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Pharmacological Screening of Gastro Protective Activity of *Chrysanthemum morifolium* Flowers in Rodent Model



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ABSTRACT

Objective: The present study was designed to investigate the anti-ulcer activity of methanolic extract of *Chrysanthemum morifolium* flowers using animals. **Methods:** Methanolic extract of *Chrysanthemum morifolium* was tested for acute toxicity studies on female rats at the dose of 2000 mg/kg b.wt. *p.o.* The working dose was considered as 1/10th *i.e.*, 200 mg/kg body weight, second dose selected was double dose of 1/10th *i.e.* 400 mg/kg body weight. The animals were divided into five groups in which each group contain six animals (n=6). First group was served as normal control group, second group as a disease control, third and fourth groups were of 200mg/kg and 400mg/kg, and fifth group as a standard group, using Omeprazole as a standard drug. Anti-ulcer activity was evaluated using two models such as Ethanol induces and Aspirin induced respectively. **Results:** In the phytochemical constituent screening, the flowers of *Chrysanthemum morifolium* showed the presence of alkaloids, steroids, flavonoids, triterpenoids, tannins & phenolic compounds, saponins, glycosides. The data obtained were analyzed by One-way ANOVA followed by Dunnett Multiple Comparisons test using GraphPadInStat. $p < 0.05$ and $p < 0.001$ was considered to be significant. The results obtained from anti-ulcer activity collectively demonstrated that the methanolic extract of *chrysanthemum morifolium* showed a significant anti-ulcer effect and was dose dependent (400 mg/kg body weight). **Conclusion:** It was concluded that the test drug possesses better and significant effect in alleviating the ulcer.

INTRODUCTION

Peptic ulcer disease is a term which describes a condition with ulcerations. It is a heterogeneous disorder characterized by the disruption of the mucosal integrity of the esophagus, stomach, or duodenum [1]. Ulcers can occur at any age, including infancy and childhood, but are most common in middle-aged adults. Ulcers (gastric and duodenal) occur most commonly in patients aged 30 to 50 years, although patients > 60 years of age account for 80% of deaths. Infection by *Helicobacter pylori*, a spiral bacterium of the stomach, remains an important epidemiological factor in causing peptic ulcer [2]. It affects 10%-15% of the population totally at any time. Ulcers are primarily caused by an imbalance between some endogenous aggressive and protective factors in the stomach such as acid-pepsin secretion, integrity of the mucosal barrier, mucus secretion, blood flow, cellular regeneration, prostaglandins and growth factors [3]. The treatment for peptic ulcer is targeted at either counteracting aggressive factors (acid, pepsin, active oxidants, platelet aggravating factor "PAF", leukotrienes, endothelins, bile or exogenous factors including NSAIDs) or stimulating the mucosal defenses (mucus, bicarbonate, normal blood flow, prostaglandins (PG), nitric oxide). The goals of treating peptic ulcer disease are to relieve pain, heal the ulcer and prevent ulcer recurrence. Currently, there is no cost-effective treatment that meets all these goals. Hence, efforts are on to find a suitable treatment from natural product sources. Since hundreds of years, the flower of *Chrysanthemum morifolium* Ramat. (FC) has been used in oriental countries and is widely consumed as a medicinal herbal tea [4]. FC is reported to have ethnomedicinal importance like cardiovascular protection, antitumorigenesis, and anti-inflammation. *Chrysanthemum* species have been shown to contain a wide variety of flavonoids, phenols, and phenolic acids [5]. Significant amounts of flavonoids and hydroxycinnamoylquinic acids are considered to be the biologically active components. Keeping in view of the anti-oxidant and anti-inflammatory property, an attempt was made to investigate the anti-ulcer effect of the *Chrysanthemum morifolium* [6]. The inflammation and ulcer have a relation, inflammation being an initiating factor for healing process, and also considered as a protective mechanism, but if exceeds or prolonged can effect adversely to a diseased condition. Proton pump inhibitors (PPIs) play a key role in the treatment of ulcers as it suppresses stomach acid secretion by specific inhibition of the H⁺/K⁺-ATPase system found at the secretory surface of gastric parietal cells. The most common side effects of proton pump inhibitors are headache, diarrhea, constipation, abdominal pain, flatulence, fever, vomiting, nausea. Initially, PPIs were proven to be safe and effective and healing

