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PHARMACOLOGICAL EVALUATION OF AGERATUM CONYZOIDES. LINN LEAVES EXTRACTS FOR ITS ANTI-ULCER ACTIVITIES

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ABSTRACT

For the treatment of gastric ulcer disease and peptic ulcer disease may chemical drugs are available in market such as Proton pump inhibitors, H_2 Antihistaminic Drugs Anticholinergics The most serious side effect of proton pump inhibitors are Bacterial infections, Bone fractures, Damage to arteries, Dementia, Heart attack or heart failure, Kidney disease or injuries, Premature death, Stroke. The serious side effects H_2 blocker are heart palpitations, galactorrhoea, gynecomastia, difficulty in breathing. From last 20 years people of world are move towards the herbal medicine because it will produce is very less toxic effect when we compare to chemical drugs. Loss on drying 2.68% w/w, Total Ash 17.5% w/w, Acid Soluble Ash 6.33% w/w, Water soluble Ash 11.8% w/w, Extractive values of Methanol 23.1% w/w, Water 20.76% w/w, Chloroform 2.41% w/w. The Phytochemical Tests shown Alkaloids, Carbohydrate, Glycosides, Phytosterols/Terpens Oils Protein, Tannins and Saponins. The TLC studies displayed the presence of compound such as, Flavonoid, Terpenoids and alkaloid with the significant Rf values. The pre-clinical pharmacological anti-ulcer impacts had seen by applying numerous extracts of *Ageratum conyzoides. L* such as chloroform, methanol and aqueous on different gastric-ulcer models, are pylorus ligation, Stress induced, Aspirin induced, and Ethanol induce ulcers models. These test sample had administered thru oral route at a dose of 400mg/kg. Entirely extracts improved the ulcer healing of all gastric ulcers models ($P< 0.05$). But methanol extract had more significant when we equate with standard drug ranitidine ($P< 0.001$). In the pylorus ligation, stress induce ulcer, ethanol induces ulcer and aspirin induce ulcer showed remarkable anti-ulcer activities ($P< 0.05$). From this experiment and biochemical test result methanolic leaves extract of *Ageratum conyzoides. L* had shown more significant ulcer healing activity.

KEYWORDS: *Ageratum conyzoides. L*, Ulcer index, anti-ulcer models, ulcer protection and histopathology.

INTRODUCTION

Gastric ulcer is breakdown of the gastric mucosa as well as duodenum mucosa that occurs whenever the normal mucosal defensives factors becomes weakened and overcome through antagonistic luminal factors are gastric acid & pepsin. The characterization, ulcers spread over the muscularis mucosa are generally 2.5 mm in radius.

The pathogenesis of peptic ulcer is depending upon several factors when these factors imbalanced then it will lead to peptic ulcer disease. aggressive factors are-If the person is suffering from helicobacter pillory, taking medicine such as NSAIDs e.g. Asprin, taking corticosteroids for long period of time, taking alcohol regularly, taking Tabaco smoke. mucosal defensive factors are- If less surface mucus production, less bicarbonate production on the mucus membrane of stomach, less mucosal blood flow, less working apical epithelial cell transport system less epithelial reformative capacity, less production of prostaglandins.

Approximately 11.7% of world population is suffering from gastric ulcer, peptic ulcer and gastritis out of this, In the United States, every year 5 lakhs new cases of peptic ulcer and 40 lakhs ulcer reappearances; occurrence of peptic ulcers in an individual in his/her lifetime is approximately 10%. Ulcers occurrence 5x time more in the patient's duodenum. In the antrum region more than 60% benign ulcer is more common whereas in the antrum region of lesser curvature ulcer are less than 24%.[1]

Ulcers is more common in male when relate with female. Even though ulcers can happen in any stage of life, duodenal ulcers more in patients 30 -55 years, whereas gastric ulcers is more in patients having age in between 55 to 70 years. in smokers and the individual are taking medicine such as NSAIDs are prone to ulcer.[2]

According to research most recent by WHO Exactly who data information had been released in May 2014 Peptic Ulcer Disease mortality rate in India achieved 85,487 or 0.96 percent of mortalities rate. In this the United State Of America got rank 161 and Death rate was 0.6 percent in 100,000 peoples. Peptic ulcer is the huge problems in world and everyday lots of peoples are dying due to peptic ulcer.[3,4] There are several nations come under red zone in this India got 26 rank.

In India Gastric ulcer disorder is common problem. The India frequency of gastric ulcer disease is nearly 5 in 869 which is 12, 25,614 public disease from Gastric ulcer diseaes from the entire 120 crore population. The Rate of Gastric ulcer is diminishing in developed nations but growing in emerging nations.

For the treatment of gastric ulcer disease and peptic ulcer disease may chemical drugs are available in market such as Proton pump inhibitors like Omeprazole, Rabeprazole, Pantoprazole, Lansoprazole, Esomeprazole H_2 Antihistaminic drugs are Ranitidine, Famotidine, Nizatidine, Cimetidine, Roxatidine. Anticholinergics Pirenzepine, Telenzepine, Propantheline, and Oxyphenonium Misoprostol, Emprostil. The most serious side effect of of PPIs are Bacterial infections, Bone fractures, Damage to arteries, Dementia, Heart attack or heart failure, Kidney disease or injuries, Premature death, Stroke. The serious side effects H_2 blocker are heart palpitations, galactorrhoea, gynecomastia, difficulty in breathing.

