



Received on 23 May, 2010; received in revised form 17 August, 2010; accepted 17 September, 2010

STUDY OF PHYTO CHEMICAL, ANALGESIC AND ANTI ULCER ACTIVITY OF EXTRACTS OF AERIAL PARTS OF *CARDIOSPERMUM HALICACABUM* LINN.

P. Muthumani*¹, R. Meera ¹, S. Venkatraman ¹, Sundara Ganapathy ¹ and P. Devi ²

Department of Pharmaceutical Chemistry ¹, Department of Pharmacognosy ², K M College of Pharmacy, Uthangudi, Madurai, Tamil Nadu, India

ABSTRACT

Keywords:

Cardiospermum halicacabum
Linn,
Aerial parts,
Anti ulcer,
Analgesic

The dried aerial parts of *Cardiospermum halicacabum* Linn were subjected to extraction using the solvents (petroleum ether, chloroform, Ethyl acetate and ethanol) in increasing order of polarity. The prepared extracts were then subjected to preliminary phytochemical analysis. It was found plant possesses carbohydrates, alkaloids, sterols, flavanoids and saponins. All extracts were selected for further study. The analgesic activity of all extracts of aerial parts was assessed in albino mice using thermal stimulus model. morphine and Paracetamol were used as standard. The results indicate that, petroleum ether extract showed 34% (0.15mg/ml) and 58 % (0.3mg/ml) significant activity, when compared with morphine. Comparison with Paracetamol the pet ether extract showed 48% (0.3mg/ml) and 82% (0.3mg/ml) significant activity. The ulcer activity was determined by pylorus ligation technique. Ranitidine (50mg/kg) used as standard. The ethanol extract showed 48.2% (18.75mg/2ml) significant antiulcer activity compared with standard drug. From the present study it may be concluded that the constituents present in all the extracts may be responsible for both activities.

Correspondence to Author:

P. Muthumani

Department of Pharmaceutical Chemistry, K M College of Pharmacy, Uthangudi, Madurai, Tamil Nadu, India

INTRODUCTION: *Cardiospermum halicacabum* Linn, Family: Sapindaceae. As a wild climber through out the plains of India, ascending to 1300 m in the North Western Himalaya. *Cardiospermum halicacabum* Linn is a small genus of ornamental, herbaceous or shrubby vines. An annual or sometimes perennial climber, 3.5 m in height commonly found as a weed throughout India, ascending upto 1200m. Leaves deltoid, biternate, 3-8 cm long, leaflets deeply cut, acuminate, laterals oblong or ovate, terminal rhomboid- lanceolate, flowers white in umbellate cymer, with a pair of peduncles modified into tendrils; capsules depressed – pyriform, covered with bladder like calyx, winged at the angles; seeds globose, black, smooth, 4-6mm, with a small, white, heart shaped aril. In literature review it was found that the Plant used as amenorrhea, anti arthritis, anti-inflammatory, analgesic, antispasmodic, antihemolytic and anti rheumatic. The root used as aperient in orchitis, diuretic, used in liver disorders and dysentery. The leaf juice used for asthmatic treatment and drooped into nostrils relives one side head-ache^{1,2}.

The dried plant powder is being used for bronchitis by oral route. The plant is being to reduce acute rheumatism and used as tincture³⁻¹⁴. *Cardiospermum halicacabum* Linn contains flavonoids, alkaloids, steroids, fatty acids, terpenoids, saponins, sugars, sterol, an essential oil, resin, non glucosidal bitter substance, tannin, large amount of potassium nitrate and other constituents^{15, 16, 17, 18}. However, there are no reports on the diuretic activity of the plant. Hence, the present study was designed to verify the claims of traditional and use in Unani system of medicine.

MATERIALS AND METHODS: Fresh aerial parts of *Cardiospermum halicacabum* Linn. were collected during the month of September 2007, from Ottanchatiram, Dist. Dindugal, Tamil Nadu. The plant was identified and authenticated by Dr. Stephen Botanist Professor in American college, Madurai and herbarium specimen

deposited at K.M.College of Pharmacy, Madurai. The fresh plant material was then dried under shade. Dried plant material was powdered using mechanical grinder and passed through 60# sieve to get the powder of desired coarseness. Powdered material was preserved in an air tight container.

