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EVALUATION OF ANTIULCER ACTIVITY OF ACONITUM HETEROPHYLLUM ON EXPERIMENTAL ANIMAL

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ABSTRACT

In present era peptic ulcer is a worldwide problem and its prevalence is quite high in India. Some present data shows that in different part of India its occurrence is 4 to 10 % per thousand populations. The exact etiology of peptic ulcer is not known, the disease results in chronic suffering, loss of working hours and occasional fatality. Smoking habit, alcoholism, stress & spicy food make the severity of the disease which leads serious complication of ulcer. Aconitum heterophyllum is one of the most commonly use in different medical conditions has been documented. Traditionally, Aconitum heterophyllum roots or tubers are beneficial in the treatment of diseases related to lungs & airways, blood, skin, stomach, intestines, and liver. As no reports are available on the possible antiulcer effects of Aconitum heterophyllum. The present work was carried out to antiulcer activity of Aconitum heterophyllum by cold stress induced gastric ulcers in wister albino Test drug Aconitum heterophyllum (low dose) and Aconitum heterophyllum (high dose) have shown result in comparison to standard drug omeparazole and control drug. Thus study has provided documentary evidence for antiulcer property of Aconitum heterophyllum for its activity.

KEYWORDS: Aconitum heterophyllum, peptic ulcer, antiulcer property.

INTRODUCTION

Charaka made fifty groups of ten herbs each of which, according to him, would suffice an ordinary physician's need. Similarly, Sushrutha arranged 760 herbs in 7 distinct sets based on their common properties. A large portion of the Indian population even today, depends on the

Indian System of Medicine - 'Ayurveda'- "An ancient science of Life". The well known treaties in Ayurveda are Charaka Samhita and Sushrutha Samhita. In the nineteenth century, the term 'Materia Medica' was used for the subject now known as Pharmacognosy. Pharmacognosy is derived from the two Greek words viz. Pharmakon (a drug) and Gignosco (to acquire the knowledge of). Pharmacognosy is an objective study of crude drugs from natural sources treated scientifically and it encompasses the knowledge of the history, distribution, cultivation, collection, processing for market and preservation, the study of sensory, physical, chemical and structural characters and the uses of crude drugs. Pharmacognosy is an important link between 'Pharmacology' and 'Medicinal Chemistry'. As result of rapid development of phytochemistry and pharmacological testing methods in recent years, new plant drugs are finding their way into medicine as purified phytochemicals, rather than in the form of traditional galencial preparations. India is a veritable emporium of medicinal plants. Nearly three fourths of the drug mentioned.

The pathophysiology of the gastric ulcer has not been completely elucidated, but it is known that an imbalance between aggressive factors (acid and pepsin secretion) and cyto-protective factors of the gastric mucous membrane (mucus and bicarbonate secretion) result in gastric ulceration. It is also known that several endogenous factors are involved in the pathophysiology of the gastro-protection which includes prostaglandin E_2 (PGE_2), somatostatin, nitric oxide (NO) and sulthydryl compounds. The etiology of gastric ulcer involves environmental factors such as alcoholic beverages and non-steroidal anti inflammatory drugs (NSAIDs) use, Helicobacter pylori, genetic factors, among others Alcohol is known as a necrotizing substance and its excessive ingestion may result in gastritis, characterized by mucous membrane edema, sub epithelial haemorrhages, cell exfoliation and inflammatory cells infiltration .Thus, gastrointestinal tract diseases related to excessive alcohol use play an important role in the clinical gastroenterology.

PLANT PROFILE OF ATIVISHA

Synonym

Aruna, Ardra, Upavisa, Kasaya Krsna,Ghuna.

Part Used

Roots.

Habitat

Maharashtra & Himalayas.

Ativisha grows in the Himalayas at an attitude of 2000 to 5000 metres. It is a characteristic species of Sikkim, Nepal and chumbi area.

ATIVISHA

Ativisha grows in colder parts of India. It is abundant in the alpine regions growing up to a height of 2000 feet above sea level. The roots of the plant are the source of most of the alkaloids obtained from the plant such as aconitine, atisine, heterophyllin, heterophyllisin etc. The roots of the plant are paired and tuberous. They may be white or grey in color. Stem is simple or branched, growing up to a height of about 15 to 20 cm. Leaves are heteromorophous and glabrous. The flowers usually occur as inflorescence which may be white or violet in color. Seeds may be pyramidal, blackish or brownish in color.