peptic ulcer disease became one of the most-prescribed medications by healthcare providers. This contributed to their overuse and misuse, prolonged use and even lifetime use. It inclined to serious adverse effects like hypergastrinemia, pneumonia, fractures (due to calcium deficiency), Vit B12 deficiency, hypomagnesimia, dementia and SLE (Systemic lupus erythematosus). This lead to the focus on the phytotherapy and the beneficial effects of herbal medicines in treating ulcers. Although conventional regimens are effective, their side effects are often unavoidable and limit the clinical utility [7]. However, both clinical and experimental studies have demonstrated that herbal medicines exhibit therapeutic benefit for gastric ulcer with fewer side effects. Moreover, the cost of herbal medicine for gastric ulcer is only about 1/6th of that of Western medicine. Despite a concern for herb-drug interactions, some herbs can cause severe side effects and are used to treat gastric ulcer are generally safe in both animal models and humans [8]. This was demonstrated primarily in various animal models, including ulcers induced by NSAIDs, ethanol, cold-restraint stress, pylorus ligation, as well as erosive agents. In the present study, two models were selected to evaluate the anti-ulcer activity of methanolic extract of *Chrysanthemum morifolium* flowers.

METHODOLOGY:

Collection of Plant material and extraction [9]

The Flowers of *Chrysanthemum morifolium* were collected from a local market during the month of October 2018. This material was identified and authenticated by a botanist at SV University, Tirupati, Andhra Pradesh, India. The freshly collected flowers of the plant *Chrysanthemum morifolium* were cleared from dirt and then the flowers were dried under shade for about 10 days and coarsely powdered in a mixer grinder. The powdered material was stored for extraction process. The powder was subjected to methanol extraction, in the Soxhlet apparatus and was run about 10 cycles. After filtration through Whatman filter paper, the filtrates were dried in desiccator.

Chemicals: Carrageenan was procured from Sigma Aldrich, Bombay, India. Diclofenac was a gift sample from Dr. Reddy's Laboratories; Omeprazole was procured from Aurobindo Pharma, Hyderabad. Aspirin was procured from Sigma labs, Mumbai. Acetic anhydride, Ascorbic acid, chloroform, formalin and hydrogen peroxide were procured from SD Fine Chem Limited, Mumbai. Ammonia, carboxymethylcellulose, ferric chloride and glacial acetic acid from Himedia laboratories, Mumbai.

Preliminary Phytochemical Screening: [10]

The flowers of *Chrysanthemum morifolium* was screened for the presence of various phytoconstituents like alkaloids, flavonoids, steroids, tannins, glycosides, triterpenoids and saponins.

Acute Toxicity Studies of METS [11]

Acute toxicity studies were carried out in order to check the toxic effects for methanolic extract of flowers of *Chrysanthemum morifolium*. The studies were performed as per Organization for Economic Cooperation and Development (OECD). The method is used to evaluate the acute oral toxicity is up and down procedure (OECD guideline-425). Up and down procedure (OECD guideline-425) acute toxicity studies were carried out as per the OECD 425 guidelines.

Animals: Animal Protocol was approved by IAEC (Institutional Animal Ethical Committee) of CPCSEA (Committee for Purpose of Control and Supervision of Experimentation on Animals) through its reference no: IAEC/MNRCP/2018/003, Dated: 27/2/18. Male Wistar rats, weighing (180-250 gms) were obtained from NIN (National Institute of Nutrition, Hyderabad). The animals were acclimatized to the experimental room at a temperature of $23\pm 2^{\circ}$ C, controlled humidity conditions (50-55%) and 12hr light and 12hr dark cycles. They were fed with standard food pellets (Hindustan Lever, Hyderabad) and water *ad libitum*.