From last 10-15 years people of world are move towards the herbal medicine because it will produce is very less toxic effect when we compare to chemical drugs. When any chemical drugs are taken by the patient for the treatment or management of any disease, it be cure the disease but along with this it will produce acute and chronic toxic effect and developed of numerus new disease. So, it is necessary to perform the researches for investigation or development of new Phyto-biochemical compound form plants. Minerals.

Ageratum conyzoides Linn

Ageratum conyzoides Linn Is belong to family Asteraceae the domain is Eukaryota kingdom Plantae, category is class Dicotyledonae, order is Asterales and taxonomic group is Ageratum. Ageratum conyzoides Linn.is regularly recognized as goat wildflower in English, Pumpillu in Tamil and Visadodi in Hindi. It is a polymorphic, sweet-smelling, yearly herb local to tropical rain forest. It is a naturalized as a weed all through India and distinctive verities of this spics are found in various piece of india. Ageratum conyzoides Linn. likewise found in lower subansiri region of Arunachal Pradesh. These are some countries where Ageratum conyzoides. L is present in abundant quantity India, Brazil, Cuba, Fiji, Gambia, Germany, Ghana, Indonesia, Italy, Japan.

The entire herb is calming and antiallergic.[4] The extract of the young plant, or a concentrate of the dry herb, is utilized as a part of the therapy for unfavorably susceptible rhinitis and sinusitis.[4] The extract to their new herb is likewise helpful in curing baby blues uterine

discharge.[4] The extract of the root is antilithic.[5,6] A glue of their root, blended with all the bark of Schinus wallichii, is linked to set disjoined bones.[7] The leaves are styptic.[5] They are dried up and connected as a powderize to cuts, wounds and the bursts brought about by uncleanliness,[7] The powdered assimilates the dampness regarding the disease and structures a layer that is expelled after one to two days.[7] A successful treatment for many cuts and bruises, however it doesn't impact a total treatment for disease.[7] The leaves are additionally utilized remotely as a part of the treatment of ague.[5,8] The juice of the plant is utilized to treat cuts, wounds and wounds.[7] A glue of the leaves is utilized as a poultice to expel thistles from the skin.[7]

It is practice traditionally for gastric ulcers but there is no pharmacological-clinical data is available. Hence, evaluation of anti-ulcer activity of *Ageratum conyzoides. L* and make obtainable preclinical data of it.

MATERIAL AND METHODS

Pharmacognostic Study

The leaves of *Ageratum conyzoides. L* collection number **[30604(ARUN)]** for the present studies were collected from forest of Yazali, Lower subansiri, Arunachal Pradesh, India. The plant was identified, and authenticated by Dr. Umeshkumar L. Tiwari Scientist of Botanical Survey of India, Arunachal Pradesh Reginal center, Itanager-791111 (INDIA).

After the authentication plant was dried at room temperature until they become free from moisture.

Pharmacognostics study of *Ageratum conyzoides. L* leaves

Table no. 1: Pharmacognostic Study of *Ageratum conyzoides. L (leaves)*.

Sr.no	Parameters studied	Ageratum conyzoides(leaves)
1	Loss on drying	2.68% w/w
2	Ash value	
	Total Ash	17.5% w/w
	Acid soluble Ash	6.33% w/w
	Water soluble Ash	11.8% w/w
3	Extractive values	
	Methanol	23.01% w/w
	Water	20.76% w/w
	Chloroform	2.30% w/w

EXTRACTION

Chloroform, Methanol And Aqueous extracted of *Ageratum conyzoides. L.*

PERCENTAGE YIELD OF EXTRACTS[11]

Table no. 2:-Extracts Yielded and Percentage yielded of *Ageratum conyzoides. L* Leaves.

Sl. No.	Extracts	Colour of extract	Yield in gm	Percentage Yield
1.	Chloroform	Dark greenish paste	15	3 %
2.	Methanol	Dark greenish clumps	17.2	3.44%
3.	Aqueous	Brown powder	33.6	6.72%

PRELIMINARY PLANTS BIOLOGICALLY ACTIVE COMPOUNDS TESTING OF *AGERATUM CONYZOIDES. L* EXTRACTS

Table no. 3: Phytochemical compounds Testing of *Ageratum conyzoides. L* leaves Extracts.

Sl. No.	Test	Chloroform extract	Methanolic extract	Aqueous extract
I	Alkaloids	+	+	+
II	Carbohydrates	-	+	+
III	Flavonoids	-	+	+
IV	Tannins	+	+	+
V	Proteins and amino acid	-	+	+
VI	Glycoside	+	+	+
VI	Saponins	-	+	+
(- Absent) (+ Presence)				

THIN LAYER CHROMATOGRAPHY OF *AGERATUM CONYZOIDES. L* LEAVES EXTRACT

Table no.3:- Rf values of methanolic extract of *Ageratum conyzoides. L* Leaves.