2.3.3. General Information about Ativisha

Ativisha is the ayurvedic name of an herb known as atis in Hindi. It is extensively discussed in the ancient ayurvedic texts written by Charaka and Sushruta. It is one of the most befitting herbs for digestive problems in children. It has a carminative action and is superb for the maintenance of a healthy digestive system. Ativisha means one that is toxic but in spite of the toxic properties, Ativisha is considered as one of the best medicinal herbs in Ayurveda.

The Latin name of the plant is Aconitum heterophyllum and it belongs to Ranunculaceae family.

Ativisha Purification

Ativisha Purification is done using an ayurvedic technique called SWEDANA and base material used in this technique is GOMAYA RASA (cow dung juice). This process helps to make it consumable for humans and removes its impurities and detoxifies it.

Internal Uses

Respiratory system

The juice of roots along with milk is an expectorant Root powder is given orally in cervical lymphadenitis.

Digestive system

Seed and root are used in ascites. Seeds are laxative.

Urinary system

The seeds are diuretic; the root decoction reduces burning of urinary tract. It increases volume of urine.

Reproductive system

Root is used in sperrnatorrhoea. The decoction of roots is also used in burning of vagina.

Circulatory system

The juice of leaves along with juice of zingier reduce perspiration.

Toxic Effects

Over dosage (More than 5-6g) produces symptoms like dryness of mouth, tremors etc. Pre-treatment of A. palmatum root in cow's milk and urine reduced the cardio-toxicity (Singh L.B. et al., 1985).

PartUsed

The tuberous root is medicinally used both alone and in combination. Yogaratnakara mentioned that Haritaki may be used as the substitute for Ativisa.

Dosage

For adults: l-3 Gms per day.

For children: 1 gm per day, in divided doses.

MATERIAL AND METHOD

Collection & Authentication of Plant Material

The medicinal roots of Aconitum heterophyllum have been collected from the Amruta Herbals Pvt. Ltd. Indore, Madhya Pradesh 452015, India, in Nov. 2016. The plant was authentified by Amruta Herbals Pvt. Ltd. Indore, Madhya Pradesh with their truthful label.

Drugs and Chemicals

Standard Drug

Omez 20 Tablet (Omeprazole 20mg). This is an allopathic formulation of Dr Reddy's Lab, Baddi-solan, and Himachal Pradesh. Used mainly in treatment of peptic ulcer and acidity.

Other Chemicals

Ethanol (90%), Anesthetic ether, HCl, 0.1N NaOH, Phenolphthalein indicator, Formal saline all these chemicals were procured from S.D. Fine Chemical Ltd. Mumbai, Maharashtra. The chemicals used and other solutions were all of analytical grade. All drugs and reagents were prepared immediately before use.

METHODS

Extraction method

For the extraction of plant material the soxhlet extraction method may be used. Requirements of extraction process are as follows:

Solvent: Ethanol was used as solvent.

Apparatus: Soxhlet Extraction Assembly.

Procedure

The collected roots were air dried under shade at room temperature and milled to a coarse powder. The obtained dried powder was subjected to continuous extraction with 80% ethanol in a Soxhlet apparatus. The powdered root material was packed in a tumble made of Whatmann's filter paper. It was extracted with ethanol for 40 cycles. The extract thus obtained was concentrated to dryness in a flash evaporator under reduced pressure and controlled temperature.

The yield of ethanolic extract of roots of A. heterophyllum was 12.91%. The Obtained residue was a brown color thick and sticky paste. The extract was stored in refrigerator and reconstituted in gum acacia before administration to animals.

Experimental Animals

The experiment is performed on albino Wistar rats (weighing 150-200g), which are obtained from the animal house of Department of Pharmacology, Vidyabharati college of pharmacy, Amravati. All the animals are acclimatized to the animal house prior to use. They are kept in cages in animal house with a 12 h light: 12 h dark cycle. Animals are fed on pellets and tap water ad libitum. The care and handling of rat were in accordance with the internationally accepted standard guidelines for use of animals (CPCSEA). Permission and approval for animal studies was obtained from the Institutional Animal Ethics Committee (IAEC) of Vidyabharti college of Pharmacy, Amravati. SGB Amravati University. (1504/Po/Re/S/11/CPCSEA-09/08/2016).

Selection of Animal species & housing

For the acute toxicity study the Female rats were used, as Female rats are more sensitive than Male rats. All the test animals were kept in separate cages at least 5 days before the commencement of toxicity test. Animals were maintained at 22 ± 3^0C in (12:12) light & dark cycle with free access of Food and Water.