Experimental protocol:

Table No. 1: Study design for Ethanol induced ulcer model

S. No	Groups	Treatment
1	Group – I	Control (0.9% Normal saline)
2	Group – II	Ethanol (90% v/v, 1 ml/200g)
3	Group – III	MECM (200 mg/kg, b.wt, <i>p.o.</i>)
4	Group – IV	MECM (400 mg/kg, b.wt, <i>p.o.</i>)
5	Group – V	Omeprazole (20mg/kg <i>p.o.</i>)

Table No. 2: Study design for Ethanol induced ulcer model

S. No	Groups	Treatment
1	Group – I	Control
2	Group – II	Aspirin (200 mg/kg b.wt) <i>p.o.</i>
3	Group – III	MECM (200 mg/kg, b.wt, <i>p.o.</i>) for 1-8 days
4	Group – IV	MECM (400 mg/kg, b.wt, <i>p.o.</i>) for 1-8 days
5	Group – V	Omeprazole (20mg/kg <i>p.o.</i>) for 1-8 days.

The *in vivo* evaluation of Anti-ulcer activity of the methanolic extract of Flowers of *Chrysanthemum morifolium* were done using two models -

1. Ethanol induced ulcer model
2. NSAID'S (Aspirin) induced ulcer

Ethanol induced ulcer model: [12]

Albino Wistar rats were divided into five groups of 6 animals each. All animals received treatment for 5 days. Group-I served as normal control, received 0.9% normal saline solution (1ml/kgb. wt), Group II: disease control received ethanol (90% v/v, 1 ml/200g), Group III: received with MECM of 200 mg/kg body weight, *p.o.*, Group IV: received MECM of 400 mg/kg body weight, *p.o.*, and Group V served as a standard group which received Omeprazole 20mg/kg *p.o.* Gastric ulcers were induced in rats by administration of 1ml 90% v/v ethanol *p.o.* Animals were fasted for 24 h with free access to water prior to the test. MECM and the standard drug (Omeprazole) were given orally 30 minutes before administration of ethanol (90% v/v, 1 ml/200g) and were sacrificed after 15 minutes. The stomach was dissected out, gastric juice was collected, and its volume was measured. The free and total acidity was also determined. The stomach was opened along the greater curvature, rinsed under a stream of water and pinned flat on a corkboard. Erosions formed on the glandular portion of stomach were counted and each was given a severity rating on 1-3 scale, based on diameter of the ulcer. The overall total diameter of ulcers in one stomach divided by factor 10 was designated as ulcer index (UI) (Gosh, 2005; Hollard *et al.*, 1985).

NSAID'S (Aspirin) induced ulcer: [12]

In the aspirin – induced ulcer experiment, 5 groups of albino rats (150-180 g), with each group of 6 animals were used. The first group served as a normal control group, group 2 served as a disease control group which received aspirin (200 mg/kg b.wt) *p.o.*, group third and fourth served as test groups and fifth group served as a standard group receives Omeprazole (20mg/kg *p.o.*). The third and fourth group received MECM of 200 and 400 mg/kg b.wt. *p.o.* respectively by oral route for 8 days. After 8 days of treatment, animals were fasted for 24 h. Ulcer was produced by administration of aqueous suspension of aspirin (a dose of 200 mg/kg b.wt. orally) on the day of sacrifice. The animals were sacrificed 4 hrs later and stomach was opened to calculate the ulcer index, free acid total acid, the pH of the gastric juice is recorded by using a pH meter (Maruthappan *et al*, 2010).

RESULTS

Methanolic flower extract of *Chrysanthemum morifolium* was explored for its *in vivo* anti-ulcer activity using two animal models. All the results obtained in this study were depicted in the tables and figures respectively.

The preliminary phytochemical investigation for methanolic extract of *Chrysanthemum morifolium* flower heads showed the presence of Alkaloids, steroids, flavonoids, triterpenoids, tannins & phenolic compounds, saponins, glycosides. The results were showed in Table 3.

Table No 3: Preliminary Phytochemical analysis for MECM flower heads

Phytoconstituents	Results
Alkaloids	+
Carbohydrates	-
Flavonoids	+
Triterpenoids	+
Saponins	+
Phenolic compounds	+
Glycosides	+

Note: + indicates present; - indicates absent

In vivo Anti-Ulcer Activity

Methanolic extract of *Chrysanthemum morifolium* flower heads was explored for its anti-ulcer activity in Ethanol induced ulcer model and NSAID'S (Aspirin) induced ulcer in rodent models. All the results obtained in this study were discussed as follows.