Preparation of Extracts: The aerial parts of *Cardiospermum halicacabum* Linn was dried in the shade. Then the shade dried leaves were powdered to get a coarse powder. About 750g of dry powder was extracted first with petroleum ether (40-60°C) by hot continuous percolation using Soxhlet apparatus. The extractions were continued for 72 hours. The petroleum ether extract was filtered and concentrated to a dry mass by using vacuum distillation. A dark brown residue was obtained (8.4g). The marc left after the petroleum ether extract was taken and subsequently extracted with chloroform up to 72 hours. The chloroform extract was then filtered and concentrated to a dry mass. A dark brown residue was obtained (8.1g). The marc left after the chloroform extraction was dried and extracted with ethyl acetate. The extraction was continued up to 72 hours. The ethyl acetate extract was filtered and concentrated by vacuum distillation. A black residue was obtained (8.7g). Finally the marc was extracted with ethanol in the above manner and processed. A black residue was obtained (9.2g).

Preliminary Phytochemical Studies: All the extracts were screened for the presence of various secondary metabolites like steroids, alkaloids, carbohydrates, flavonoids, essential oil and tannins using standard methods.

Animals: Male albino rats weighing 200-300 gm of either sex were procured from Cadila Health Care Ltd., Dholka, Ahmedabad. All the animals were kept in standard polypropylene cages and maintained at 27°C ± 2°C under 12 h. dark/light cycle. The animals were fed with standard rat feed and water was given *ad libitum*. Ethical

clearance for handling the animals and the procedures used in the study was obtained from the institutional animal ethical committee.

Analgesic Sctivity^{19, 20, 21, 22, 23}: The technique of Janssn and Jageneau (1957) was employed to detect the effect, using thermal stimulus. The three male albino mice weighing 20-25gm were selected. The analgesiometer was maintained at 55°C and the animals were paced over it. The reaction time i.e, the time between placing animals on the analgesiometer and the beginning of licking the fore or hind paw by the animals was recorded for all the mice. After the fist attempt the number of attempts to lick the hind paw per 30seconds was also recorded.

Preparation of Injection, Administration and Observation: The extracts were dissolved in poly ethylene glycol and the solution for injection was prepared according to the body weight of animal, however 1g of each extract was dissolved in 100ml of polyethylene glycol which gives the concentration of 10mg/ml. from this 10ml was taken and diluted to 100ml which given the concentration of 1mg/ml. from the solution, the test solution was prepared in two different concentrations, i.e. 30ml and 15ml were taken and diluted to 100ml to give the concentration of 0.3mg/ml and 0.15mg/ml respectively.

Then the animals were divided into four groups. The first group of animals (three animals) received the poly ethylene glycol (blank) intraperitonially. The second group of animals (three animals) received the Morphine hydrochloride 10mg/kg and third group of animals were given (three animals) paracetamol at the dose of 15mg/kg. The fourth group animals (24 animals) again divided into 4 sub groups each of six animals each. The first sub group three animals received the petroleum ether extract 15mg/kg and another three animals received the petroleum ether extract 7.5mg/kg. In the same manner the remaining 3 sub groups of animals were given with the three

extracts such as chloroform extract, ethyl acetate extract and ethanol extract in the two different doses (15mg/kg and 7.5mg/kg). After administering the drugs the animal was placed on the analgesiometer maintained at 55°C after one hour of the administration. The reaction time was recorded. After the first attempt, the numbers of subsequent attempts to lick the hind paw which was recorded for 30 seconds intervals.