Acute Oral Toxicity Study

In order to decide the dose range of herbal formulation, toxicity study was carried out as per OECD guidelines No 425 (Annexure 2c, Annexure 2d, 2001) of CPCSEA for acute oral toxicity. No mortality and no sign of toxicity were found after the administration of 250 mg/kg; 500mg/kg; 1000mg/kg; 1500mg/kg and 2000mg/kg of herbal formulation by oral route. No death observes up to dose of 2000mg/kg. Therefore the $LD^{[50]}$ of ethanolic roots extract of Aconitum Heterophyllum was found to beyond 2000 mg/kg.

So, for present experimental studies the 225 mg/kg as a low dose, 450 mg/kg as a medium dose & 900 mg/kg as a high dose of Aconitum Heterophyllum was selected.

Preparation of doses

During each study procedure Fresh aqueous solution of root extract of Aconitum heterophyllum was made and each time same volume of dose was administered by varying the conc. of the drug extract.

Test procedure

The required dose is administered in animal one at a time by using oral gavages. The animal (Rats) was fasted overnight but water was not withdrawn. The fasted body weight of rat is determined and Dose is calculated on body weight basis after administration of Aconitum heterophyllum extract the food is withheld for further 3-4 h. For limit test 2000 mg/kg dose was administered in one animal and then the animal was observed for mortality for a period of 48 k the tested rat was survived therefore test was continue by taking 4 more animals.

In main test dose of 250,500, 1000, and 1500 was selected and was administered in animal one at a time. The animal was observed for any toxic symptoms initially for 1h. Interval for 4 h. then periodically for up-to 14 days.

Selection of Dose groups

On the basis of acute toxicity study data. It was conclude that $LD^{[50]}$ of Aconitum

heterophyllum ethanolic extract is more than 2000mg/kg. 225mg/kg of dose was selected and was examine for its Antiulcer efficacy. It was found to be effective.

Therefore the test groups were divided as 225mg (low dose), 450 mg (medium dose), 900mg (high dose).

Determination of Antiulcer Activity

The Antiulcer potential of ethanolic roots extract of *Aconitum heterophyllum has* been carried out by using Ethanol induce ulcer model in Albino wistar rat of either sex weighing 150-250 gm.

Ethanol Induced Ulcer

Rats were divided into five groups with six animals in each. The rats were fasted 24 h prior to start of experiment. Then the first groups receive an oral dose of the vehicle (10 ml/kg), in the second group Omeprazole (20mg/kg) & 3^{th}, 4^{th} and 5^{th} group receive 225,450 and 900 mg/kg body weight of root extract of Aconitum heterophyllum. After 60 min, all groups were orally treated with 1 ml of ethanol solution for gastric-ulcer induction. Animals were killed 1h after the administration of ethanol and the stomachs were excised and gastric damage (score for ulcer) determined as described below.

Treatment Protocol

Briefly, the animals were divided into five groups (n = 6) and treated with the respective test solutions as given below:

1. Group 1 (negative control group) –Ethanol + vehicle.
2. Group 2 (Standard group) - Ethanol + 20 mg/kg Omeprazole.
3. Group 3(Low dose group) - Ethanol + 225 mg/kg ERAH.
4. Group 4 (Moderate dose group) - Ethanol + 450 mg/kg ERAH.
5. Group 5 (High dose group) - Ethanol + 900 mg/kg ERAH.

Ulcer Scoring

Scoring for the ulcer is made according to the severity of ulcer as follows.

Table No.1: Observation Table for Scoring of Ulcers.

Score	Observation
0	Normal, No ulcer
0.5	Red Coloration
1	Spot ulcer
1.5	Hemorrhagic Streak
2	Deep ulcer
3	Perforation

Determination of Ulcer Index

After scoring Ulcer according to their severity, the mean ulcer score for each animal was expressed as ulcer index. Ulcer index was measured by using following formula:

Ulcer Index (UI) = UN + US + UP X 10^{-1}

Where,

UI = Ulcer Index.

UN = Average number of ulcers per animal.

US = Average number of severity score.

UP = Percentage of animals with ulcers.

% Inhibition of Ulceration

Percentage inhibition of ulceration was calculated as below:

% Inhibition of Ulceration = (Ulcer index Control-Ulcer index Test) ×100/Ulcer index Control.

Determination of Total Acidity and pH

The stomachs were removed and the content was subjected to centrifugation at 3000 rpm for 10 min. The total acidity of the gastric secretion was determined by titration with 0.01 N NaOH and phenolphthalein as indicator.

