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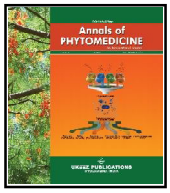

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Protective effects of *Fagonia cretica* L. aqueous extract on experimentally induced gastric and duodenal ulcers in wistar rats

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Abstract

Changes in mucosal integrity of the stomach and duodenal lining are hallmarks of the condition known as a stomach ulcer. Nausea, blood in the stools or vomit, perforations, loss of appetite, and weight loss are a few of its symptoms. Many therapy choices for ulcer care, including antihistamines, proton pump inhibitors, antacids, and prostaglandins, are all associated with side effects, according to prior research findings. Alternatives to synthetic medicines for various pharmacological disorders include herbal or natural products. *In vivo* ulcer preventive efficacy of the *Fagonia cretica* L. plant's aqueous extract against indomethacin as well as cysteamine caused ulcer models were examined in wistar rats with the help of two distinct doses of 200 mg/kg b. w. and 400 mg/kg b. w. In both ulcer models, *F. cretica* aqueous extract significantly increased percentage protection while reducing stomach lesions. Additionally, the indomethacin-induced gastric ulcer model prevented mucin from the stomach mucosa from being lost, improved gastric pH, and decreased gastric volume. The current findings indicate that the *F. cretica* aqueous extract in a dose 400 mg/kg b. w. significantly prevented gastric as well as duodenal lesions in wistar rats. The outcome of this investigation demonstrated that the *F. cretica* aqueous extract prevented gastric and duodenal lesions caused by indomethacin and cysteamine, respectively.

1. Introduction

A gastric ulcer sometimes referred to as a stomach lesion, is a rupture in the gastrointestinal mucosa's normal integrity that penetrates to the submucosal layer or deeper. Stomach ulcers are caused by a dissymmetry among the defensive agents at gastric mucosal layer (prostaglandins, bicarbonate, blood flow and mucus,) and the aggressive agents (acid, pepsin, nonsteroidal anti-inflammatory drugs and H. pylori) (Ahmed *et al.*, 2012; Adinortey *et al.*, 2013). First-line treatment for gastric ulcers largely uses proton pump inhibitors like omeprazole and H_2 receptor antagonists like ranitidine to decrease stomach acid secretion. However, current findings from the study suggest that prolonged usage of medications that suppress stomach acid elevates drug-related side effects, *e.g.*, enhanced chance of bone fractures, nutrient shortages and *Clostridium difficile* caused enteric infections (Cryer and Mahaffey, 2014). Altogether, these extended impacts could lead to changes in the stomach and intestinal pH (da Luz *et al.*, 2021). Consequently, emerging natural product alternatives may produce fewer drug-related adverse effects than synthetic equivalents (Vijayalakshmi *et al.*, 2022; Parveen *et al.*, 2020). Hence, many plants have been investigated for various pharmacological activities (Khare and Andrew, 2020).

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Fagonia cretica L. (Zygophyllaceae) is a plant utilized in Ayurvedic remedies to treat skin ulcers, mouth ulcers and inflammatory diseases (Puri and Bhandari, 2014; Rehman *et al.*, 2015). The ethnobotanical information and the profile of the active compounds suggest that *F. cretica* is a valuable plant that needs further investigation (Rajani *et al.*, 2022).

2. Materials and Methods

2.1 Chemical substance and drugs

Indomethacin (Aleid *et al.*, 2014) was procured from Jagsonpal Pharmaceuticals Limited, India, and omeprazole (Rahim *et al.*, 2014) was purchased from Dr. Reddy's Laboratories Limited, India. Ethanol, cysteamine hydrochloride, sodium carbonate, hydrogen peroxide, carboxymethyl cellulose, potassium permanganate, ether, hydrochloric acid, sulphuricacid, sodium bicarbonate, thiobarbituricacid and sucrose was collected from central store of Shree N.L.Patel College of Pharmacy, Umrakh.

2.2 Plant material collection and authentication

The *F. cretica* was procured from Phoenix medicaments Private Limited, Ahmedabad and validated at the Patidar Gin Science College, Department of Botany, Bardoli, Dist. Surat, India. The herbarium was kept and the No. PGSC/BOT/AUTH/1/2021/138 was issued.