Ethanol induced ulcer model

Table No. 4: Effect of methanolic extract of flowers of *Chrysanthemum morifolium* (100 mg/kg and 200 mg/kg) on the Gastric volume and pH

Treatment	Gastric volume	pH
Control	1.475±0.09	6.04±0.29
Ethanol (1ml/200g)	3.55±0.08**	1.52±0.10**
MECM (200 mg/kg)	2.80±0.15*	3.62±0.13**
MECM (400 mg/kg)	2.48±0.16**	4.54±0.15**
Omeprazole (20mg/kg)	2.01±0.21**	5.46±0.12**

Values are expressed as Mean ± SEM, (n=6). Statistical analysis was performed by using ANOVA followed by Dunnett's test. Results were compared with diseased control (** p<0.001, * p<0.05) and standard (*p<0.001, * p<0.05).

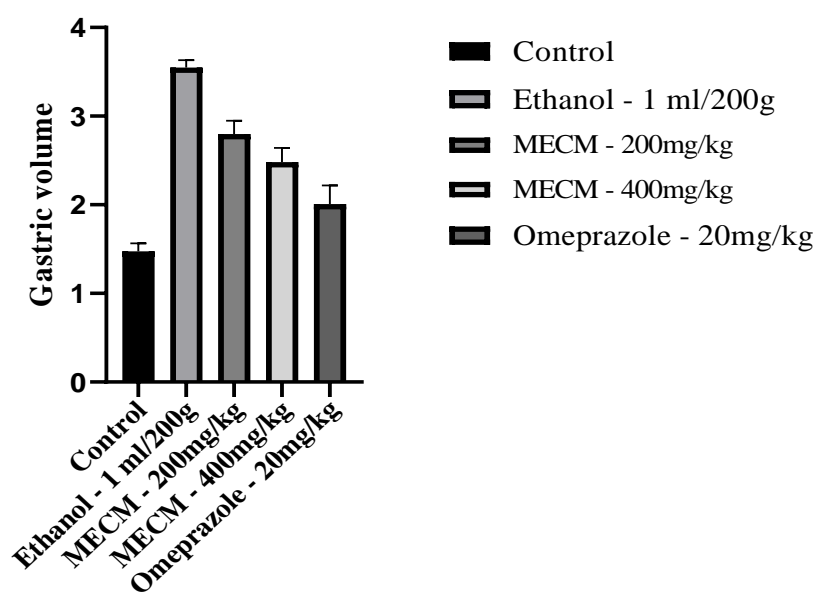


Figure No. 1: Effect of test extracts on the gastric volume

Table No. 5: Effect of methanolic extract of flowers of *Chrysanthemum morifolium* (100 mg/kg and 200 mg/kg) on the free and total acidity

Treatment	Total acidity	Free acidity
Control	25.08±0.30	19.16±0.30
Ethanol (1ml/200g)	63.62±0.61**	52.43±0.35**
MECM (200 mg/kg)	54.006±0.54**	34.70±0.69**
MECM (400 mg/kg)	42.82±0.93**	28.15±0.61**
Omeprazole (20mg/kg)	31.57±0.34**	23.91±0.77**

Values are expressed as Mean ± SEM, (n=6). Statistical analysis was performed by using ANOVA followed by Dunnett’s test. Results were compared with diseased control (** p<0.0001, * p<0.05) and standard (*p<0.0001, *p<0.05).