The total acidity is expressed as equiv./1using the following formula:

Total Acidity = n X 0.01 X 40 X1000

Where,

n is volume of NaOH quantified,

40 s the molecular weight of NaOH,

0.01 is normality of NaOH and

1000 is the factor represented in litre.

Determination of pH

pH of the gastric secretion was recorded with calibrated pH meter.

Statistical Analysis

The data were expressed as mean±SEM. Results were analyzed statistically by One-way ANOVA followed by DUNNETT's TEST using Primer of Biostatistics, Version 4, The difference was considered significant if $P<0.05$.

RESULT AND DISCUSSION

Table no. 2: Analytical Report of Aconitum Heterophyllum.

Specified test	Result	Specification
1)Physiochemical		
a) Description	Brown or grey coloured dry powder with bitter and astringent taste and odourless.	light ash-grey, White or grey-brown coloured dry powder with bitter and astringent taste and odourless.
b) Solubility in water	86.27%	NLT 60.00%
c) pH of 1.0%w/v solution	5.32	3-7
d) Loss on drying	4.73%	NMT 7.00%
e) Ash content	2.04%	NMT 10.00%
f) Heavy metals	Complies	NMT 20 ppm
2) Microbiological		
Total plate count	580Cfu/gm	NMT 1000Cfu/gm
Total yeast mould	20Cfu/gm	NMT 100Cfu/gm
E.coli	Absent	Absent
Salmonella spp.	Absent	Absent
S.aereus	Absent	Absent

Photochemical Investigation

Table.No. 3: Observation table for Phytochemical Investigation of Aconitum heterophyllum.

Sr. No.	Natural Product	Test Performed	Inference
1	Alkaloid	Dragendorff's Test	-
		Mayer's Test	+
		Hager's Test	+
2	Steroids	Salkowask'y test	-
3	Phenol	Lead acetate test	+
4	Flavone	Shinoda test	+
5	Enzyme test	Catalyst test	+
6	Carbohydrate	Molisch's test	-
		Fehling's test	+
		Benedict's test	-

7	Saponine	Soap Formation with water	+
8	Glycoside	Brontragar's test	-
		Flavonoid Glycoside	+
9	Tannin	Gllotannin	+
		Catechin	-
10	Protein and Amino Acid	Ninhydrin test	+
11	Quinones		-
12	Terpenoids		+

\+ Indicates presence

\- Indicates absence

Phytochemical testing was carried to find out the secondary metabolites because secondary metabolites possess biological activity. The data of above table reveals that alkaloids, flavonoids, carbohydrates, glycoside, tannins & phenolic compounds were present in Aconitum Heterophyllum roots.

Microbial Load Analysis

For the safe use of plant drugs, microbial load was tested for raw materials which include total aerobic count, total yeast and moulds count, absence of Escherichia coli, Salmonellae, S.aereus. As per WHO guidelines. Microbial load was tested for *Aconitum Heterophyllum* which includes, total plate count, total yeast and moulds count, absence of Escherichia coli, Salmonellae, S.aereus. As per WHO guidelines 5.

Table No. 4: Microbial Analysis of *Aconitum Heterophyllum*.

Parameters	Results	Limit as per WHO
Total Microbial Count	580Cfu/gm	NMT 1000 Cfu/gm
Yeast and Moulds	20Cfu/gm	NMT 100 Cfu/gm
Escherichia coli	Absent	Should be absent
Salmonellae	Absent	Should be absent
S.aereus	Absent	Should be absent

PHARMACOLOGICAL STUDY

ETHANOL INDUCED ULCER

A. ULCER SCORE

Table No. 5: Mean Ulcer Score in Ethanol induced ulcer.

Treatment Group	Dose mg/kg	Mean Ulcer Score
Control Group	10ml/kg	2.25±0.25
Omeprazole	20 mg/kg	0.83±0.16***
ERAH	225 mg/kg	1.75±0.11 ns
ERAH	450 mg/kg	1.66±0.16 ns
ERAH	900 mg/kg	1.25±0.21**

Each group consist of six animals, Data is presented in mean±SEM.

Here ** means significant difference ($p<0.05$) as compared to Negative control group.

Ns= no significant ERAH=Ethanolic Root Extract of Aconitum Heterophyllum.

