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Evaluation of anti ulcer activity of *ecliptaalba* extract in experimental animal model

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ABSTRACT

The cause of ulceration in patients is mainly due to hyper secretion of gastric juice and also due to hyper secretion of pepsin. In traditional system of medicine a number of herbal preparations have been used for the treatment of peptic ulcers. There are various medicinal plants has been used for the treatment of gastrointestinal disorders. In view of this, in present study we have to evaluate the anti-ulcer activity of *Eclipta Alba*. Study was carried out, by using three methods i.e., alcohol, paracetamol and stress induced ulcers in rats pretreated with the doses of 250 mg/kg AQEA and ALEA, 10mg/kg Omeoprazole and 50 mg/kg Ranitidine.
To evaluate the antiulcer activity of aqueous and alcoholic extracts of *Eclipta Alba* leaves (AQEA and ALEA) at 250 doses using different experimentally induced gastric ulcer models in rats. Gastric ulcers were induced in rats by 80% alcohol, paracetamol and forced immersion stress induced methods. In alcohol induced ulcer model, paracetamol induced ulcer model and stress induced model the ulcer index was determined. Where as in stress induced ulcers stress plays an important role in ulcerogenesis.In alcohol-induced ulcers, AQEA and ALEA were effective in reducing lesion index and increasing the gastric mucus content. It was also effective in decreasing ulcer index in paracetamol-induced ulcers. All the results obtained with *Eclipta Alba* were dose dependent. The results suggest that AQEA and ALEA possesses significant and dose dependent antiulcer activity. The antiulcer activity of AQEA and ALEA can be attributed to its cytoprotective and antisecretory action.

Keywords: *Eclipta Alba*, antisecretory, cytoprotective, gastric ulcer, alcohol induced ulcers, paracetamol-induced ulcers and stress induced ulcers.

INTRODUCTION

Peptic ulcer and other acidic symptom affect up to ten percentages of the humans with sufficient severity to prompt victims to seek medical attention. The more significant disease condition requiring medical fuscous is ulcer and gastro esophagealdisease1. In the US, approximately 4 million people have peptic ulcer (duodenal and gastric types), and 350 thousand new patient are diagnosed in each year, around 180 thousand peoples are admitted to hospital and treated with drugs yearly, and about five thousand patient from this case die each year as a result of ulcer condition. The lifetime of human being developing a peptic ulcer is about 10 percentages for Americans males and four percentages for female population2.

Peptic ulcers is wound in the lesions that are most often affected in younger to older adults population, but this may diagnosed in young adult life. They often appear without obvious sign and symptom, after a period of days to months of active phase of disease, it may heal with or without drug treatment. It also affect because of bacterial infections with H. Pylori.

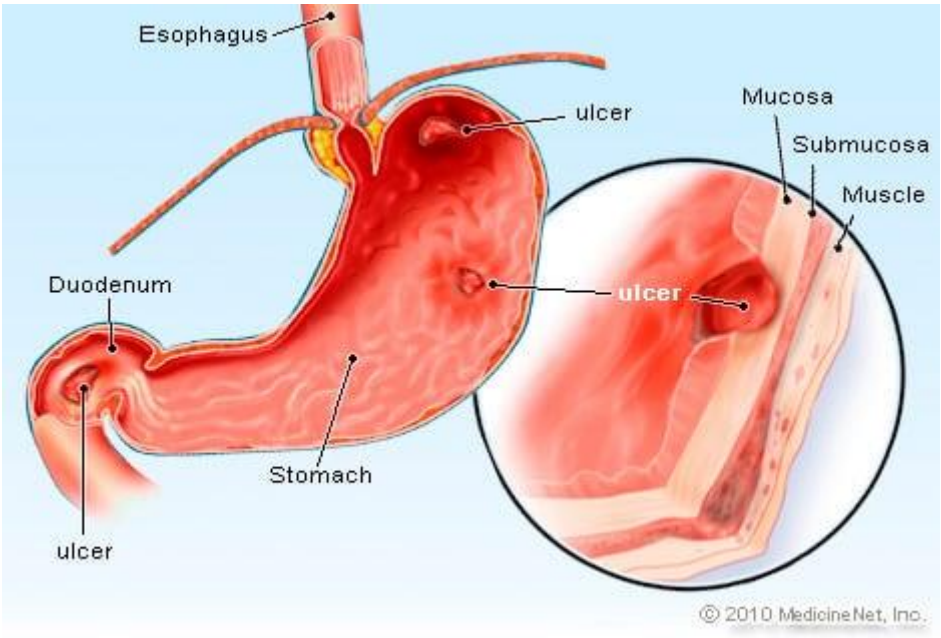

Figure 1-Diagram of Peptic Ulcer[3]