Anti ulcer activity^{24, 25, 26, 27, 28, 29}: The method of Shay et al was employed to evaluate the anti ulcer activity by Pylorus Ligation technique. Three albino rats weighing 150g to 250 g for each group were selected and housed in individual cages and were fasted (water allowed) for 48 hours prior to pyloric ligation, care being taken to avoid coprophagy. The animals were divided into four groups. The first group of animals (three animals) received the 1% carboxyl methyl cellulose suspension (control) and the second group of animals (three animals) received ranitidine 50mg/kg orally at 30 minutes before of pyloric ligation. The third group of animals (12 animals) gain divided into four sub groups of each of three animals. In it the first sub group (three animals) received petroleum ether extract, the second sub group (three animals) received chloroform extract, the third sub group (three animals) received ethyl acetate extract and the fourth sub group(three animals) received ethanol extract in the concentration of 18.75mg/2ml (75mg/kg.)

The test solution was prepared by dissolving 0.5gm of each extract in 50ml (10mg/ml) of 1% carboxyl methyl cellulose suspension and administered according to the body weight in the oral route. Under light ether anaesthesia the abdomen was opened by small midline incision below the xiphoid process; pyloric portion of the stomach was slightly lifted out and ligated correctly to avoid traction to the pylorus or to its blood supply and they are deprived of both food and water during the postoperative period. After four hours of pyloric

ligation, the stomach was excised and the gastric juice was collected into test tubes. The stomach was inflated by injecting saline (10ml) and fixed in 5% formalin for 30 minutes. Then the stomach was cut open along the greater curvature and the inner mucosal membrane surface was examined under 6.4 binocular magnifiers.

The degree of ulceration was estimated using the following scoring systems. No ulcer is Grade zero, 1 to 5 ulcers in 1mm diameter is Grade 1, 6-10 ulcers (1mm diameter) is Grade 2, more than 10 ulcers (1mm diameter) is Grade 3, 1-5 Streaked ulcers indicated Grade 4, 6-10 streaked ulcers indicated Grade 5, more than 10 streaked ulcers indicated Grade 6. The ulcer Grade was obtained from the sum of the number ulcers multiplied by the corresponding score.

Total Acidity: The gastric juice was titrated against 0.01N sodium hydroxide using phenolphthalein as indicator until the pale pink colour observed and the acidity was expressed as equivalent mg HCl/100 g body weight.

Free Acidity: It was determined in a similar manner of total acidity using Toper's reagent as indicator and 0.01N Sodium hydroxide was run until the canary yellow colour observed.

Ulcer Index: The gastric ulcers were measured by scoring of affected lesions of stomach mucosa and the ulcer index was determined.

Ulcer index = $10/x$

$$\text{Where } x = \frac{\text{Total area of stomach mucosa}}{\text{Total ulcerated area}}$$

Statistical Analysis³⁰: All the results are expressed as mean \pm standard error. The data was analyzed statistically using ANOVA followed by Dunnett's Multiple Comparison Test.

RESULTS: The phytochemical tests revealed the presence of flavonoids, saponins, carbohydrates in methanol and aqueous extracts. When compared with Morphine (0.2mg/ml), petroleum ether extract showed 34% and 58% activity, chloroform extract showed 26% and 42% activity, ethyl acetate extract showed 22% and 40% activity and Ethanol extract showed 24% and 45% activity for 0.15mg/ml and 0.3mg/ml concentrations of each extract respectively. When compared with paracetamol (0.3mg/ml), petroleum ether extract showed 48% and 82% activity, chloroform extract showed 36% and 59% activity, ethyl acetate extract showed 32% and 57% activity and Ethanol extract showed 34% and 64% activity for 0.15mg/ml and 0.3mg/ml concentrations of each extract respectively. Generally these extracts showed considerable analgesic activity at the concentration of 0.3mg/ml. when dilute the sample that is at 0.15mg/ml concentration, the extracts showed only minimum percentage of analgesic activity.

Standard drug Ranitidine (6.25mg/ml) showed of 67.2% anti ulcer activity when administered orally. When compared with Ranitidine (6.25mg/ml), petroleum ether extract (18.75mg/2ml) showed 33.6%, chloroform extract (18.7mg/2ml) showed 27.4%, ethyl acetate extract (18.75/2ml) showed 36.8% and ethanol extract (18.75mg/ml) showed 48.2% of anti ulcer activity by the oral administration. Generally, these extracts showed medium percentage of anti ulcer activity then standard drug.