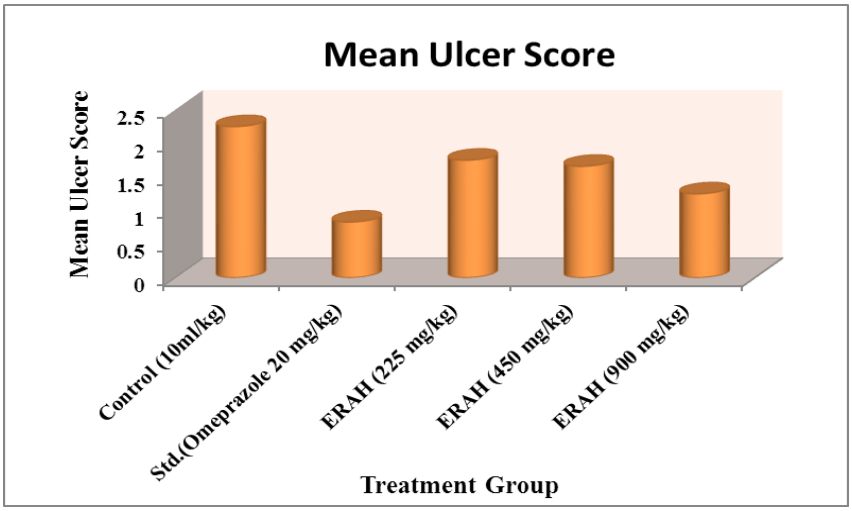

Figure No.01: Bar chart of Mean Ulcer Score.

Ulcer score is the counting of spots and severity of damage in gastric part by any moiety such as ethanol. This present study showed that all drug groups showed protection against ethanol damage by significant level ($P<0.05$) as compared to vehicle treated group. Single drug treatment (225 mg/kg, 450 mg/kg and 900 mg/kg of ERAH) was effective up to significant level ($P<0.05$) as compared to vehicle treated group.

B. ULCER NUMBER

Table No. 6: Observation table for Ulcer number in Ethanol induced ulcer.

animal	Control group	Std.(omeprazole 20 mg/kg)	ERAH(225 mg/kg)	ERAH(450 mg/kg)	ERAH(900 mg/kg)
1	4	0	5	1	0
2	5	0	3	2	1
3	7	1	3	1	1
4	5	0	4	1	1
5	6	2	5	1	1
6	4	0	3	2	1
mean±SEM	5.16±0.477	0.50±0.341***	3.83±0.401 ns	1.33±0.21***	0.83±0.166***

ULCER INDEX AND % INHIBITION OF ULCER

Table No 7: Observation table for Ulcer Index and % of Inhibition in Ethanol induced ulcer.

Group	Treatment	Ulcer Number	Mean ulcer score	Incidence of ulcers (%)	Ulcer Index	% Of Inhibition
Control	Vehicle 10 ml/kg	5.16±0.477	2.25±0.25	100 %	10.74	-
Standard	Omeprazole 20 mg/kg	0.50±0.341***	0.83±0.16***	33.33 %	3.46	67.78
ERAH	225 mg/kg	3.83±0.401 ns	1.75±0.11 ns	100 %	10.55	1.76
ERAH	450 mg/kg	1.33±0.21***	1.66±0.16 ns	100 %	10.29	4.18
ERAH	900 mg/kg	0.83±0.166***	1.25±0.21**	83.33 %	8.54	20.48

Each group consist of six animals, Data is presented in mean±SEM. Here ** means significant difference ($p<0.05$) as compared to Negative control group. Ns= no significant ERAH=Ethanolic Root Extract of Aconitum Heterophyllum.

A. ULCER INDEX

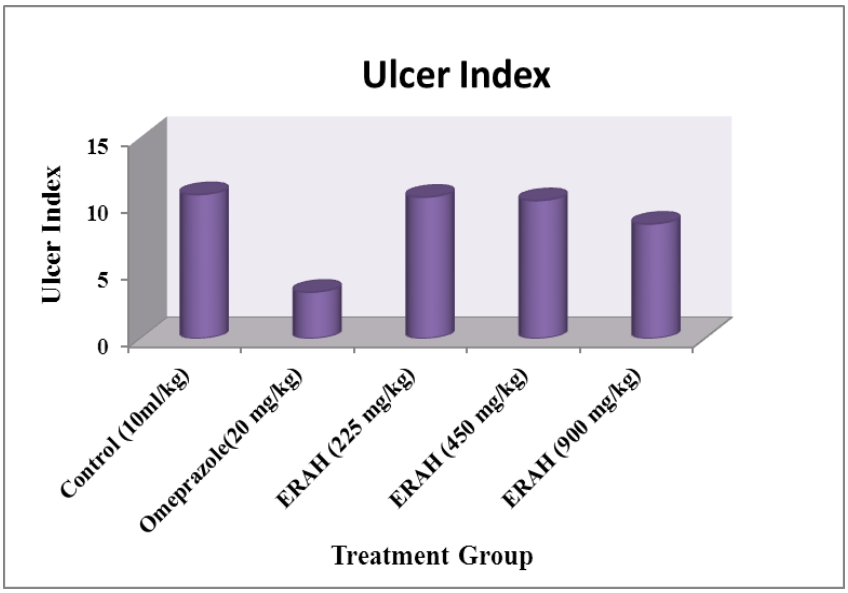

Figure No.02: Bar chart of ulcer Index in Ethanol induced ulcer.