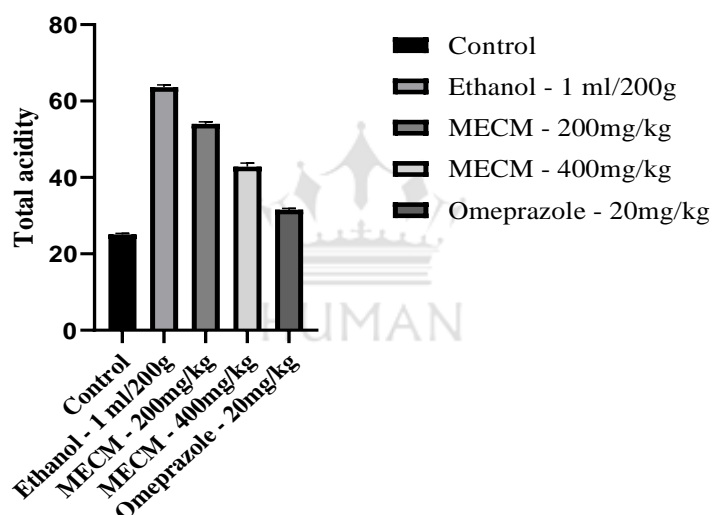


Figure No. 2: Effect of test extracts on the total acidity

Table No. 6: Effect of methanolic extract of flowers of *Chrysanthemum morifolium* (100 mg/kg and 200 mg/kg) on the Ulcer Index

Treatment	Ulcer Index	% Protection of Ulcer index
Ethanol (1ml/200g)	11.68±0.43**	--
MECM (200 mg/kg)	5.14±0.21*	55.99
MECM (400 mg/kg)	4.28±0.28 ^{ns}	63.35
Omeprazole (20mg/kg)	3.46±0.11**	70.37

Values are expressed as Mean \pm SEM, (n=6). Statistical analysis was performed by using ANOVA followed by Dunnett's test. Results were compared with diseased control (** p<0.001, * p<0.05) and standard (A p<0.001, B p<0.05).

NSAID'S (Aspirin) induced ulcer model

Table No. 7: Effect of methanolic extract of flowers of *Chrysanthemum morifolium* (100 mg/kg and 200 mg/kg) on the Gastric volume and pH

Treatment	pH	Gastric volume
Control	5.50 \pm 0.09	1.69 \pm 0.09
Aspirin (200 mg/kg)	2.44 \pm 0.10**	4.35 \pm 0.12**
MECM (200 mg/kg)	3.45 \pm 0.09**	3.40 \pm 0.06**
MECM (400 mg/kg)	4.47 \pm 0.09**	3.18 \pm 0.07**
Omeprazole (20mg/kg)	5.15 \pm 0.03**	2.34 \pm 0.07**

Values are expressed as Mean \pm SEM, (n=6). Statistical analysis was performed by using ANOVA followed by Dunnett's test. Results were compared with diseased control (** p<0.0001, * p<0.05) and standard (A p<0.0001, B p<0.05).

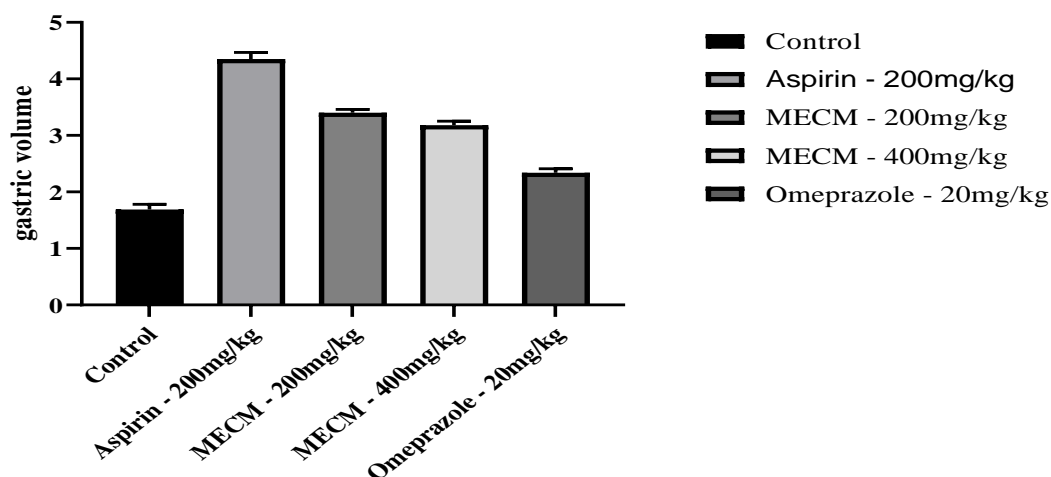


Figure No. 3: Effect of test extracts on the Gastric volume

Table No. 8: Effect of methanolic extract of flowers of *Chrysanthemum morifolium* (100 mg/kg and 200 mg/kg) on the free and total acidity