Compound	Mobile phase	Ratio	Rf value
Flavonoid	Chloroform: Methanol	18:2	0.65
Terpinoids	Benzene: Ethyl acetate	1:1	0.35, 0.72
Alkaloid	Methanol: sodium hydroxide	17:3	0.86
Saponins	Chloroform: methanol: water	7:3:1	0.06

EXPERIMENTAL ANIMALS

Albino Wistar rats weight 160-220g had taken from **Biogen laboratory animal facility CPCSEA Registration No. (971/bc/06)**, Bangalore. These rats were breeding and preserved in animal household of "**East Point College of Pharmacy"** for experimental function. Rats had been well-maintained under calculated condition of heat at $27^{o} \pm 2^{o}$ C that is and 24 hours light-dark rounds for starters week. these rats had kept in polypropylene cages and paddy that is containing as sheet. That they had an access that is free standard pellets and water advertising libitum,

ACUTE TOXICITY STUDIES (LD_{50})

In equally stage I and Stage II procedures, no one of the mices didn't express any toxicity as will death when given the dosage administration of CECA, MECA and AECA 250, 500, 1000,2000 and 4000mg/kg according to acute toxicity guideline 423 given by Organization of Economic Cooperation and Development. Thus, $1/10^{th}$ of supreme dose (400 mg/kg) tested had selected this present study

PYLORUS LIGATION ULCER MODEL

Albino Wistar rats of either gender weighing between (120- 180gms) are divided in to groups of an animal. In this process albino rats are fasted in specific cages every day and night for 24 hours. *Ageratum conyzoides. L* extracts , standard drugs or control vehicle is administered 30 minutes just before ligation that is pyloric. The abdomen is opened and the pylorus was ligated under light ether anaesthesia. The stomach will be sutured. The animals are assassinating with excess of anaesthetic ether, and the stomach is dissected out gastric juice is collected had drained into tubes and had centrifuged at 1000 rpm for 10 minutes and the volume is noted at the end of 4 hours afterward ligation. The pH of gastric juice is recorded by pH meter. Then articles are afflicted by analysis at no cost and acidity that is total. The stomachs are then washed with operating water to see for ulcers into the portion that is glandular of belly. The number of ulcers per stomach are noted and extent for the ulcers scored microscopically by using 10x lens.

Histopathological studies had been carried out by repairing belly cells in 10% formalin for 24 h. The formalin fixed specimens are embedded in section and paraffin(3-5µm) and stained with haematoxylin and eosin dye. The sections that are histochemical examined by light microscopy[9,10]

ULCER INDEX

0 means – without gastric ulcer

1 means- light surface gastric ulcer

2 means- serious gastric ulcer

3 means-puncture gastric ulcer

4 means- wide puncture gastric ulcer

i.e,

Nil abscess-**0**

Abscess is less then 1mm diameter-**1**

Abscess is in between 1-2 mm diameter -**2**

Abscess is in between 2-4 mm diameter-**3**

Abscess is greater then 4 mm diameter-**4**

Calculation of ulcer Index

$$UI = UN + US + UP \times 10\text{-}1$$

Where as

UI = Ulcer Index

UN = Average of number of ulcer per animal

US = Average of severity score

UP = Percentage of animal with ulcer

PERCENTAGE OF ULCERS PROTECTION

Percentage Inhibition of Ulcer =

(Ulcer index of Control-Ulcer Index of Test) × 100 ÷ Ulcer index of Control

ASPIRIN INDUCED ULCER MODEL

Albino rats of either gender with a weight in between 120-180 gms are split into five groups. in every category of six rats in a group. The rats are fasted every day and night for 24 hours. The test *Ageratum conyzoides. L* extracts at a dose of 400mg/kg in design associated with test is administered orally 30 minutes moment just before aspirin at dosage of 200 mg/kg. 4 hours later on the rats are assassinating by utilizing ether that is an aesthetic their stomachs dissected as well as addition they had been exposed along greater curvature for the dedication of gastric lesions. Ulcer index determined by noting the true wide range of ulcers per animal and extent scored by watching the ulcers microscopically with the aid of 10x lens and scoring is performed below.[11]

SWIMMING STRESS INDUCED MODEL

Stress instigated ulcers were acquired by constrain swimming the glass chamber (tallness 45cm breadth 35cm) containing water up to 35cm kept up at 35^0C for 3 hrs. Rats were not eat for 24 hrs preceding the test. After the medicine treatment (standard/test) creatures were middle of the road to swim for 3hrs then rats were investigated stomachs were expelled. Every stomach had opened over the greater curvature ulcer index record.

ETHANOL INDUCED ULCERS

Albino rats of either gender with a weight in between (120-180 grams) are isolated into group. The rats kept fasted for 24 hours through free get to water. rats are given test *Ageratum conyzoides. L* extracts or standard medication. after 1-hour 1ml/ 200grams of 99.80% liquor is offered orally to every individual. The rats anesthetized had been assassinating 60 minutes final with ether and stomach had been cut across the greater curvature and movement and ulceration had been scored. The total amount of ulcers together with amount of every ulcer had been fixed. Ulcer list had been ascertained seriousness that is utilizing and normal quantity of ulcers per creature. Severity ratings as under.[12]

STATISTICAL ANALYSIS

ANOVA followed by non-parametric Dunnett's test was used by IBM SPSS STATISTCS VERSION 20. values are expressed as mean + S.E.M, n=6 and *p<0.05, **P<0.01, ***P<0.001 was considered significant and graph was plotted by Excel (Microsoft office 2016).

RESULT

All the *Ageratum conyzoides. L* extracts has shown a significant anti-ulcer activity

Table no. 4:- Impact of AEAC, MEAC and CEAC on Ulcer Index in Pylorus Ligation.