2.3 IAEC approval and experimental animals

After receiving approval from the Institutional Animal Ethics Committee (IAEC) of Shree N.L. Patel College of Pharmacy, Umrakh which is governed by the committee for the purpose of

control and supervision of experiments on animals (CPCSEA), Government of India. The animals, wistar rats between weight of 180-200 g were purchased from Jai Research Foundation, Vapi, India. A certified number CPCSEA/IAEC/21/01/119 was supplied for the research work.

2.4 Extract preparation

500 g powdered sample of *F. cretica* was extracted for 48 h in 5000 ml of distilled water with continual orbital shaking at 300 rpm. It was then filtered using whatman No.1 filter paper using supplied solution. The resulted filtrate was specifically reconstituted in distilled water to provide the needed dose (200 mg and 400 mg/kg body weight) to test in animals.

2.5 Indomethacin caused gastric lesions

All animals were separated into five groups. Group I received only vehicle and acted as a normal. Group II animals given only indomethacin (30 mg/kg p.o.). Group III animals administered with omeprazole (20 mg/kg p.o.) after pre-treatment with indomethacin. Group IV ulcerated rats received *F. cretica* aqueous extract at 200 mg/kg dose. Group V ulcerated rats were given treatment of 400 mg/kg b.w. of *F. cretica* aqueous extract. 6 h following the indomethacin administration, the animals were sacrificed as per CPCSEA guidelines. A stomach dissection was performed, the greater curvature was assessed and the ulcerated area was calculated. The ulcer index was obtained by determining mean ulcer score of individual animal and percentage inhibition of ulcer was computed by using Eq. 1 and Eq. 2, respectively (Sabiu *et al.*, 2015).

$$\text{Ulcer index (U.I.)} = \frac{\text{Ulcerated area}}{\text{Entire stomach area}} \times 100 \quad \text{... (1)}$$

$$\%\ \text{Inhibition of ulcer} = \frac{\text{U.I. in control - U.I. in test}}{\text{U.I. in control}} \times 100 \quad \text{... (2)}$$

2.6 Assessment of gastric juice acidity

The gastric volume of each rat was assessed by collection of gastric contents into the centrifuge tubes and continuously centrifuging at a speed of 200 rotations per minute (rpm) for 15 min. 1ml sample of gastric juice was combined with 1ml of distilled water and the pH of the resulting mixture was measured using a pH meter (Fu *et al.*, 2022).

2.7 Mucin content

The stomach's glandular segments were taken out, weighed, and stained at room temperature for 2 h in 10 ml of 0.1%w/v alcianblue solution. The extra dye was eliminated twice in a succession using 10 ml of 0.25 M sucrose solution for 15 and 45 min each time then after 2 h of intermittent shaking with 10 ml of 0.5 M magnesium chloride, the dye that had combined with the mucus was extracted. The blue extract was then combined with an equal amount of diethyl ether, and the combination was centrifuged for 10 min at 3600 rpm. The amount of alcianblue extracted per gram of glandular tissue was estimated by measuring the aqueous layer's absorbance at 580 nm using a spectrophotometer and putting the values in Eq. 3 (Ahmed *et al.*, 2022).

$$\text{Mucin content} = \frac{\text{alcianblue}(\mu g / ml)}{\text{glandular tissue}(g)} \quad \text{.... (3)}$$

2.8 Cysteamine induced acute duodenal ulcers

At a dose of 300 mg/kg p.o., two doses of cysteamine HCl at 4 h intervals in distilled water were given to produce acute duodenal ulcers in rats. Oral administration of *F. cretica* extract, and the standard medication began one hour before the cysteamine challenge. In addition to maintaining a control group with cysteamine HCl, a normal group got only vehicle treatment. 48 h after the final dosage of cysteamine was administered, all animals were sacrificed. The duodenum was then evaluated for lesions and given the following scores: 0 for protected duodenum score 1 for each lesion on the mucosal surface; score 2 for marked ulcer or necrosis and score 3 for perforation (Kuldeep *et al.*, 2022; Gurbuz and Yesilada, 2007).