Treatment	Total acidity	Free acidity
Control	27.38±0.25	14.33±2.57
Aspirin (200 mg/kg)	58.45±0.44**	53.05±0.63**
MECM (200 mg/kg)	44.11±1.05**	32.29±0.75**
MECM (400 mg/kg)	37.86±0.37**	27.49±0.59**
Omeprazole (20mg/kg)	24.11±0.29**	18.71±0.37**

Values are expressed as Mean ± SEM, (n=6). Statistical analysis was performed by using ANOVA followed by Dunnett’s test. Results were compared with diseased control (** p<0.0001, * p<0.05) and standard (*p<0.0001, *p<0.05).

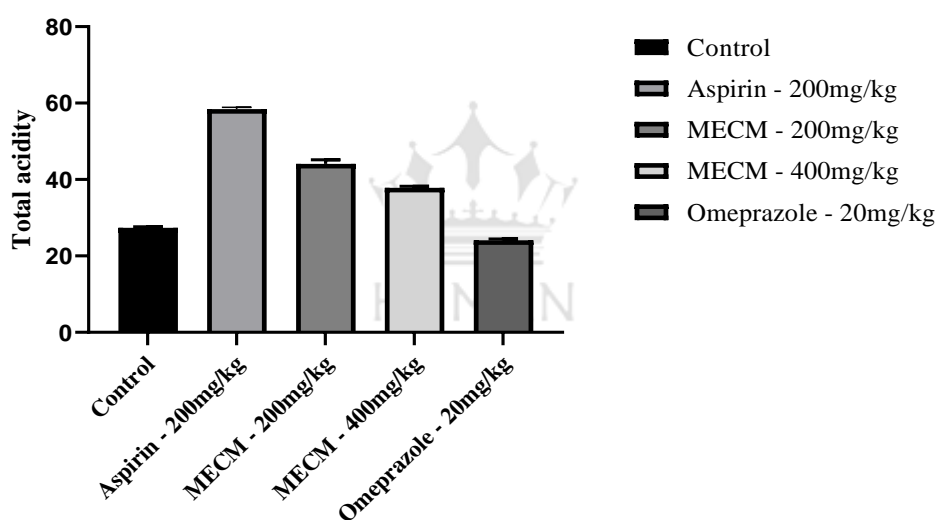


Figure No. 4: Effect of test extracts on the total acidity

Table No. 9: Effect of methanolic extract of flowers of *Chrysanthemum morifolium* (100 mg/kg and 200 mg/kg) on the Ulcer Index

Treatment	Ulcer Index	% Protection of Ulcer index
Aspirin (200 mg/kg)	11.3±0.24**	--
MECM (200 mg/kg)	7.03±0.36**	37.78
MECM (400 mg/kg)	5.34±0.17**	52.74
Omeprazole20mg/kg)	3.90±0.20**	65.48

Values are expressed as Mean \pm SEM, (n=6). Statistical analysis was performed by using ANOVA followed by Dunnett's test. Results were compared with diseased control(** p<0.001, * p<0.05) and standard (*p<0.000, * p<0.05).