Ulcer Index

Group	**Treatment**	**Ulcer index**	
Control	Pylorus ligation for 5 hours	11.85±0.21***	***0***
Ranitidine	100mg/kg b.wt, suspended in vehicle+ pylorus ligation.	4.02±0.14**	***66.07***
AEAC	400mg/kg b. wt, suspended in vehicle+ pylorus ligation.	5.34±0.24***	***54.93***
CEAC	400mg/kg b. wt, suspended in vehicle+ pylorus ligation.	7.24±0.16***	***38.90***
MEAC	400mg/kg b. wt, suspended in vehicle+ pylorus ligation.	4.45±0.15***	***62.44***

values are expressed as mean + S.E.M, n=6 and *p<0.05, **P<0.01, ***P<0.001 was considered

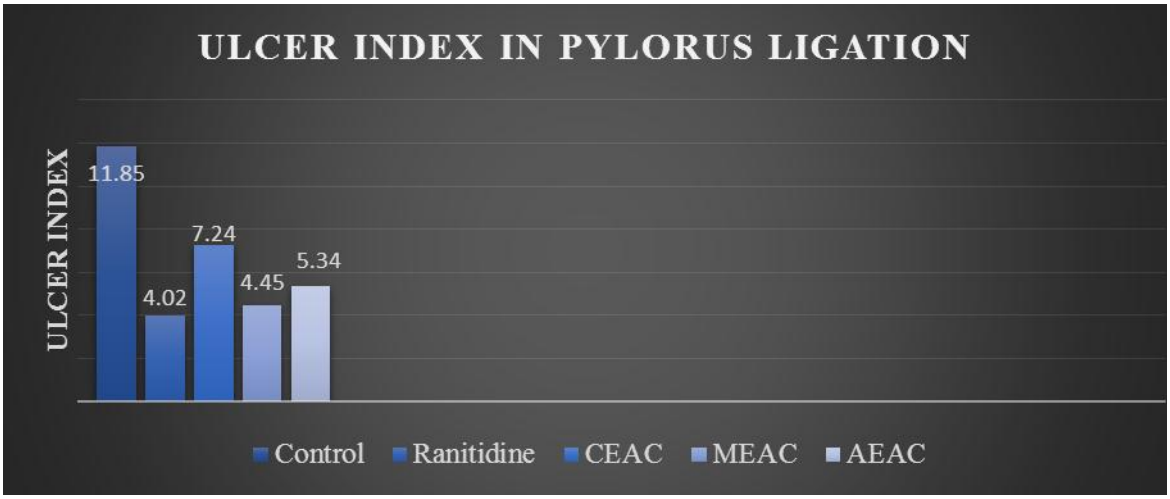

Fig. No.1: Impact of various extract of *Ageratum conyzoides. L* in Ulcer index at Pylorus Ligation caused Ulcer in Rat model.

Table No. 5: Impact of AEAC, MEC and CEAC in pH, Gastric Volume, Free Acidity and Total Acidity in Pylorus Ligation Ulcer Screening Model.

SI. No	Treatment	Dose	Ph	Gastric volume	Free acidity	Total acidity	Total Protein
1	**Control**	-	1.41±0.1607	7.6±01956	89.17±1.858	98.26±3.220	6.47±0.015
2	**Ranitidine**	100mg/kg	4.23±0.2275***	2.93±0.1606***	40.13±1.940***	28.36±1.665***	12.32±0.002**
3	**MEAC**	400mg/kg	4.5±0.2386***	3.78±0.1249***	52.70±2.141***	41.37±1.245***	10.47±0.042***
4	**AEAC**	400mg/kg	4.81±0.2171***	4.21±0.1183***	66.79±1.718***	47.12±1.196***	9.76±0.023**
5	**CEAC**	400mg/kg	2.11±0.1155***	4.91±0.1312***	55.45±1.782***	65.21±1.760***	7.51±0.065***

values expressed as mean + S.E.M, n=6 and *p<0.05, **P<0.01, ***P<0.001 was considered.

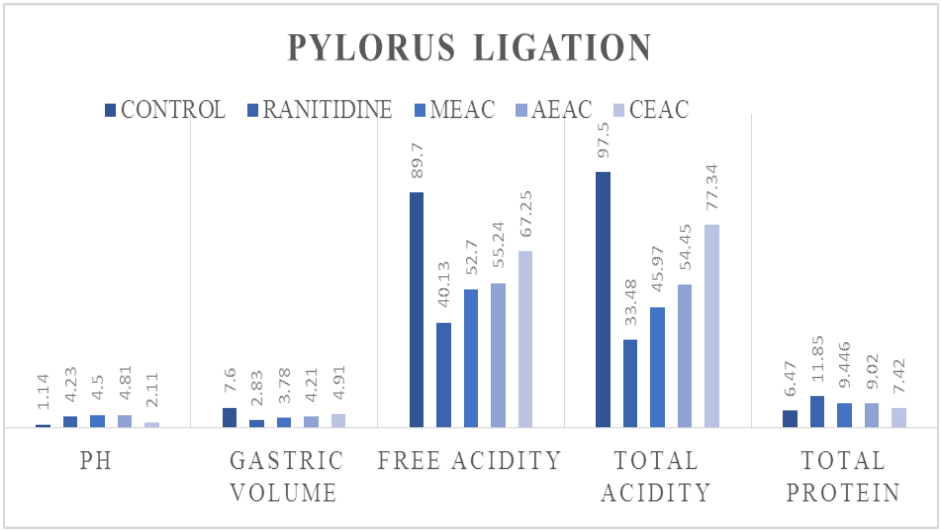

Fig No.2: Impact of various extract of *Ageratum conyzoides. L* in pH, Gastric Volume, Free Acidity, Total Acidity and total protein at Pylorus Ligation caused Ulcer in Rat models.