2.9 Statistical analysis

The results were expressed as mean ± SEM. The statistical difference in mean ulcer index between treated group and that of control was computed using ANOVA complied by Dunnett's Multiple Comparison Test with the help of GraphPad Prism Software. $p<0.05$ value was considered statistically significant.

3 Results

3.1 Indomethacin caused gastric ulcers

Table 1 displays impact of *F. cretica* aqueous extract on ulcer index and percent inhibition of ulcer in animal's groups. The level of ulcers (ulcer index) in the rats raised significantly ($p<0.05$) following administration of indomethacin. However, after receiving extracts, there was a noticeable increase in the level of ulceration inhibition. In comparison to 200 mg/kg body weight dose, the extract with a dose of 400 mg/kg b.w. provided greater protection against ulceration and performed well with the standard medication (Omeprazole).

Table 1: Effect of *F. cretica* aqueous extract in indomethacin ulcerated rats

Groups	Treatments	Ulcer index	% Protection	Gastric volume (ml)	pH	Mucin content (µg/ml)
1	Distilled H_2O (normal)	-	-	1.9 ± 0.01	6.53 ± 0.13	394 ± 0.70
2	Ind (ulcerated control)	0.560 ± 0.05	-	8.44 ± 0.11	2.55 ± 0.12	193 ± 0.67
3	Ind+ Ome (20 mg/kg)	0.210 ± 0.02	62.5 %	2.54 ± 0.15	5.48 ± 0.11	381 ± 0.37
4	Ind+ AQFC (200 mg/kg)	0.333 ± 0.02	40.5 %	5.62 ± 0.09	3.58 ± 0.12	306 ± 0.13
5	Ind+ AQFC (400 mg/kg)	0.270 ± 0.01	51.7 %	4.47 ± 0.12	4.87 ± 0.0	345 ± 0.32

Values are represented as Mean ± SEM; n = 6.

Ind; Indomethacin, Ome; Omeprazole, AQFC; Aqueous extract of *F. cretica*.