B. % INHIBITION OF ULCER.

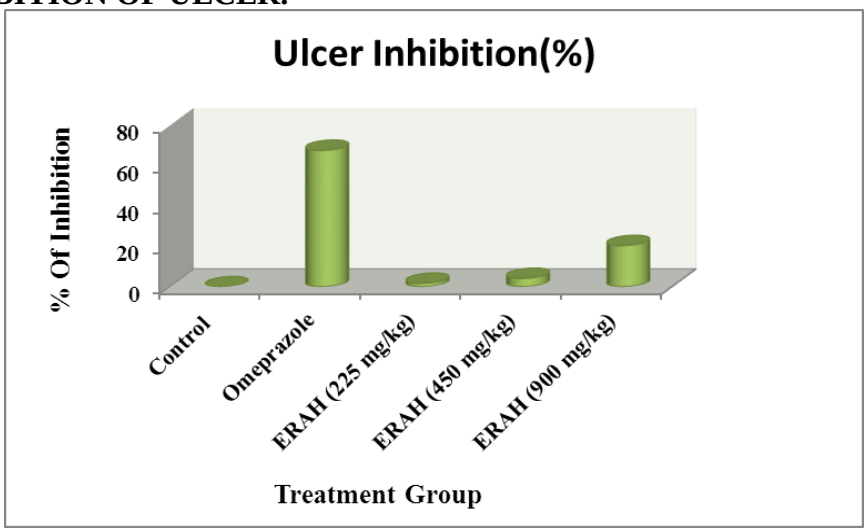

Figure No.03: Bar chart of % Inhibition of Ulcer in Ethanol induced ulcer.

The % of occurrence of ulcers in stomach is significantly inhibited by the standard drug (omeprazole) and ERAH in dose dependent manner.

DETERMINATION OF pH AND TOTAL ACIDITY OF GASTRIC JUICE

Table No 8: Observation of pH, Free Acidity, Total Acidity and Volume of Gastric Juice.

Treatment group	Ph	Free acidity Meq/L	Total acidity Meq/L	Volume of astric Juices (ml)
Control group	1.36±0.049**	33.33±0.66	84.83±1.19	6.77±.09
Omeprazole (20 mg/kg)	2.85±0.089**	19.00±0.68***	45.67±.91***	4.38±.10***
ERAH(225 mg/kg)	2.36±0.045**	26.83±0.60***	61.67±.95***	6.20±.05***
ERAH(450 mg/kg)	2.66±0.072**	24.50±.88***	49.00±1.15***	5.15±.04***
ERAH(900 mg/kg)	2.75±0.068**	22.67±.71***	48.67±.61***	4.88±.06***

Each Group consist of six animals, Data is presented in mean±SEM. Significant at P<0.05*, 0.01**, ns= not significant.

ERAH= Ethanolic Root Extract Aconitum Heterophyllum.

A. Determination of pH of Gastric Juice.

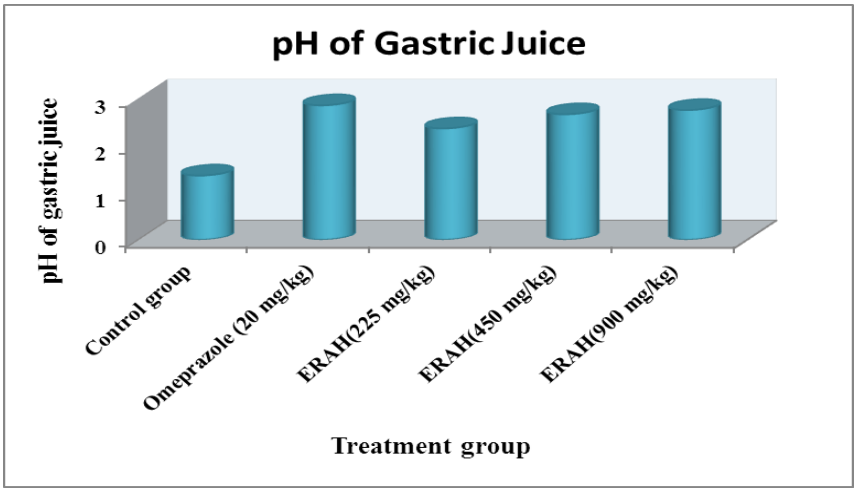

Figure No.04: Bar chart of pH of Gastric Juice.