MATERIALS AND METHODS

The designing of methodology involves a series of steps taken in a systematic way in order to achieve the set goal(s) under the prescribed guidelines and recommendations. It includes in it all the steps from field trip to the observation including selection and collection of the medicinal plant, selection of dose value, standardization of protocol, usage of instruments, preparation of reagents, selection of specific solvents for extraction, formation of protocols and final execution of the standardized protocol. All this requires good build of mind and a good and soft technical hand to handle the materials and procedure in a true scientific manner.

Drugs and Chemicals

Drugs and Chemicals used in this study were of analytical grade and of highest purity procured from standard commercial sources in India.

Table 1: Drugs and Chemicals

S.No	*Materials*	*Company Name*
1.	Cimetidine	Cipla
2.	Omeoprazole	Cipla
3.	Ranitidine	Cipla
4.	Alcohol	Merck

Experimental animals

Wistar rats (150-200 g) and were procured from Animals were housed in appropriate cages in uniform hygienic conditions and fed with standard pellet diet (Amrul Laboratory Animal Diet) and water ad libitum. All the animals were maintained under standard conditions, that is room temperature 26 ± 1°C, relative humidity 45 - 55% and12:12 h light – dark cycle. The animals were housed in large spacious hygienic cages during the course of the experimental period. Animal studies had approval of IAEC.

Plant Material Collection

The leaf of Eclipta Alba was collected from the Botanical garden and was identified and authenticated from Department. The plant material was cleaned, reduced to small fragments, air dried under shade at room temperature and coarsely powdered in a mixer. The powdered material was stored or taken up for extraction process.

Preparation of plant extracts

Preparation of Aqueous Extract:

Fresh leaves of *Eclipta Alba* were collected and washed under tap water. The leaves extract used was prepared by taking 20gms of finely cut leaves into 250ml beaker containing 200ml of water. The contents were mixed well and then the mixture was boiled up to 80-100^{0}C for 4-5hrs. Further the extract was filtered with whatmann filter paper. The filtrate was boiled until the concentrated residue is formed. The concentrated product was sealed in sample covers and stored under room temperature and used for further experiment to check the activities.

Preparation of Alcoholic Extract

Fresh leaves of *Eclipta Alba* were collected and washed under tap water. The leaves extract used was prepared by taking 20gms of finely cut leaves into 250ml beaker containing 200ml of alcohol. The contents were mixed well and then the mixture was boiled up to 50-60^{0}C for 4-5hrs. Further the

extract was filtered with whatmann filter paper. The filtrate was boiled until the concentrated residue is formed. The concentrated product was sealed in sample covers and stored under room temperature and used for further experiment to check the activities.

Selection of dose for animal study

The dose considered for the experiment on rats was obtained from conversion of human dose of *Eclipta Alba* (3-5 g/kg). The conversion factor of human dose (per 200 g body weight) is 0.018 for rats. Hence the calculated dose for the rats (considering human dose3 and 5 g/kg) is 200 mg/kg. Acute toxicity was done at dose of 2000mg/kg body weight.

Pharmacological evaluation

Preparation of extracts

The aqueous and alcoholic extracts of *Eclipta Alba* suspended in water in presence of 3%v/v Tween-80 solution.All the drugs were administered orally for experimental purpose. Each time preparations of the extracts were prepared when required. The drugs were administered at a constant volume of 10ml/kg for each animal.

ACUTE ORAL TOXICITY

The acute oral toxicity of aqueous and alcoholic extracts of *Eclipta Alba* was determined by using rats which were maintained under standard conditions. The animals were fasted 12 hour prior to the experiment, up and down procedure OECD guideline no. 425 were adopted for toxicity studies. Animals were administered with single dose of individual extract up to 2000mg/kg and observed for its mortality during 7days and 21days study period (long term) toxicity and observed up to 7days for their mortality, behavioral and neurological profiles.

RESULTS

Phytochemical screening test

The freshly prepared extract of the leaves of *Eclipta Alba* was subjected to phytochemical screening tests for the detection of various active constituents. The extract showed the presence of alkaloids, tannins, steroids, phenolic and flavonoids, carbohydrates, and glycosides in crude extract of *Eclipta Alba* leaves as depicted.