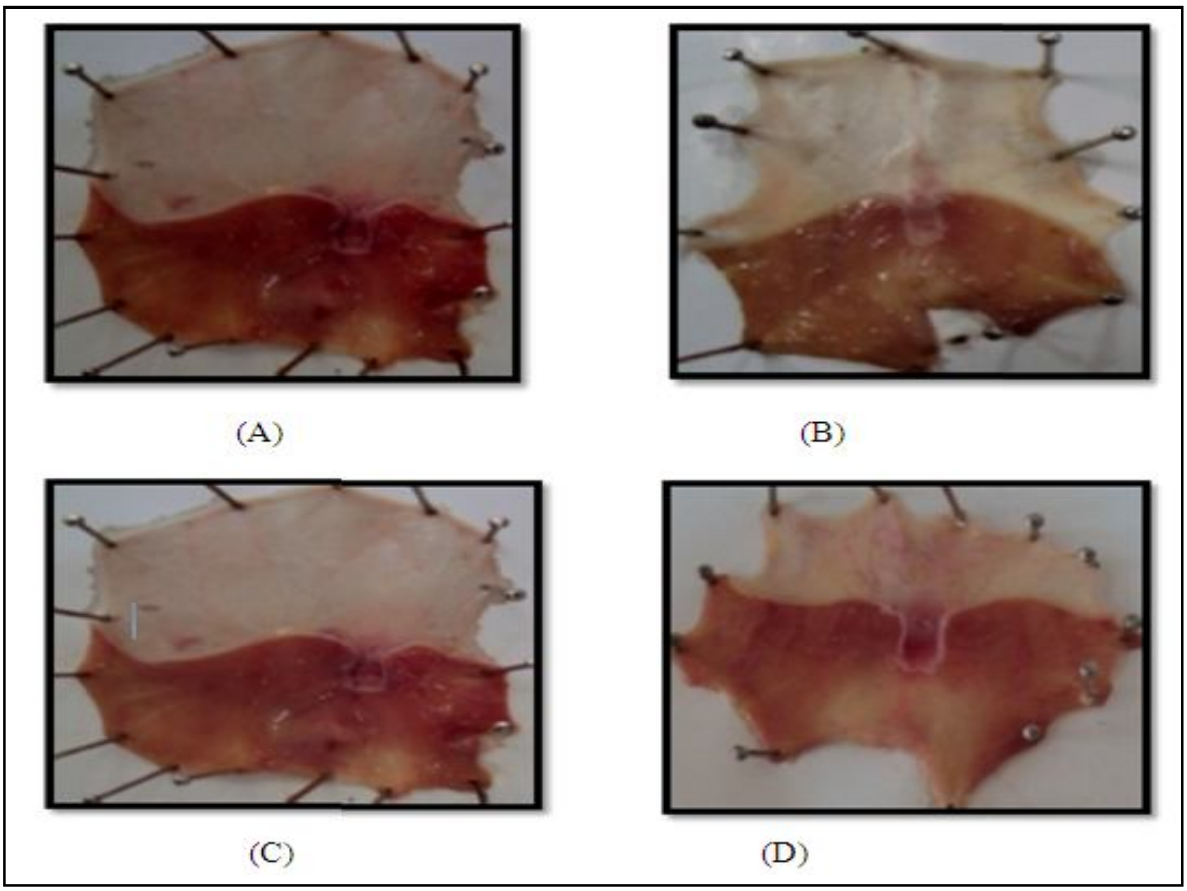

Figure 1: Gross examination of gastric mucosal layer in rats. (A) Rats pretreated with indomethacin (30 mg/kg, ulcer control). Severe lesions are seen in gastric mucosal layer. (B) Rats pre-treated with omeprazole (20 mg/kg, standard). Very mild lesions of gastric mucosa are observed as compared to lesions in ulcer control. (C) Rats pre-treated with low dose of *F. cretica* aqueous extract (200 mg/kg). (D) Rats pre-treated with high dose of *F. cretica* aqueous extract (400 mg/kg). Very mild lesions of gastric mucosa are observed as compared to lesions in control.

3.2 Cysteamine induced acute duodenal ulcers

Using the cysteamine method, rats were tested for the effect of *F. cretica* aqueous extract on duodenal ulcers. The aqueous extract treatment decreased mean ulcer size in a dose-dependent fashion. When compared to ulcerated control, omeprazole treatment significantly decreased mean ulcer size at $p<0.001$ as shown in Table 2.

Table 2: Effect of *F. cretic a*aqueous extract on ulcer index and % protection in cysteamine induced ulcers

Groups	Treatment	Ulcer index	% Protection
1	Distilled H_2O (normal)	-	-
2	Cys (ulcerated control)	0.423 ± 0.03	-
3	Cys + Ome (20 mg/kg)	0.205 ± 0.07	51.53%
4	Cys + AQFC (200 mg/kg)	0.306 ± 0.01	27.65%
5	Cys + AQFC (400 mg/kg)	0.273 ± 0.01	35.46%

Values represented as Mean ± SEM; n = 6.

Cys; Cysteamine, Ome; Omeprazole, AQFC; Aqueous extract of *F. cretica*.