Low pH is responsible for more damage in gastric portion. In this study the pH is increase by significant level in both standard (omeprazole) and test (225, 450 & 900 mg/kg of ERAH) group as compare to control group.

B. TOTAL ACIDITY

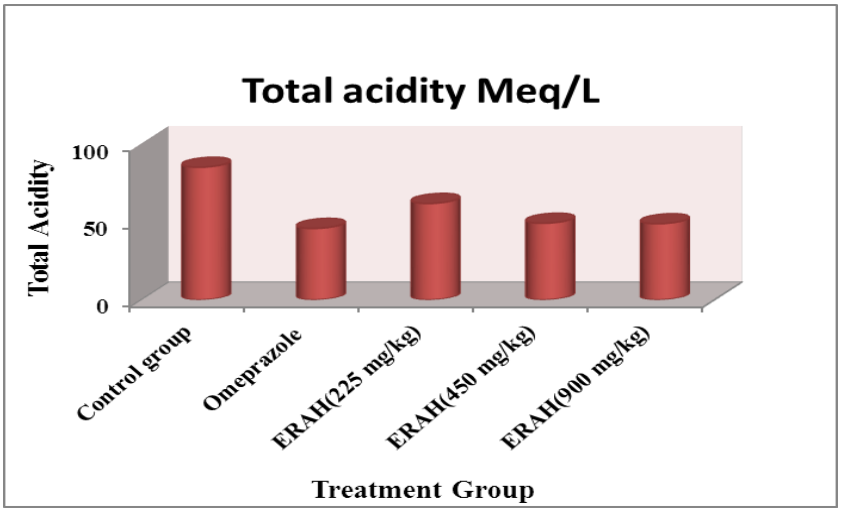

Figure No.05: Bar chart of Total Acidity of Gastric Juice.

Total acidity has relation with amount of HCl present in the gastric fluid and responsible for gastric environmental because it is inversely proportional to the gastric pH. The volume of gastric juice in stomach is also significantly reduced by the standard drug (omeprazole) and ERAH dose dependent manner.

DISCUSSION

The main cause of gastric ulcer is destruction of the gastric mucosal barrier which consists of the surface epithelium and mucosal coat. This destruction may be due to either, an increase in gastric acid secretion, a decrease in mucus production or a decrease in mucosal blood flow. It is generally accepted that gastric ulcers results from an imbalance between aggressive factors and the maintenance of the mucosal integrity through the endogenous defense mechanism.

Prostaglandins (PG) offer protection to duodenum through both increases in mucosal resistance as well as decrease in aggressive factors, mainly acid and pepsin.

Ethanol induced gastric ulcers have been widely used for the evaluation of gastro protective activity. Ethanol is metabolized in the body and releases superoxide anion and hydroperoxy free radicals. The incidence of ethanol induced ulcers is predominant in the glandular part of stomach. It was reported to stimulate the formation of leukotriene C_4 (LTC_4), mast cell secretory products and reactive oxygen species resulting in the damage of rat gastric mucosa. It has been found that oxygen derived free radicals are implicated in the mechanism of acute and chronic ulceration in the gastric mucosa and scavenging these free radicals can play an appreciable role in healing these ulcer. Despite the availability of many pharmaceutical products for the treatment of gastric ulcers in the market as mentioned above, their successes were limited by presence of several adverse effects (e.g. anaphylaxis reactions, gynecomastia, hematopoietic changes, thrombocytopenia, acute interstitial nephritis, nephrotoxicity & hepatotoxicity).

Due to the reported side effects of available antiulcer drugs, focused have been shifted towards natural products as the new sources of antiulcer agents. With the increasingly growing interest in natural medicine, various plants have been studied based on the traditional knowledge of their pharmacological properties and confirmed to be useful in treating and managing ulcer. Furthermore, medicinal plants have been known to be amongst the most attractive sources of new drugs, and have been shown to give promising results in treatment of various diseases including gastric and duodenal ulcers.

Different therapeutic agents including plant extracts are used to inhibit the gastric acid secretion, or to stimulate the mucosal defense mechanism. Mucosal defense mechanism by increasing the mucus production protecting the surface epithelial cells, or interfering with the PG synthesis.