Pylorus ligation model All the *Ageratum conyzoides. L* extracts has shown a significant anti-ulcer activity there is reduction in ulcer index when equated to control. The percentage of ulcer protection is increase when compare to standard drug ranitidine. The more activity shown by the MEAC at a dose 400mg/kg body weight significant reduction of ulcer index, Gastric volume, Free acidity, Total acidity and rise in P^H and Total Protein. (Table 4, Figure 1 and Table 5, Figure 2).

Pictures demonstrating impact of various extract of Ageratum conyzoides *L* on ulcer recuperating in Pylorus Ligated Rat's gastric ulcers

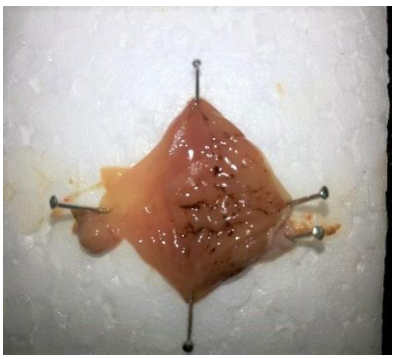

Figure 3

GROUP I CONTROL.

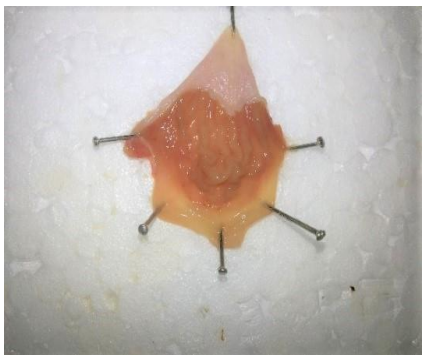

Figure 4

GROUP II RANITIDINE (100mg/kg).

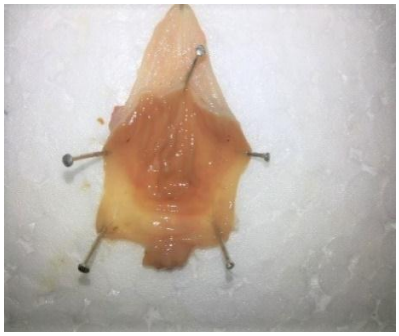

Figure 5

GROUP III AEAC (400mg/kg).

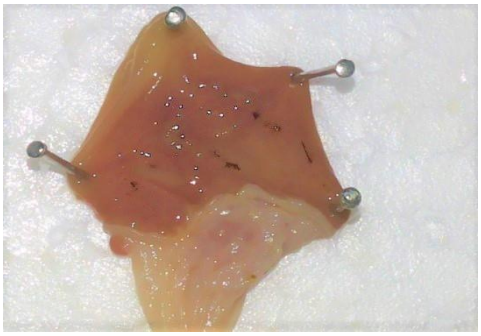

Figure 6

GROUP IV MEAC (400mg/ kg).

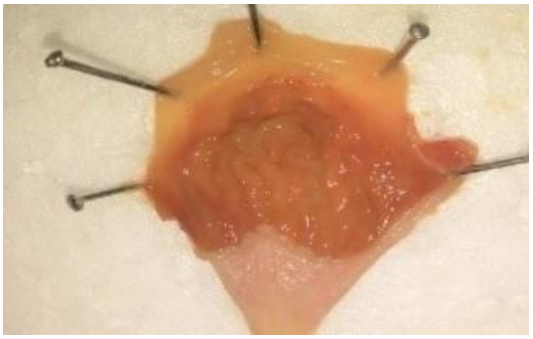

Figure 7

GROUP III MEAC (400mg/kg).

GROUP-I The ulcer produce in anterior serosal surface of stomach, mucosa get harm and lot of blood clotes are seen. More ulcer range found. (Figure.3).

GROUP-II The ulcer create in anterior serosal surface of the stomach, less mucosa get harm here and encompassing areas. The group contain the Ranitidine. Less ulcer are found. (Figure.4).

GROUP-III The ulcer happen in anterior serosal surface of the stomach. mucosa get harm around there and encompassing areas. The group contain the Aqueous extracts of Ageratum conyzoides. The stomach contain less ulcer as compaire to control (Figure.5).

GROUP-IV The ulcer occurs in anterior serosal surface of the stomach. The group contain the Chloroform extracts of Ageratum conyzoides. The stomach get patch the harming segment of ulcer. (Figure.6).

GROUP-V The ulcer occurs in anterior serosal surface of the stomach. the Methanolic extracts of Ageratum conyzoides. The stomach gets repair the harming segment of ulcer. Easley envisioned more practicable extract. (Figure.7).

Histopathological Studies of various Extracts of *Ageratum conyzoides. L* on the Pylorus Ligated Ulcer Models

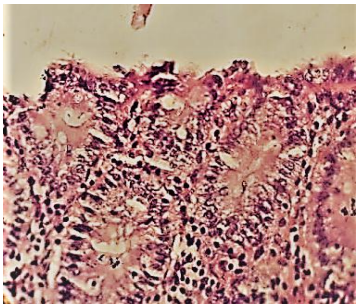

Figure 8
Group-I: Control (Non-treated group).