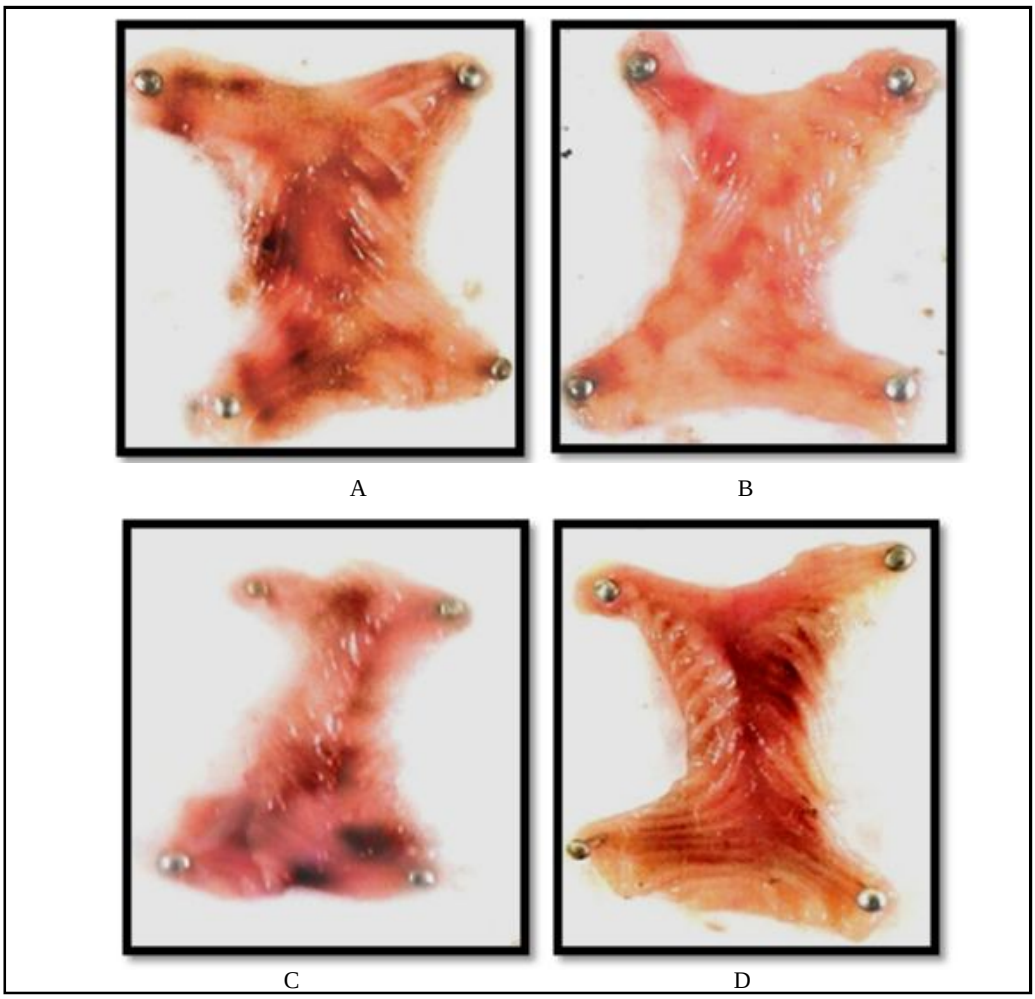

Figure 2: Gross observation of duodenum in rats. (A) Rats pre-treated with cysteamine (300 mg/kg) (ulcer control). Severe lesions are seen in duodenum. (B) Rats pre-treated with omeprazole (standard). Very mild lesions are observed in duodenum as compared to lesions seen in ulcer control. (C) Rats pre-treated with lower dose of *F. cretica* aqueous extract (200 mg/kg). (D) Rats pre-treated with higher dose of *F. cretica* aqueous extract (400 mg/kg). Very mild lesions are observed as compared to lesions in control.

4. Discussion

Research on natural products is frequently impacted through ethno pharmacological information, and introduction of new chemical substances and/or its mechanism of action has contributed significantly to developing new medications (Augustine *et al.*, 2014). Natural plant and herb extracts are favored due to their extensive safety limits and less or no harmful health effects (Abo *et al.*, 2022). In present study, *F. cretica* aqueous extract was evaluated for its ulcer preventive ability in indomethacin caused gastric ulcer model and cysteamine caused duodenal ulcer model, respectively.

Non-steroidal anti-inflammatory (NSAID) drug, indomethacin, is extensively used worldwide for managing pain, fever and inflammation has been linked to cause gastric ulcer as a side effect and it has a higher propensity for causing ulcers than other non-steroidal medications (Sabiu *et al.*, 2016). Indomethacin is distinguished by inhibiting prostaglandin formation, which is a key stage of etiology of gastric ulcers (Sheeba *et al.*, 2016). The existing study revealed that oral administration of aqueous extract of *F. cretica* significantly decreased the ulcer lesion index in indomethacin caused gastric ulcers when compared with ulcerated control group. Furthermore, compared to ulcerated control rats, treatment with the *F. cretica* extracts resulted in a considerable increment in pH value and a significant reduction in gastric volume.