DISCUSSION: In most of the cases the etiology of the ulcer is unknown. It is generally accepted that it results from an imbalance between aggressive factors and the maintenance of the mucosal integrity through the endogenous defense mechanism³¹. To regain the balance, different therapeutic agents including plant extracts are used to inhibit the gastric acid secretion or to encourage the mucosal defense mechanisms by increasing mucus production,

stabilizing the surface epithelial cells, or interfering with the prostaglandin synthesis.

Even though many products in the market for the treatment of gastric ulcers, including antacids, proton pump inhibitors, anti cholinergic and histamine H₂-antagonists, are used, most of these drugs produce several adverse reactions, such as gynecomastia, hematopoietic changes, acute interstitial nephritis³², thrombocytopenia³³, anaphylaxis reactions³⁴, nephrotoxicity and hepatotoxicity³⁵. Medicinal plants are amongst the most attractive sources of new drugs, and have been shown to give promising results in treatment of gastric and duodenal ulcers³⁶.

Most of the cases the etiology of the ulcers is unknown, it is accepted that they result from an imbalance between aggressive factors and maintenance of mucosal integrity through endogenous defense mechanisms. Also it has been reported that non-steroidal anti inflammatory drugs (NSAIDs) associated gastric ulceration occurs in 30 percent of users that leads to hospitalization and is also associated with high mortality. Aspirin (ASP) is one of the most widely used NSAIDs, which damages

gastrointestinal mucosa by irritant action, causing alterations in mucosal permeability and/or suppression of prostaglandin synthesis³⁷. Most of the commonly used drugs such as H₂-blockers (ranitidine, famotidine etc), M₁-blockers (pirenzepine, telenzepine etc), proton pump inhibitors (omeprazole, lansaprazole etc), decrease secretion of acid while, drugs like sucralfate and carbenoxolone promote mucosal defenses. Not long, the role of these drugs on the defensive factors is gaining importance. It is now assumed that these drugs ultimately balance the aggressive factors (acid, pepsin, H.pylori, bile salts) and defensive factors (mucin secretion, cellular mucus, bicarbonate secretion, mucosal blood flow and cell turnover). Although these drugs have brought about remarkable changes in ulcer therapy, the efficacy of these drugs is still debatable. Reports on clinical evaluation of these drugs show that there are incidences of relapses and adverse effects and danger of drug interactions during ulcer therapy. The search for an ideal anti ulcer drug continues and has also been extended to herbal drugs in search for new and novel molecules, which afford better protection and decrease the incidence of relapse³⁸.

TABLE 1: DATA SHOWING THE PRELIMINARY PHYTOCHEMICAL SCREENING OF THE *CARDIOSPERMUM HALICACABUM* LINN EXTRACTS

Name of the extract	Sugar	Protein	Tannin	Alkaloid	Sterol	Flavonoid	Glycoside	saponins
Petroleum ether	-	-	-	-	+	-	-	-
Chloroform	-	-	-	-	+	-	-	-
Ethylacetate	-	-	-	-	+	+	-	-
ethanol	+	-	-	+	+	-	-	+

TABLE 2: REACTION TIME WITH POLY ETHYLENE GLYCOL (BLANK)

Before administration		After administration	
Reaction time (in sec)	Reaction time (in sec)	Reaction time (in sec)	No. of attempts/30sec
4	4	4	6
4	4	4	5
5	5	5	5

TABLE 2: REACTION TIME WITH MORPHINE (0.2MG/ML)

Before administration		After administration	
Reaction time (in sec)	Reaction time (in sec)	Reaction time (in sec)	No. of attempts/30sec
4	6	20	5
3	7	22	4
5	7	20	4
4	6.6	20.6	4.3

TABLE 2: REACTION TIME WITH PARACETAMOL (0.3MG/ML)

Before administration		After administration	
Reaction time (in sec)	Reaction time (in sec)	Reaction time (in sec)	No. of attempts/30sec
5	7	14	4
4	8	16	5
6	6	14	4
5	7	14.6	4.3