This study investigated the inhibitory effects of *Aconitum heterophyllum* roots extract on gastric ulcer formation induced by ethanol, compared to omeprazole, a drug whose ulcer healing effects have been extensively studied, and to an ulcer control group (vehicle). The Aconitum heterophyllum roots extract (900mg/kg) was found to have a protective effect on the gastric mucosa similar to that of omeprazole (20mg/kg). Omeprazole and *Aconitum heterophyllum* roots extract were both found to be protective in comparison to control group (Vehicle). This suggests that Aconitum heterophyllum roots extract indeed has a significantantly-ulcer effect.

The results show that the Aconitum heterophyllum roots extract is capable of providing prophylactic anti-ulcer effects against an irritant substance. The Aconitum heterophyllum roots extract is capable of inhibiting lesion formation induced by ethanol. The accompanying significant dose-dependent decrease in Total Acidity as a dose of the drug is increased, suggests that the decrease in total acidity mechanism contributes to the acid neutralizing effect of the Aconitum heterophyllum roots extract. It is evident from the decrease in total acidity that decrease in total acidity must have largely contributed to preventive effect of the Aconitum heterophyllum roots extract. The Total Acidity of the gastric Content is thought to play an important role as a defensive factor against gastrointestinal damage. This suggests that gastro-protective effect of Aconitum heterophyllum roots extract may be mediated partly by preservation of gastric mucosal damage against acidic gastric content. This may play significant role in reducing peptic ulcer.

Absolute alcohol gets metabolized in to body, leading to increased Oxygen free radicals into the gastric mucosa. The free radicals produced cause lipid peroxidation leading to membrane fluidity. Which in turn increase the influx of ca^{+} ions and result in the reduced membrane integrity of surface epithelial cells, there by generating gastric ulcers. Free radicals have been demonstrated to be a contributing factor in tissue injury and in the modulation of pain.

The incidence of ethanol induce ulcers, predominant in the glandular part of the stomach has been reported to stimulate the form of leaukotrineC_4 (LTC_4), mast Cell secretory product and reactive oxygen species resulting in the damage of rat gastric mucosa. Oxidative stress plays an important role in the pathogenesis of various diseases including gastric ulcer, with antioxidants being reported to play a significant role in the protection of gastric mucosa against various necrotic agents. Antioxidants could help to protect cells from damage caused

by oxidative stress while enhancing the body's defense systems against degenerative diseases. Administration of antioxidants inhibits ethanol-induced gastric injury in rat.

Oxygen free radicals stimulates the proton pump, these stimulated pump then increases the secretion of acid and pepsins, which leads to increase in acidity, and thus produces ulcer. These reactive species are highly cytotoxic and can induce tissue damage.

In Ethanol induced gastric ulcers, the lesions were characterized by multiple hemorrhage red bands of different sizes along the longitudinal axis of the glandular stomach. This model is extensively used to screen drugs for cyto-protection.This study provided a substantial evidence for anti-ulcer and anti-secretory effects of an Ethanolic extract of Aconitum Heterophyllum *roots.* Aconitum Heterophyllum roots significantly inhibited the ulcerative lesions in all animals treated with necrotizing agents, which was further confirmed by histological findings in which Total Acidity, pH and ulcers were abolished in rats pre-treated with Aconitum Heterophyllum roots extract. The ability of gastric mucosa to resist injury by endogenous secretions (acid, pepsin and bile) and ingested irritant (ethanol), can be attributed to a number of factors that have been referred to collectively as mucosal defense. The gastric mucosal lesions induce by necrotizing agents such as strong alkalis are due to depression of the gastric defensive mechanisms.

8. CONCLUSION

In conclusion it appears that Aconitum Heterophyllum Roots extract may significantly decrease the acid secretion in the gastric chamber and simultaneously protect the gastric mucosa against ethanol-induced injury. Aconitum Heterophyllum Roots extracts may be exhibits an antiulcer potential activity through at least one or more possible mechanisms. Such protection was shown to be dose-dependent an as certained by the reduction or inhibition of ulcerated areas in the gastric wall as well as the reduction or inhibition of total acidity and pH of gastric content. Protection was most prominent at a dose of 900 mg/kg of the ethanolic roots extract of plant drug substances.

The anti-ulcer activity is probably due to the presence of bioactive compounds like flavonoids, alkaloids, terpenoids, tannin, protein & amino acid, saponin and phenol. Further studies are required to confirm the exact mechanism underlying for the ulcer healing and protecting property of the extract.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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