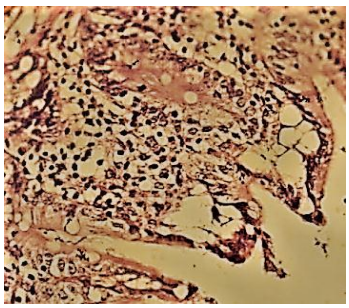

Figure 9
Group II: Ranitidine [100mg/kg].

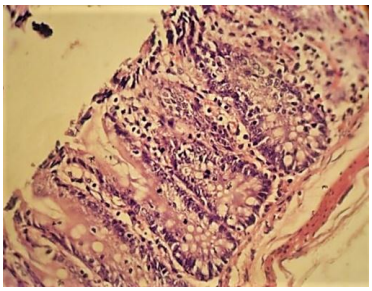

Figure 10
Group III: (AEAC) [400mg/kg].

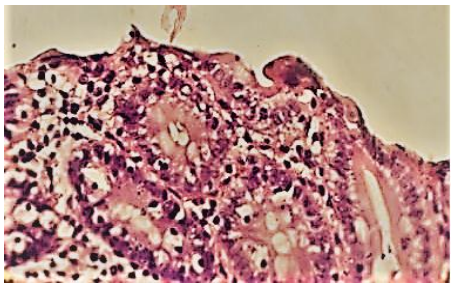

Figure11
Group V: (CEAC) [400mg/kg.

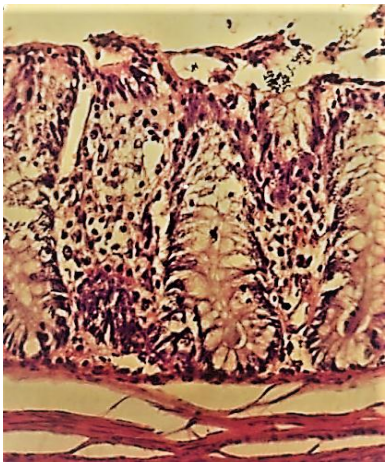

Figure 12: Group V: (MEAC) [400mg/kg].

Group-I: Control (Non-treated group)

Section studied shows mucosal ulceration consisting of predominantly necrosis, degenerated epithelial cells with moderate inflammatory infiltration comprising of aggregates of macrophages and neutrophils. The submucosa shows severe edema. (Figure.8).

Group II: Ranitidine [100mg/kg]

Section studied shows intact mucosa with regenerative epithelial cells and mild inflammatory infiltration. The submucosa and muscularis propria appears normal. (Figure.9).

Group III: (Aqueous Extract of AC) [400mg/kg]

Section studied shows focal mucosal ulceration Mediating the mucosal epithelial cells are seen direct fiery invasion with couple of regenerative epithelial cells (Figure.10).

Group-IV: (Chloroform extract of AC) [400mg/kg]

Section studied shows focal mucosal ulceration intervening the mucosal epithelial cell, are seen mild inflammatory infiltration with some regenerative epithelial cell. The submucosa shows mild edema with mononuclear inflammatory infiltration. (Figure.11).

Group – V: (Methanolic Extract of AC) [400mg/kg]

Section with regenerative epithelial cells and mild inflammatory infiltration. The submucosa and fiery cells with regenerative epithelial cells**.** The submucosa shows up close to typical. The muscularis propria seems unremarkable. (Figure.12).

Table no. 6: Impact of AEAC, MEAC and CEAC on Ulcer Index in Aspirin Induced Ulcer Models.

Group	Treatment	Ulcer index	%Ulcer Protection
Control (Aspirin)	200mg/kg p. o	12.24± 0.32***	*0*
Ranitidine	100 mg/kg p. o	4.32±0.18***	*64.7*
AEAC	400mg/kg p. o	5.23±0.05**	*57.27*
CEAC	400mg/kg p. o	7.58±0.03***	*38.07*
MEAC	400mg/kg p. o	4.92±0.05**	*59.8*

values are expressed as mean + S.E.M, n=6 and *p<0.05, **P<0.01, ***P<0.001 was considered.

All the extracts has shown a significant ulcer healing effect there is reduction in ulcer index when equated to control. However, more activity shown by the MEAC at a dose 400mg/kg body weight significant reduction of ulcer index and percentage ulcer protection which is comparable to standard drug ranitidine (100mg/kg). (Table 6, Fig. 13)

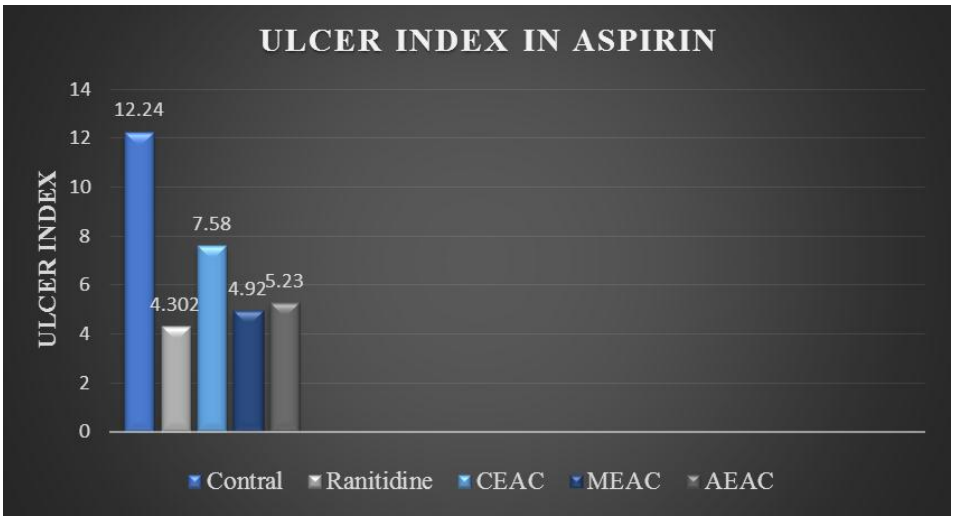

Figure No.13: Impact of various extract of Ageratum conyzoides. L in Ulcer index at Aspirin Induced Ulcer Models.