TABLE 2: REACTION TIME WITH PETROLEUM ETHER EXTRACTS (0.15MG/ML)

Before administration		After administration	
Reaction time (in sec)	Reaction time (in sec)	Reaction time (in sec)	No. of attempts/30sec
6	6	8	5
6	5	6	3
5	6	7	4
5.6	5.6	7	4

TABLE 2: REACTION TIME WITH PETROLEUM ETHER EXTRACTS (0.15MG/ML)

Before administration		After administration	
Reaction time (in sec)	Reaction time (in sec)	Reaction time (in sec)	No. of attempts/30sec
6	6	8	5
6	5	6	3
5	6	7	4
5.6	5.6	7	4

TABLE 2: REACTION TIME WITH PETROLEUM ETHER EXTRACTS (0.3MG/ML)

Before administration		After administration	
Reaction time (in sec)	Reaction time (in sec)	Reaction time (in sec)	No. of attempts/30sec
4	7	13	4
6	6	11	3
5	6	12	4
5	6.3	12	3.6

TABLE 2: REACTION TIME WITH POLY ETHYLENE GLYCOL (BLANK)

Before administration		After administration	
Reaction time (in sec)	Reaction time (in sec)	Reaction time (in sec)	No. of attempts/30sec
4	8	4	6
4	8	4	5
5	7	5	5
4.3	7.6	4.3	7.6

TABLE 2: REACTION TIME WITH CHLOROFORM EXTRACTS (0.15MG/ML)

Before administration		After administration	
Reaction time (in sec)	Reaction time (in sec)	Reaction time (in sec)	No. of attempts/30sec
4	8	5	7
4	8	5	7
6	7	6	6
4.6	7.6	5.3	6.6

TABLE 2: REACTION TIME WITH MORPHINE (0.2MG/ML)

Before administration		After administration	
Reaction time (in sec)	Reaction time (in sec)	Reaction time (in sec)	No. of attempts/30sec
4	6	20	5
3	7	22	4
5	7	20	4
4	6.6	20.6	4.3

TABLE 2: REACTION TIME WITH CHLOROFORM EXTRACTS (0.3MG/ML)

Before administration		After administration	
Reaction time (in sec)	Reaction time (in sec)	Reaction time (in sec)	No. of attempts/30sec
4	7	8	5
5	7	9	4
5	8	9	4
4.6	7.3	8.6	4.3

TABLE 2: REACTION TIME WITH PARACETAMOL (0.3MG/ML)

Before administration		After administration	
Reaction time (in sec)	Reaction time (in sec)	Reaction time (in sec)	No. of attempts/30sec
5	7	14	4
4	8	16	5
6	6	14	4
5	7	14.6	4.3

TABLE 2: REACTION TIME WITH ETHYLACETATE EXTRACTS (0.15MG/ML)

Before administration		After administration	
Reaction time (in sec)	Reaction time (in sec)	Reaction time (in sec)	No. of attempts/30sec
4	8	5	7
4	8	5	7
6	7	6	6
4.6	7.6	5.3	6.6

TABLE 2: REACTION TIME WITH ETHYLACETATE EXTRACTS (0.3MG/ML)

Before administration		After administration	
Reaction time (in sec)	Reaction time (in sec)	Reaction time (in sec)	No. of attempts/30sec
5	8	8	6
6	8	9	5
5	8	8	5
5.3	8	8.3	5.3

TABLE 2: REACTION TIME WITH ETHANOL EXTRACTS (0.15MG/ML)

Before administration		After administration	
Reaction time (in sec)	Reaction time (in sec)	Reaction time (in sec)	No. of attempts/30sec
4	6	4	6
6	6	6	5
6	6	5	6
5.3	6	5	5.6

TABLE 2: REACTION TIME WITH ETHANOL EXTRACTS (0.3MG/ML)

Before administration		After administration	
Reaction time (in sec)	Reaction time (in sec)	Reaction time (in sec)	No. of attempts/30sec
4	8	9	6
4	7	10	6
6	7	6	6
4.6	7.6	5.3	7.3

