, 2014; Rathi SS et al, 2013)**.

Soomro AL et al examined the effect of *Fagonia indica* on experimentally produced tumours in rats. They were found that the endurance of the rats administered *Fagonia* extract was significantly longer than the control group. In the treated group the survival of female rats was 83.2+12.67 days (range 55- 118 days), while that of the treated male rats was 59.4+ 10.07 days (range 39-98). The survival of untreated female rats was 38.9+4.16 days (range 21-57 days) while the non-treated males survived for 17.0+2.55 days (range 10-27 days). The difference in survival between the treated and untreated rats was statistically significant (P <0.01) with the females significant (P<0,.01) in both the male and female rats. In treated group the difference between the survival of female and male rats surviving longer. In the non-treated group no such difference was found between the survival of male and female rats (P>0.1). This initial experiment has shown that an aqueous infusion of Fagonia indica has a tumourostatic effect which is more significant in the females **(Soomro AL et, 2003).**

- Anti diabetic activity

Rehman UA et al conducted study of anti diabetic activity of various solvent extract (n hexane, chloroform,methanol, and water) of *F.indica* by in-vivo and in-vitro.Hypoglycemic potential was investigated by alpha-amylase inhibitory assay and assessment of anti-hyperglycemic potential exhibiting in-vitro alpha amylase inhibition was carried out in Wistar albino rat model.Results shows chloroform fraction has more action **(Rehman UA et al, 2019)**.

Nazir I et al investigated the anti diabetic activity of aqueous extract of *F.cretica* L in pre clinical model and analyzed via LC/MS and also it inhibit alpha-glucosidase in vitro, the hypoglycemic effect was evaluated in normoglycaemic and streptozotocin treated rats.Various portions of preparation was managed (250-500 mg/kg) when daily for 21 days. The portion of 500 mg/kg was efficient in the management of the disease ,causing a 45% decrease in the plasma glucose level **(Nazir I et al, 2017)**.

Kamran SH et al examined methanolic extract of *Fagonia cretica* and Citrus paradisi juice (grapefruit juice) in alloxan induced diabetic rabbits and determine anti-hyperglycemic and renal protective effect. Diabetes was actuated in rabbits by alloxan monohydrate (150 mg/kg, i.p.). The treatment including *Fagonia cretica* methanolic extract (500 mg/kg), Citrus paradisi juice (7 mL/kg) and sitagliptin (10 mg/kg) were administered (p.o.) to diabetic groups for 14 days. *Fagonia cretica* extract and grapefruit juice therapy significantly ($p<0.05$) reduced glucose levels in diabetic rats. *Fagonia cretic*a extract was more effective anti-hyperglycemic agent than Citrus paradisi juice and sitagliptin **(Kamran SH et al, 2017)**.

- Androgenic activity

V Abirami et al studied on the alcoholic extract of the arial parts of *F. cretica*, and they were investigated the effect of it on estrous cycle and implantation in female albino rats. In the examination they were discovered that *Fagonia critica* generate deformation in the regularity of the estrous cycle of the rats and there is random omission of the heat period (estrous phase). Its disappearance index +53.33 which represents the decrease of the craving of the females to mate with males.Further it significantly acted as an anti-implantation agent,at the administered dose of 250 mg/kg p.o . In comparison of the weights of both seminal vesicles and ventral prostate to the control value , the weight seems to be increased. It cleared that the drug suspension has shown significant androgenic activity . It does not seem to possess any anti-androgenic activity as the values obtained by treatment with testosterone propionate were not significantly altered when the combination of the two was given **(Abirami V et al,1996).**

- Anti allergic property

Tahya AYMA et al examined the anti-allergic property of *Fagonia bruguieri*. In this the whole plant *Fagonia bruguieri* was extracted with boiling water and freeze-dried. The LD50 estimation values of the dried extract were found 11.5 and 10.75 g/kg i.p. in mice and rats, respectively. Treatment of albino guinea-pigs were done with the extract in doses of 200 mg/kg i.v, orally antagonized histamine (20 µg/kg i.v.) and capsaicin (100 µg/kg i.v.) and induced bronchoconstriction without influencing those ones instigated with ACh and 5-HT. The percentages of antagonisms were found that 72 ± 0.9 and 65 ± 4% against histamine and capsaicin respectively ($P < 0.01$, $N = 10$). When cognizant guinea-pigs are subjected to expose on histamine aqueous aerosols (10 mg/ml) ,it resulted that induced initial graspings and reversible loss of consciousness within 5 minutes. Treatment of the guinea-pigs with the extract in dose of 1.25 g/kg (i.p.) for 20 minutes or orally for 2 hours ensured altogether the animals against histamine-induced grasps and loss of consciousness ($P < 0.01$, $N = 11$) (**Tahya AYMA et al, 2007)**.