Table 2: Result of chemical group tests of the Aqueous and Alcoholic Extract of *Eclipta Alba* leaves.

Test	Aqueous Extract	Alcoholic Extract
Carbohydrates	+	+
Tannins	++	++
Flavonoid	+	++
Saponins	++	++
Phenols	+	+
Steroids	++	++
Alkaloids	++	++
Glycosides	+	++

Aqueous and Alcoholic extract; (+): Present; (-): Absent; (+++); Reaction intensity is high; (++): Reaction intensity is medium; (+): Reaction intensity is normal;

ACUTE TOXICITY STUDY

Administration of the *Eclipta Alba* extracts *in* rats at doses of 250 mg/kg by oral gavage did not reveal any adverse effects or signsof toxicity.Observations twice daily for fourteen days also did not reveal any drug related observable changes or mortality. Accordingly, the acute oral LD50 of the extractives was concluded to exceed 2000 mg/kg body weight, the highest dose tested in the study.

Effect on alcohol induced gastric ulcers

Oral administration of 80% alcohol produced haemorrhagic gastric lesions in glandular portion of stomach. Pretreatment with AQCR and ALCR at the dose of 250 mg/kg and Omeprazole (10 mg/ kg) significantly ($p<0.001$) protected the gastric mucosa as shown by reduced values of lesion index (17.5 ± 0.19 and 26.01± 0.61 respectively) against alcohol challenge as compared to solvent control (29.14 ± 0.63).

Table 3: Effect of *Eclipta Alba* at various doses on alcohol induced gastric ulcer in rats

Treatment (n=6)	Dose mg/kg (p.o.)	Lesion index	% Inhibition of ulcer	Mucus content (μgAlcian blue/g wet tissue)
1% CMC	-	29.14 ± 0.63	-	0.55 ± 1.62
Ulcer control	-	37.29±1.21	-	0.61±2.01
Omeprazole	10	26.01± 0.61	21.08	0.68 ± 0.18
AQEA	250	32.20 ± 0.26	7.19	0.26 ± 0.52
ALEA	250	17.5 ± 0.19	44.21	0.851± 0.10

Values are mean ± S.E.M. n=number of animals in each group. Significant differences with respect to solvent control group were evaluated by Student's *t* – test. ($p<0.05$, $p<0.01$ and $p<0.001$).

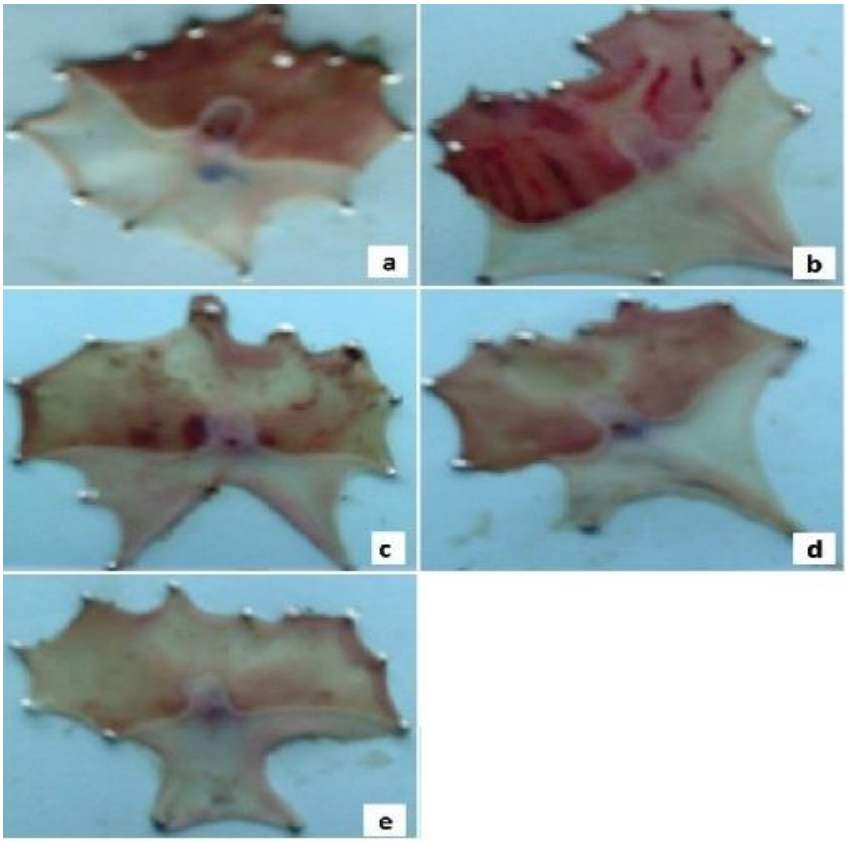

Fig1: Effect of *Eclipta Alba* on alcohol induced ulcers in the rats in the study (a) Normal Control (b) Ulcer Control (c) *AQEA* (250 mg/kg) treated (d) *ALEA* (250 mg/kg) treated (e) Omeprazole (10 mg/kg treated).