TABLE 3: AVERAGE REACTION TIME BEFORE ADMINISTRATION OF DRUGS (AVERAGE BASAL REACTION TIME)

Drugs and Extracts	Reaction time (in sec)	% of action	No. of attempts/30sec
Blank	4.3	-----	7.6
Morphine (0.2mg/ml)	2.6	100%	4.3
Petroleum ether extract			
0.15mg/ml	7.6	34%	4.0
0.3mg/ml	12.0	58%	3.6
Chloroform extract			
0.15mg/ml	5.3	26%	6.6
0.3mg/ml	8.6	42%	4.3
Ethyl acetate extract			
0.15mg/ml	4.6	22%	6.3
0.3mg/ml	8.3	40%	5.3
Ethanol extract			
0.15mg/ml	5.0	24%	6.6
0.3mg/ml	9.3	45%	5.6

TABLE 4: COMPARISON OF ANALGESIC ACTIVITY OF LEAF EXTRACTS OF *CARDIOSPERMUM HALICACABUM* LINN WITH MORPHINE

Drugs and Extracts	Reaction time (in sec)	% of action	No. of attempts/30sec
Blank	4.3	-----	7.6
Morphine(0.2mg/ml)	2.6	100%	4.3
Petroleum ether extract			
0.15mg/ml	7.6	34%	4.0
0.3mg/ml	12.0	58%	3.6
Chloroform extract			
0.15mg/ml	5.3	26%	6.6
0.3mg/ml	8.6	42%	4.3
Ethyl acetate extract			
0.15mg/ml	4.6	22%	6.3
0.3mg/ml	8.3	40%	5.3
Ethanol extract			
0.15mg/ml	5.0	24%	6.6
0.3mg/ml	9.3	45%	5.6

TABLE 5: COMPARISON OF ANALGESIC ACTIVITY OF LEAF EXTRACTS OF *CARDIOSPERMUM HALICACABUM* LINN WITH PARACETAMOL

Drugs and Extracts	Reaction time (in sec)	% of action	No. of attempts/30sec
Blank	4.3	-----	7.6
Paracetamol (0.3mg/ml)	14.3	100%	4.3
Petroleum ether extract			
0.15mg/ml	7.0	48%	4.0
0.3mg/ml	12.0	82%	3.6
Chloroform extract			
0.15mg/ml	5.3	36%	6.6
0.3mg/ml	8.6	59%	4.3
Ethyl acetate extract			
0.15mg/ml	4.6	32%	6.3
0.3mg/ml	8.3	57%	5.3
Ethanol extract			
0.15mg/ml	5.0	34%	6.6
0.3mg/ml	9.3	64%	5.6

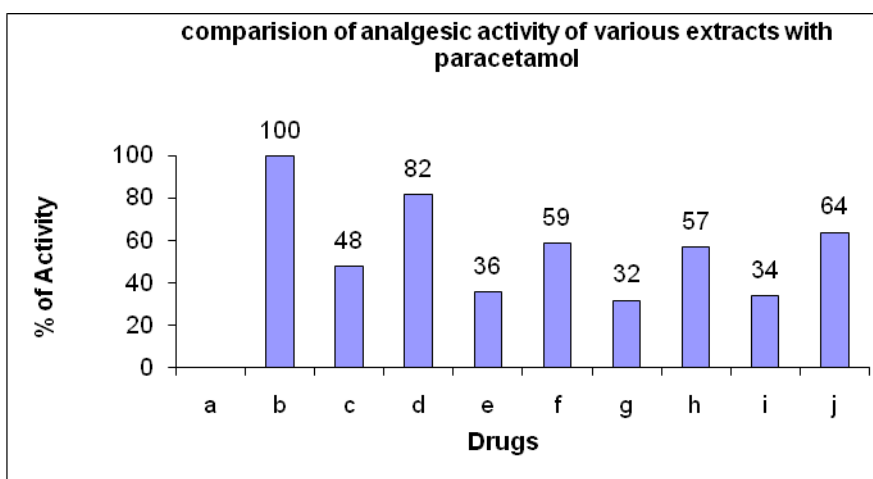


FIG. 1: COMPARISON OF ANALGESIC ACTIVITY OF VARIOUS EXTRACTS WITH PARACETAMOL

TABLE 6: FOR CONTROL (1% CARBOXY METHYL CELLULOSE)