- Neuro protective activity

Rawal AK et al detailed the neuroprotective action of three species *Rubia cordifolia* (RC), *Fagonia cretica linn* (FC) and *Tinospora cordifolia* (TC). The study were cinducted by subjecting Hippocampal Slices to OGD (oxygen glucose deprivation) further they were divided into 3 groups such as control, OGD and OGD + drug treated. Cytosolic Cu-Zn superoxide dismutase (Cu-Zn SOD), glutathione peroxidase (GPx),reduced glutathione (GSH), nitric oxide (NO) was estimated as nitrite (NO2) in the supernatant,and also the protein assays were acted in the respective groups at different time intervals. EPR was utilized to set up the the antioxidant effect of R.cordifolia, F.Cretica and T.cordifolia regarding superoxide anion, hydroxyl radicals, nitric oxide radical and peroxynitrite anion created from pyrogallol, menadione, DETA-NO and Sin-1 respectively. Finally RT-PCR was performed for the three groups taken for GCLC, iNOS, Cu-Zn SOD and also GAPDH gene expression. In the result they were discovered that all the three species were effective in hoisting the GSH levels, expression of the gamma glutamyl cysteine ligase and Cu-Zn SOD genes. The species likewise displayed strong free radical scavenging properties against reactive oxygen and nitrogen species as studied by electron paramagnetic resonance spectroscopy (**Rawal AK et al, 2004).**

- Endocrinological property

Saeed MA et al Evaluated the powdered formulation of *Fagonia cretica* plant and studied the impacts of its two major triterpenoid saponins found such as saponin-I and saponin-II on different blood endocrinological parameters. For the study they were researched normal male rabbits about prolactin namely serum prolactin, serum thyrotropin, serum thyroxine and serum cortisol. From the ethanolic extract by repeated chromatography on silica gel, sephadex LH-20 and on biogel P-2 they were confined two major triterpenoid compounds, saponin-I and saponin-II. Further compared their values of 1H NMR and 13C NMR chemical shifts with previously reported values of similar compounds to identify these compounds.Radio-immunological assay were used to estimate the blood hormones of crude drug and saponin-treated animals by using radioactive I125.With the help of NE-1612 gamma scintillation counter the radioactivity of the standard and the unknown specimen was then measured for 90 seconds.Based on the evidences obtained, in the final results they were includes the activities and effects of the two saponins in different doses.The saponins obtained in 30 mg doses had showed significant decrease in prolactin and in the serum TSH levels on comparing with crude drug treatment and control groups.Saponin-II in a 30 mg dose significantly reduced the thyroxine level while the crude drug and saponin-I had non-significant effects on thyroxine after 16 days. A significant increase in serum cortisol occurred with the crude

drug in a 1g dose and with both saponins in 30 mg doses. Maximum increase in the serum cortisol occurred with saponin-II after 16 days (**Saeed MA et al, 2003).**

- Thrombolytic agent

Prasad S et al studied An in vitro thrombolytic model was wont to check the clot lysis effect of six aqueous herbal extracts viz *Fagonia Arabica*, *Rubia cordifolia*, *Hemidesmus indicus*,*Tinospora cordifolia*, *Glycyrrhiza glabra Linn*, and *Bacopa monnieri Linn* along with *Streptokinase* . Among the herbs studied *Fagonia arabica* showed significant percentage(75.6%) of clot lysis with reference to *Streptokinase* (86.2%). It possesses thrombolytic properties that could lyse blood clots in vitro (**Prasad S et al, 2007).**

The synopsis of the pharmacological activities are depicted in the Table 3

Table 2: Pharmacological activity studied, respective extract of *Fagonia* genus used and its plant part

Pharmacological activity	Extract used in the study	Plant parts
Analgesic activity	Alcoholic extract of *F.indica*	Whole plant
Analgesic activity	Ethanolic and aqueous extract of *F.indica*	Leaves
Anti inflammatory	Alcoholic extract of *F.schweinfurthii*	Whole plant
Anti oxidant	Alcoholic and acetone extract of *F.arabica*	Whole plant
Anti oxidant	Methanolic extract of *F.criticus* and *F.mollis*	Whole plant
Anti microbial	Ethanolic and aqueous extract of *F.indica*	Leaves
Anti microbial	Methanolic extract of *F.cretica*	Whole plant
Anti tumor	Methanolic extract of *F.cretica*	Aerial parts
Anti diabetic	Aqueous extract of *F.cretica*	Whole plant
Anti allergic	Aqueous extract of *F.bruguieri*	Whole plant

CONCLUSION

Huge number of phytochemicals and pharmacological examinations vehicles ried out over recent years and affirmed the huge medicinal values of plants of *Fagonia* genus. Various kinds of extracts separated from these plants proved the presence of numerous phytochemical compounds inclusive newly discovered compounds and clinically verified its pharmacological effects. All these details reveals its immense medicinal value.

The area covered in the study and the resulted data will be beneficial for the future analysis of the compounds, qualitative and quantitative analysis of drug in herbal preparation since the review haighlights all the plant parts of various species of *Fagonia* genus. Nowadays everyone prefer advances in the health with eco-friendly system. Hence the vast potentiality can gave a path to the advanced studies and to develop effective strategies, varied formulations which will be beneficial for treating various ailments.

The herb grasps attention in every aspects for more detailed research works. The comprehensive and comparative studies can explore in much depth of the plant.

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