Effect on Paracetamol induced gastric ulcers

In *Eclipta Alba* treated groups (250 mg/kg), the ulcer index values (0.45 ± 0.06 respectively) were significantly reduced ($p<0.001$) when compared to solvent control (0.73 ± 0.05), while the ulcer index for ranitidine treated group was 0.26 ± 0.01 ($p<0.001$). The %inhibition of ulcer showed by AQTV and ALTV (250mg/kg) and ranitidine was 52.1%, 35.6% and 55.8 % respectively.

Table 4: Effect of *Eclipta Alba* at various dose levels on paracetamol induced gastric ulcer in rats.

Treatment (n=6)	Dose mg/kg (p.o.)	Ulcer index	% Inhibition of ulcer
1% CMC	-	0.70 ± 0.17	-
Ulcer control	-	0.82±0.21	--
Ranitidine	50	0.25 ± 0.09	54.6
AQEA	250	0.47 ± 0.02	36.2
ALEA	250	0.32 ± 0.05	52.2

Values are mean ± S.E.M. n=number of animals in each group; Significant differences with respect to solvent control group were evaluated by Student's *t* - test. ($p<0.001$).

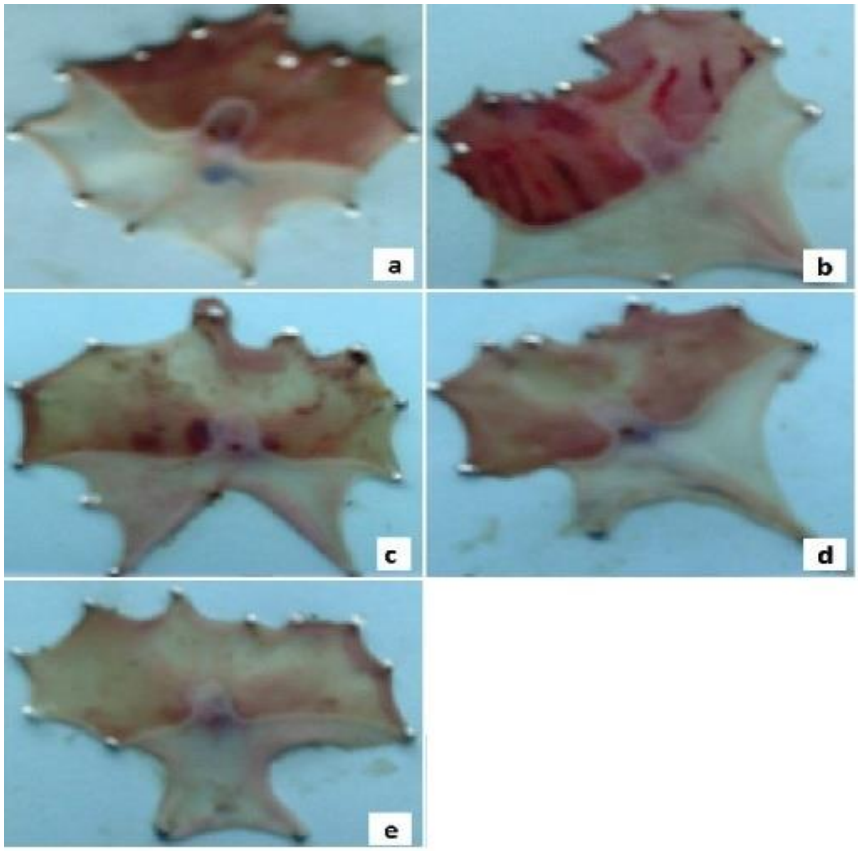

Fig2: Effect of *Eclipta Alba* on paracetamol induced ulcers in the rats in the study (a) Normal Control (b) Ulcer Control (c) *AQEA* (250 mg/kg) treated (d) *ALEA* (250 mg/kg) treated (e) Ranitidine (50 mg/kg treated)

Stress-induced ulcers

In water immersion stress induced ulcers, the mean score value of ulcer inhibition was found to be significant (P<0.001) for 250 mg/kg of the extract. The percentage ulcer inhibition was 74.91 and 93.10 for 250 mg/kg for both aqueous and alcoholic extracts, and that of the standard was found to be 89.51.