Table no.7: Impact of various extract of AEAC, MEAC and CEAC on Ulcer Index in Swimming Stress Induced Gastric ulcer models.

Group	Treatment	Ulcer index	%Ulcer Protection
Control	1 ml saline	10.25± 0.14**	*0*
Ranitidine	100mg/kg p. o	3.765±0.16***	*64.24*
AEAC	400mg/kg p. o	4.42±0.05**	*46.24*
CEAC	400mg/kg p. o	7.59±0.08***	*25.95*
MEAC	400mg/kg p. o	4.05±0.013**	*60.48*

values are expressed as mean + S.E.M, n=6 and *p<0.05, **P<0.01, ***P<0.001 was considered.

All the extracts has shown a significant ulcer healing effect there is reduction in ulcer index when equated to control. However, more activity shown by the MEAC at a dose 400mg/kg body weight significant reduction of ulcer index and percentage ulcer protection which is comparable to standard drug ranitidine (100mg/kg). (Table 7, Fig. 14)

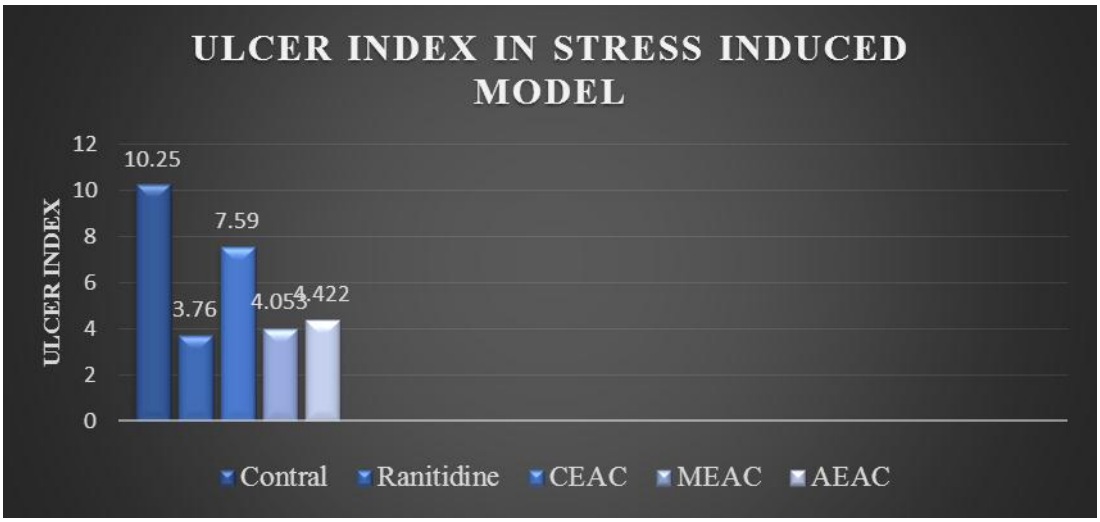

Figure No.14: Impact of various extract of *Ageratum conyzoides. L* in Ulcer index at Swimming Stress Induced Gastric ulcer models.

Table no. 8: Impact of various extract AEAC, MEAC and CEAC on ulcer index in ethanol induced ulcer model.

Group	Treatment	Ulcer index	% Ulcer Protection
Control	1 ml ethanol for 200gm body wt.	15.54±0.18	*0*
Ranitidine	100 mg/kg p.o +1ml ethanol for 200gm body wt	4.2±0.07***	*72.9*
AEAC	400 mg/kg p.o +1ml ethanol for 200gm body wt	5.51±0.14**	*64.54*
CEAC	400 mg/kg p.o +1ml ethanol for 200gm body wt	8.34±0.14**	*46.33*
MEAC	400 mg/kg p.o +1ml ethanol for 200gm body wt	4.94±0.17***	*68.21*

values are expressed as mean + S.E.M, n=6 and *p<0.05, **P<0.01, ***P<0.001 was considered.

In stress induce model methanol extract show more significant reduction of ulcer index (P<0.001**) and increase percentage ulcer protection which is comparable to standard drug ranitidine (100mg/kg). (Table 7, Fig. 15).