Cysteamine-accelerated duodenal ulcers have been linked to long-term gastric acid overproduction, which might be caused by a decline in the duodenum's buffering capacity and an increase in plasma gastrin levels which in turn due to reduced somatostatin bioavailability. Increased acid secretion, hypergastrinemia, and diminished mucosal resistance have been associated with development of cysteamine-induced duodenal ulcers (Szabo, 1978; Japundzic and Levi, 1987). Aqueous extract of *F. cretica* significantly reduced the ulcer size in the cysteamine model as well. However, the dose of *F. cretica* aqueous extract at 400 mg/kg has produced more noteworthy outcomes than the dose at 200 mg/kg b. w.

5. Conclusion

The outcome of this investigation reveals that the *F. cretica* aqueous extract exhibits promising ulcer protective action in models of gastric ulcer and duodenal ulcer caused by indomethacin and cysteamine, respectively. Additionally, the indicated ulcer protective activity was dose dependent. The findings of this study could be connected to one or more phytoconstituents found in *F. cretica*. More research is needed to identify the precise phytoconstituent accountable for ulcer protective action.

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Conflict of interest

The authors declare no conflicts of interest relevant to this article.

References

Abdel, Rahman; AlGeffari, M.A. and Barakat, H. (2021). Gastroprotective effects of *Spirulina platensis*, golden kiwifruit flesh, and golden kiwifruit peel extracts individually or in combination against indomethacin-induced gastric ulcer in rats. J. Nutrients, **13**(10):3499.

Abo, Elsoud; Ahmed, Mohamed, Abdelaziz; M. Attia, Abd., Eldaim and Hazzaa,S.M. (2022). *Moringa oleifera* alcoholic extract protected stomach from bisphenol A induced gastric ulcer in rats via its anti-oxidant and anti-inflammatory activities. J. Environmental Science Pollution Research, **8**:1-12.

Adinortey, M.B.; Ansah, C.; Galyuon, I. and Nyarko, A. (2013). *In vivo* models used for evaluation of potential antigastroduodenal ulcer agents. J. Ulcers, **1**(3):1-12.

Ahmed, M.L.; Jadhav, A.; Swamy, P.; Sanaullah, S. and Kumar, N.S. (2012). Antiulcer and hepatoprotective effects of *Semicarpus anacardium* Linn. seed extract. Ann. Phytomed., **1**(1):105-109.

Ahmed, O.; Nedi,T. and Yimer, E.M. (2022). Evaluation of antigastric ulcer activity of aqueous and 80% methanol leaf extracts of *Urtica simensis* in rats. J. Metabolism Open, **14**:100172.

Aleid, I.S.; Alfheeaid, H.A.; Aljutaily, T.; Alhomaid, R.M.; Alharbi, H.F.; Althwab, S.A.; Augustine, H.A., B.B.; Pitta, S.; Lahkar, M.; Dash,S.; Samudrala,P.K. and Thomas,J.M. (2014). Ulcer protective effect of *Leucas aspera* in various experimental ulcer models. Asian Pacific J. of Tropical Disease, **4**:S395-S402.

C.P. Khare and Andrew, Vikram, Naharwar (2020). Ashwagandha (*Withania somnifera* (L.) Dunal): A scientific review with respect to Ayurvedic perspectives. Ann. Phytomed., **9**(2):134-141.

Cryer, B. and Mahaffey ,K.W. (2014). Gastrointestinal ulcers, role of aspirin, and clinical outcomes: Pathobiology, diagnosis, and treatment. J. of Multidisciplinary Healthcare, 7:137.

Da, Luz, B.B.; Maria, Ferreira, D.; Dallazen, J.L.; de,Oliveira, A.F.; Telles, J.E.Q.; Beltrame, O.C.; Cipriani,T.R. and de, Paula, Werner,M.F. (2021). Effectiveness of the polyphenols-rich Sedum dendroideum infusion on gastric ulcer healing in rats: Roles of protective endogenous factors and antioxidant and anti-inflammatory mechanisms. J. of Ethnopharmacology, **278**:114260.