Table 5: Effect of *Eclipta Alba* at various dose levels on Stress induced gastric ulcer in rats.

Group	Dose mg/kg (p.o.)	Ulcer index	Percentage inhibition
Normal Control	-	00.00±0.00	-----
Ulcer control	-	23.19±1.53	------
Standard	50	2.61±1.26	87.29
AQTV	250	6.82±1.29	76.14
ALTV	250	4.14±3.51	82.65

Values are mean ± S.E.M. n=number of animals in each group; Significant differences with respect to solvent control group were evaluated by Student's *t* - test. (p<0.001).

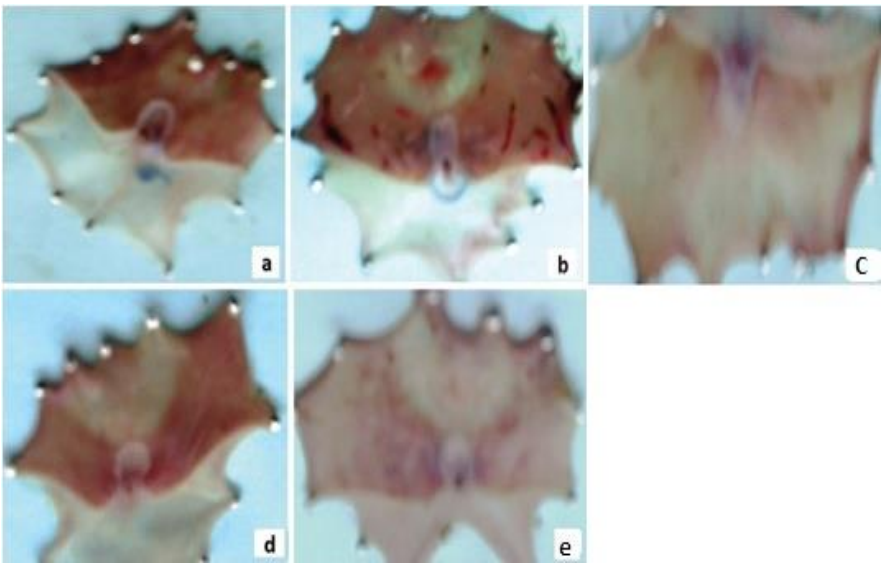

Fig3: Effect of *Eclipta Alba* on stress induced ulcers in the rats in the study (a) Normal Control (b) Ulcer Control (c) *AQEA* (250 mg/kg) treated (d) *ALEA* (250 mg/kg) treated (e) Omeprazole (10mg/kg treated)

DISCUSSION

The anti-ulcer activity of *Eclipta Alba* was evaluated by employing alcohol/paracetamol/acetic acid/stress induced gastric ulcers in rats. Alcohol and paracetamol induced ulcer models were used because they represent some of the most common causes of gastric ulcer in humans. Many factors and mechanisms are implicated in the ulcerogenesis and gastric mucosal damage induced by different models employed in the present study involving the increase of gastric acid output, vascular injury, depletion of gastric wall mucin, mucosal damage induced by non-steroidal anti-inflammatory drugs and free radical production.

Alcohol induced gastric injury is associated with significant production of oxygen free radicals leading to increased lipid peroxidation which causes damage to cell and cell membranes. *Eclipta Alba* has significantly protected the gastric mucosa against alcohol challenge as shown by reduced values of lesion index as compared to solvent control group suggesting its potent cytoprotective effect. This is further substantiated by increase in gastric mucus content produced by *Eclipta Alba* extract.

NSAID's like paracetamol, aspirin, indomethacin cause gastric mucosal damage by decreasing prostaglandin levels through inhibition of PG synthesis. *Eclipta Alba* extract was significantly effective in protecting gastric mucosa against paracetamol induced ulcers at all the dose level studied. Hence *Eclipta Alba* extract affords effective protection to gastric mucosa against various insults by increasing gastric mucus content and decreasing the acid volume, free and total acidity in rats.

Stress plays an important role in ulcerogenesis. The Pathophysiology of stress-induced gastric ulcers is complex. Stress-induced ulcers are probably mediated by histamine release with enhancement in acid secretion and a reduction in mucus production. The aqueous and alcoholic extracts of *Eclipta Alba* were effective in reducing the ulcers induced by stress.