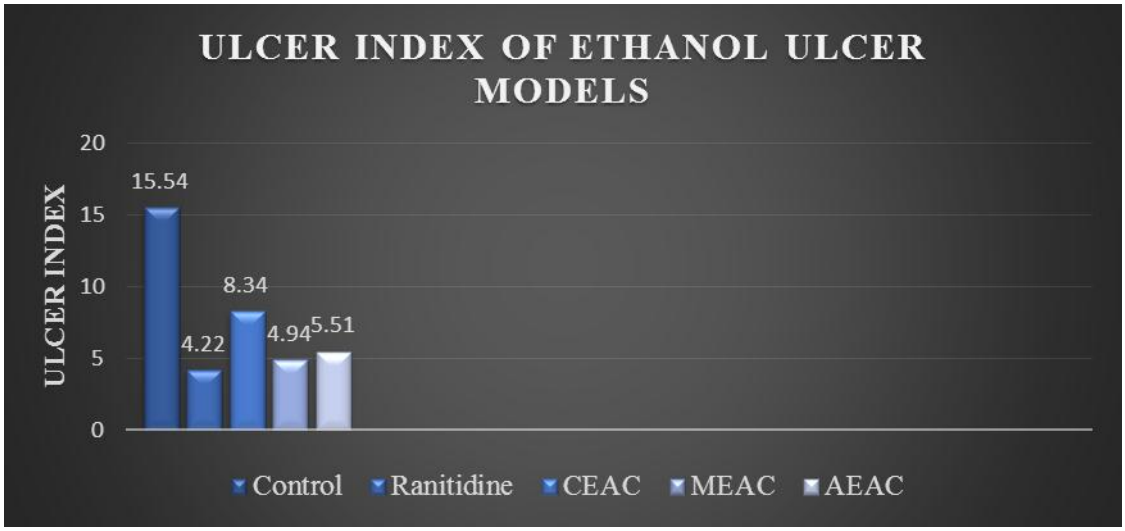

Figure No.15: Impact of various extract of *Ageratum conyzoides. L* in Ulcer index on in ethanol induced ulcer model.

DISCUSSION

The natural plants are imperative choice to for treatment peptic ulcer disease. The *Ageratum conyzoides. L leaves* extracts by Preliminary Qualitative Phytochemical Tests shown Alkaloids, Carbohydrate, flavonoids, Glycosides, Phytosterols/Terpens oils Protein, tannins and saponins and TLC shown Alkaloids, flavonoids and terponids.

The Phytochemical constituent of such as flavonoids, tannins, saponins, terpenoids may show anti-ulcer activity due to their cytoprotecting, antisecretory and antioxidant property. The Phyto-biochemical compounds which assist as drugs, may be providing newer path and evidences for modern drug design through synthesise. Thus, plant base drugs are better source for our society and show minimize toxic effect as well as improved outcome to treatment peptic ulcer, dyspepsia and may more diseases in future.

The Pylorus ligated model had utilized to estimate gastric anti-secretory effects. In pyrolus ligation method, the ulcer is caused due to accumulation of pepsin, gastric acid and hydrochloric acids in stomach due to which at the ligated pyloric end. An increase in acid pepsin accumulation due to pyloric obstruction and subsequent mucosal digestion is the known mechanism of the induction of ulcer. The anti-ulcer activities of laves of Ageratum conyzoides. Methanolic extracts reduce gastric in pH, total acidity, free acidity, gastric volume and ulcer index. Ulcer protection is more in methanolic extracts<aqueous extracts<chloroform extracts as compare to control.

Aspirin model is formed ulcer due to the COX-1 blockage which results the decrease of prostaglandin synthesis. So there will be an enhancement in the lipoxigenase pathway and leukotriene. This leukotriene's will cause ulcer in aspirin induced model. An increase in acid secretion and back diffusion of H+ is reasonable for the gastric mucosal lesion induced by aspirin. In the control group of aspirin treatment has shown severe ulcer scores by ulcer index. The different extracts of Ageratum conyzoides such as MEAC, AEAC and CEAC were shown a significant reduction of ulcer index compared with the control and the ranitidine as standard.

Restraint water immersion stress model is one of the models to produce ulcer by stress. Stress is having a major role in the ulcer etiology. It is probably mediated by histamine release by enhancement in acid secretion and a reduction in mucin production. The enhanced motility of stomach by swimming is also a reason for inducing ulcer. The evidently increased lipid peroxides and mucosal damages cause the increase of ulcer scores in the control group.In the present study, the MEAC were shown more active compared with other extracts in controlling ulcer score numbers.

Ethanol induced screening model the incidents were predominant in the glandular part of stomach tissues. It is due to the increased secretion of protein by the gastric wall, reduces glutathione level in gastric mucosa and increases the production of free radical by ethanol. The studies revealed that the ethanol is always having the ulcer modulatory action in the stomach. Treatment with different extracts of Ageratum conyzoides were having a significant reduction of ulcer score by comparing with the control. The activities were shown that the Methanol extracts of Ageratum conyzoides is more efficient to treat ulcer compared to other extracts. The 400 mg/kg of extract has given for treated groups. The activity found with respect of control and Ranitidine.

Pharmacologic activities which could be a hint to investigate use of herbal as therapeutic effect. Hence, this may be useful to discover safer substitute for Ulcer management for numerous diseases.

CONCLUSION

The chloroform, methanolic and aqueous extracts of *Ageratum conyzoides. L* for anti-ulcer activities was concluded with a positive response in ulcer induced models such as pylorus ligation, aspirin induced, swimming stress and ethanol induced models and with standard

drug i.e., ranitidine. The activity is shown in all the three extracts at a dose of 400 mg/kg body weight. The standard drug dose was took at 100 mg/kg of animal body weight. In acute toxicity studies the extracts were shown safety upto the dose of 4000mg/kg body weight.

From this research I am conclude that entirely extract of *Ageratum conyzoides. L* having significant anti-ulcer activity in gastric ulcer model of rats but out of that methanolic extracts had more potent.

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