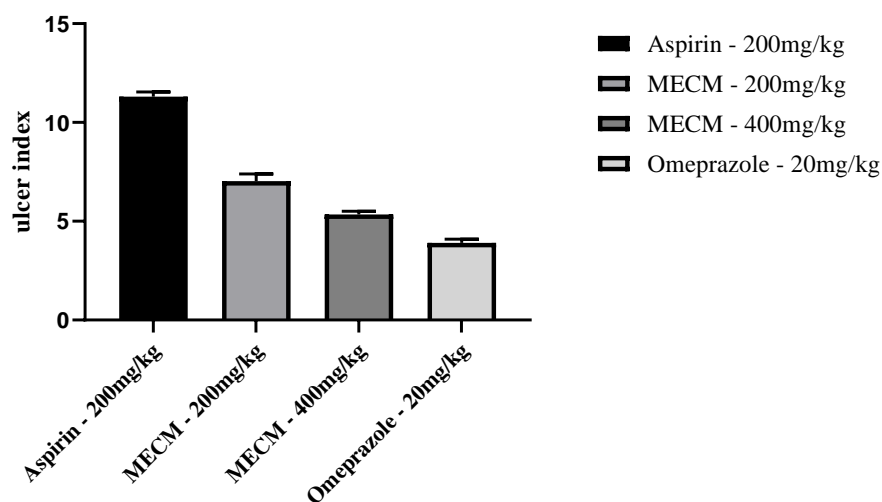


Figure No. 5: Effect of test extracts on the ulcer index

The phytoconstituents like flavonoids, tannins, terpenoids, and saponin have been reported in several anti-ulcer literatures as possible gastroprotective agents. Flavonoids, tannins and triterpenes are among the cytoprotective an active material for which anti ulcerogenic efficacy has been extensively confirmed [13].

In this study, anti-ulcer activity of MECM has been studied. The anti-ulcer activity was evaluated by using two models-Ethanol induced and Aspirin-induced ulcer models. Gastric ulceration is a major limitation to the use of non-steroidal anti-inflammatory drugs (NSAIDs). NSAIDs can cause damage to the gastric mucosa via several mechanisms, including their topical irritant effect on the epithelium, impairment of the mucosal barrier function, suppression of gastric prostaglandin synthesis, reduction of gastric mucosal blood flow and interference with the repair of superficial injury [14]. The presence of acid in the lumen of stomach also contributes to the pathogenesis of NSAIDs-induced ulcers and bleeding by impairing the restitution process, interfering with haemostasis and inactivating several growth factors that are important in mucosal defense and repair. In the present study, Ethanol induced and aspirin-induced gastric lesions were extensively prevented by methanolic extract of *Chrysanthemum morifolium* flower. Ethanol induced formation of a gastric lesion and it may be due to stasis of gastric blood flow which adds to the development of necrosis and hemorrhage [15, 16].

In the present study, oral administration of MECM at the doses of 200 and 400mg/kg exhibited dose dependent inhibition percentage of 55.99% and 63.35% ($p < 0.001$) respectively as compared to the ulcer control, proving the anti ulcer activity. The standard drug omeprazole (20mg/kg) exhibited percentage inhibition of 70.37% when compared to disease control. Other parameters like Gastric volume, pH, free acidity, total acidity were also studied and showed significant protection against ethanol induced gastric ulcers. Extract treated and ulcer induced group were compared with standard group. There was a dose-dependent increase in the ulcer protective action of the extract.

In NSAID-induced gastric ulcer model: induction of gastric ulcer was a major adverse effect caused by NSAIDs. Therefore, they have been used widely to establish animal models of gastric ulcer. The MECM was evaluated by using Aspirin induced ulcer method, oral administration of MECM at doses of 200 and 400mg/kg exhibited dose dependent inhibition percentage of 37.78% and 52.74% ($p < 0.001$) respectively compared to the ulcer control, proving the anti ulcer activity. The standard drug omeprazole (20mg/kg) exhibited percentage inhibition of 65.48% when compared to the ulcer control. Other parameters like Gastric volume, pH, free acidity, total acidity were also studied and showed significant protective effect Aspirin induced gastric ulcers. Extract treated and ulcer Induced group was compared with standard group. There is a dose-dependent increase in the ulcer protective action of the extract. These results suggested that herbal medicines could be useful in treating NSAID-induced gastric ulcer.

CONCLUSION

In conclusion, it can be stated that herbal medicines were effective in treating gastric ulcer. To sum up, *Chrysanthemum morifolium* flowers presented antiulcer effects against ethanol-induced gastric lesions and also Aspirin induced ulcer in the animal model significantly and dose-dependently. It also manifested decreased acidity and upregulated the pH of gastric juice. Therefore, the methanolic extract of the species may be considered as a one of the novel antiulcer drugs. Further studies are needed for their exact mechanism of action on gastric acid secretion and gastric cytoprotection.