Fu, Y.h.; Duan, Y.z.; Sun, X.y. and Chen,S.q. (2022). Gastroprotective effect of an active ingredients group of *Lindera reflexa* Hemsl. on ethanol-induced gastric ulcers in rats: Involvement of VEGFR2/ERK and TLR-2/Myd88 signaling pathway. J. International Immuno-pharmacology, **107**:108673.

Gurbuz, I. and Yesilada, E. (2007). Evaluation of the anti-ulcerogenic effect of sesquiterpene lactones from *Centaurea solstitialis* L. sp. solstitialis by using various *in vivo* and biochemical techniques. J. of Ethnopharmacology, **112**(2):284-291.

Japundzic, I. and Levi,E. (1987). Mechanism of action of cysteamine on duodenal alkaline phosphatase. J. Biochemical Pharmacology, **36**(15):2489-2495.

Kuldeep, Singh; Lal, Ratnakar, Singh and Anuradha, Mishra (2022). Therapeutic potential of indigenous medicinal plants against gastric ulcer. Ann. Phytomed., **11**(1):206-214.

Parveen; Bushra; Abida, Parvee; Rabea, Parveen; Sayeed, Ahmad; Minhaj, Ahmad and Muhammad, Iqbal (2020). Challenges and opportunities for traditional herbal medicine today with special reference to its status in India. Ann. Phytomed., **9**(2):97-112.

Puri, D. and Bhandari, A. (2014). Fagonia: A potential medicinal desert plant. J. of Nepal Pharmaceutical Association, **27**(1):28-33.

Rahim, N.A.; Hassandarvish, P.; Golbabapour, S.; Ismail, S.; Tayyab,S. and Abdulla, M.A. (2014). Gastroprotective effect of ethanolic extract of *Curcuma xanthorrhiza* leaf against ethanol-induced gastric mucosal lesions in sprague-dawley rats. J. Bio. Med. Research International, **1**:1-10.

Rajani, V.; Divyatha, K.; Obulu, B. and Bhongiri, B. (2022). Potential health benefits and pharmacological activities of *Fagonia cretica*. International J. of Advanced Research in Medical and Pharmaceutical Sciences, **7**(3):61-65.

Rehman, K.; Khan, M.A.; Ullah,Z. and Chaudhary, H.J.J. (2015). An ethno botanical perspective of traditional medicinal plants from the Khattak tribe of Chonthra Karak, Pakistan. Journal of Ethnopharmacology, **165**:251-259.

Sabiu, S.; Garuba, T.; Sunmonu, T.; Sulyman, A. and Ismail, N.O. (2016). Indomethacin-induced gastric ulceration in rats: Ameliorative roles of *Spondias mombin* and *Ficus exasperata*. J. Pharmaceutical Biology, **54**(1):180-186.

Sabiu, S.; Garuba, T.; Sunmonu, T.; Ajani, E.; Sulyman, A.; Nurain, I. and Balogun, A. (2015). Indomethacin-induced gastric ulceration in rats: Protective roles of *Spondias mombin* and *Ficus exasperata*. Toxicology Reports, **2**:261-267.

Sheeba, M.; Sheena, P.; Greeshma, T.; Gayathri, L. and Asha,V. (2016). Comparative evaluation of the efficacy of *Cardiospermum halicacabum* Linn. on indomethacin, pylorus ligation and helicobacter pylori induced gastric ulcer in rats. Ann. Phytomed., **1**:63-72.

Szabo, S.J. (1978). Animal model: Cysteamine-induced acute and chronic duodenal ulcer in the rat. American J. Pathol, **93**(1):273-276.

Vijayalakshmi, A.; Sumitra, M.; Prabha, T.; Lalitha, V.; Sri Bhuvaneswari, S.; Hemalatha, S.; Selvamani, P. and Latha,S. (2022). Medicinal plants for the treatment of erythrasma: A review. Ann. Phytomed., **11**(1):201-205.

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