The effects in all the 3 models studied were dose dependent. In conclusion, to the best of our knowledge for the first time, we have demonstrated that Hence *Eclipta Alba* extract has gastro protective activity against experimentally induced ulcers in rats. The mechanism of gastro protective action can be attributed to its antisecretory and cytoprotective property. However further experiments are required to establish and elaborate the molecular mechanism(s) of its Anti-ulcer activity.

CONCLUSION

The anti-ulcer activity of the plant *Eclipta Alba* was evaluated by employing paracetamol, alcohol and stress induced ulcer models. These models represent some of the most common causes of gastric ulcer in humans. Many factors and mechanisms are implicated in the ulcerogenesis and gastric mucosal damage induced by different models employed in the present study involving, depletion of gastric wall, mucin mucosal damage induced by nonsteroidal anti-inflammatory drugs and free radical production.

NSAID's like aspirin and paracetamol causes gastric mucosal damage by decreasing prostaglandin levels through inhibition of PG synthesis. Alcohol and Aqueous extract of the plant of *Eclipta Alba* was significantly effective in protecting gastric mucosa against paracetamol induced ulcers at all the dose level studied.

Alcohol induced gastric injury is associated with significant production of oxygen free radicals leading to increased lipid peroxidation, which causes damage to cell and cell membrane. The extracts of the *Eclipta Alba* has significantly protected the gastric mucosa against alcohol challenge as shown by reduced values of lesion index as compared to control group suggesting its potent cytoprotective effect. It has been proposed that in pyloric ligation, the digestive effect of accumulated gastric juice and interference of gastric blood circulation are responsible for induction of ulceration.

The antiulcer activity of *Eclipta Alba* extracts in stress induced model is evident from its significant reduction in gastric volume, ulcer index and increase in pH of gastric juice. Because of animals treated with *Eclipta Alba* extracts significantly inhibited the formation of ulcer in the stomach

and also decreased both acid concentration, gastric volume and increased the pH values.

It is suggested that *Eclipta Alba* extracts can suppress gastric damage induced by aggressive factors. It is generally accepted that gastric ulcers result from an imbalance between aggressive factors and the maintenance of the mucosal integrity through endogenous defence mechanisms. The excess gastric acid formation by prostaglandin (PG) includes both increase in mucosal resistance as well as a decrease in aggressive factors, mainly acid and pepsin. Inhibitions of PG synthesis by aspirin coincide with the earlier stages of damage to the cell membrane of mucosal, parietal and endothelial cells.

The preliminary phytochemical studies revealed the presence of flavonoids in aqueous and alcoholic extracts of *Eclipta Alba* various flavonoids have been reported for its anti-ulcerogenic activity with good level of gastric protection. So the possible mechanism of antiulcer action of *Eclipta Alba* may be due to its flavonoid content. In this study we observed that *Eclipta Alba* provides significant anti-ulcer activity against gastric ulcers in rats.

On the basis of the present results and available reports, it can be concluded that the anti-ulcer activity elucidated by *Eclipta Alba* could be mainly due to the modulation of defensive factors through an improvement of gastric cytoprotection and partly due to acid inhibition.

Recommendations

The Research work can be extended:

- ✓ Further, more herbal extracts can be screened for its Anti- ulcer Activity and used for treatment.
- ✓ Anti- ulcer activity should be evaluated of Polyherabal formulation for its synergitic action.
- ✓ Clinical Trials of Polyherbal formulations should be carried out for Anti- ulcer activity.

FUTURE SCOPE OF RESEARCH WORK

- ✓ Present study mainly focused on using natural resources in greater amount both from toxicity as well as cost oriented issues.
- ✓ Natural components are easily obtainable. Hence, in future it can effectively replace synthetic derivatives.
- ✓ Benefits are like free from toxicity, needed in little quantity plus effortlessly obtainable at fewer prices in contrast to synthetic component to achieve higher yield, optimization as well as novel processes serve such purpose by providing optimal criteria to conduct experiments. Such issues should be focus in near future.
- ✓ The plant were found having activity against GI Ulcers as evident from this study.
- ✓ Pharmacologic activities which may be a hint to investigate use of herbal as therapeutic agents.
- ✓ Hence, this may be useful to discover safer substitute for Ulcer management for numerous ailments.
- ✓ However, Future work can be done for isolating its main constituents which are responsible for this activity and for elucidating its mechanism of action of Anti- ulcer activity of these plant extracts.

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