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CONFLICTS OF INTEREST:

The authors have no conflicts of interest with anyone.

REFERENCES

- 1) Chu Q, Fu L, Guan Y, Ye J. Determination and differentiation of Flos Chrysanthemum based on characteristic electrochemical profiles by capillary electrophoresis with electrochemical detection. *Journal of Agricultural and Food Chemistry*, 2003. 52;(26):7828–7833.
- 2) Kim H and YS Lee. Identification of new dicaffeoylquinic acids from *Chrysanthemum morifolium* and their antioxidant activities. *PlantaMedica*, 2005, 71 (9):. 871–876.
- 3) Freitas CS, Baggio CH, Finau J, Anginoni M, Pizzolatti MG, Santos ARS, Marquez MCA. Inhibition of H⁺/K⁺ATPase in the gastroprotective effect of *Baccharis illinita* DC. *Journal of Pharmacy and Pharmacology*, 2008; 60:1105-10.
- 4) Jiang H, Xia Q, Xu W, Zheng M. *Chrysanthemum morifolium* attenuated the reduction of contraction of isolated rat heart and cardiomyocytes induced by ischemia/reperfusion. *Pharmazie* (2004); 59 (7): 565–567.
- 5) Miyazawa M, Hisama M. Antimutagenic activity of flavonoids from *Chrysanthemum morifolium*, *Bioscience, Biotechnology and Biochemistry*, 2003, (67)10; 2091–2099.
- 6) Ukiya M, Akihisa T, Yasukawa K. Constituents of Compositae plants. 2. Triterpenediols, triols, and their 3-Omega fatty acid esters from edible *Chrysanthemum* flower extract and their anti-inflammatory effects. *Journal of Agricultural and Food Chemistry*, 2004,49(7); 3187–3197.
- 7) Beninger C W, Abou-Zaid M M, Kistner A L E. A flavanone and two phenolic acids from *Chrysanthemum morifolium* with phytotoxic and insect growth regulating activity. *Journal of Chemical Ecology*, 2004;30 (3): 589– 606.
- 8) Sung JJ, Kuipers EJ, El-Serag HB. Systematic review: the global incidence and prevalence of peptic ulcer disease. *Aliment Pharmacol Ther*,2009; 29: 938-946.
- 9) Al-Yahya MA, Rafatullah S, Mossa JS, Ageel AM, Parmar NS, Tariq M. Gastroprotective activity of ginger *zingiber officinal* rocs, in albino rats. *Am J Chin Med*, 1989;17:51–56.
- 10) Kokate C.K, Purohit A.P, Gokhale S.B, 'Text Book of Pharmacognosy', 33th Ed. *Nirali Prakashan*, 2001; Pune; 593-597.
- 11) Bruce. OECD guideline for testing of chemicals Acute Oral Toxicity- Up-and-Down Procedure, 2001: 1-26.
- 12) Shirisha Bongu, Subash Vijayakumar. Animal models in experimental gastric ulcer screening-a review, *International Journal of Pharmacological Screening Methods*, 2012;2(2):82-87.
- 13) Hollander, D., Taranawski, A., Krause, W.J., Gergely, H. Protective effect of sucralfate against alcohol-induced gastric mucosal injury in the rat. *Gastroenterology*, 1985; 88, 366–374.
- 14) Maruthappan. V and K. Sakthi Shree. Antiulcer activity of aqueous suspension of *Saraca indica* flower against gastric ulcers in albino rats. *Journal of Pharmacy Research*, 2010; 3(1),17-20.
- 15) Kumar A, Dewan B, Rama T. Evaluation of anti-ulcerogenic properties from the root of *Flemingia strobilifera*. *Journal of Basic and Clinical Pharmacy*, 2011;2(1); 33-39.
- 16) Thomas W, Hiruma-Lima CA, Guerrero RO, Brito AR. Preliminary studies of *Mammea americana* L. (Guttiferae) bark/latex extract point to an effective antiulcer effect on gastric ulcer models in mice. *Phytomedicine*, 2005; 12: 345-350.