Sl. No.	Volume of gastric juice (ml/100g)	Total acidity (mg HCl/100g)	Free acidity (mg HCl/100g)	Ulcer Index
1	5.9	16.12	3.84	30.0
2	5.8	16.15	3.80	29.0
3	5.6	16.13	3.81	30.0
average	5.8	16.13	3.81	29.7

TABLE 6: FOR STANDARD (RANITIDINE) 12.5MG/2ML

Sl. No.	Volume of gastric juice (ml/100g)	Total acidity (mg HCl/100g)	Free acidity (mg HCl/100g)	Ulcer Index
1	1.5	2.80	0.32	9.4
2	1.2	2.82	0.34	9.5
3	1.4	2.81	0.33	9.4
average	1.4	2.81	0.33	9.5

TABLE 6: For petroleum ether extract (18.75mg/2ml)

Sl. No.	Volume of gastric juice(ml/100g)	Total acidity (mg HCl/100g)	Free acidity(mg HCl/100g)	Ulcer Index
1	3.0	8.84	2.05	16.2
2	3.4	8.82	2.09	16.3
3	3.2	8.85	2.10	16.2
average	3.2	8.84	2.08	16.2

TABLE 6: FOR CHLOROFORM EXTRACT (18.75MG/2ML)

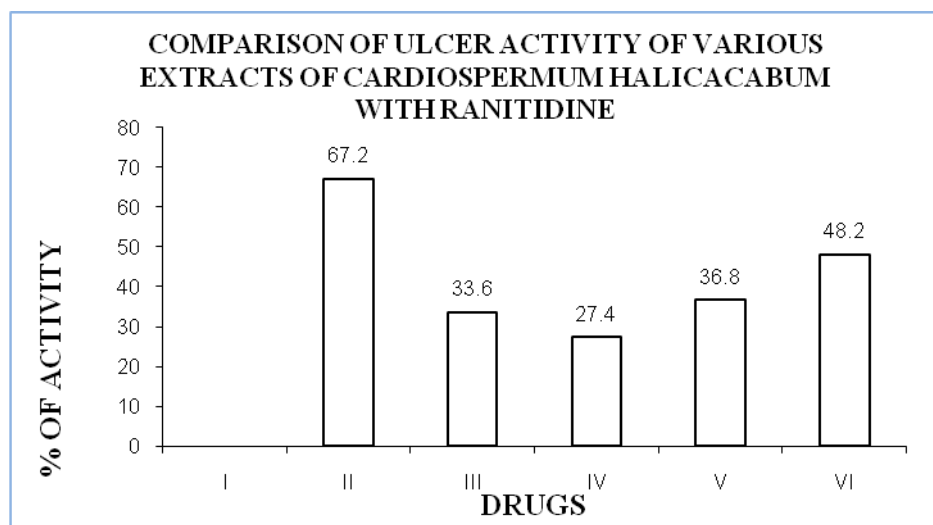
Sl. No.	Volume of gastric juice (ml/100g)	Total acidity (mg HCl/100g)	Free acidity (mg HCl/100g)	Ulcer Index
1	4.0	11.55	2.70	21.5
2	4.1	11.59	2.75	21.0
3	4.3	11.56	2.72	21.3
average	4.1	11.57	2.72	21.3

TABLE 6: FOR ETHYL ACETATE EXTRACT (18.75MG/ML)

Sl. No.	Volume of gastric juice (ml/100g)	Total acidity (mg HCl/100g)	Free acidity(mg HCl/100g)	Ulcer Index
1	2.8	8.05	1.89	15.3
2	2.6	8.07	1.92	15.0
3	2.9	8.04	1.93	14.9
average	2.8	8.05	1.91	15.0

TABLE 6: For ethanol extract (18.75mg/ml)

Sl. No.	Volume of gastric juice (ml/100g)	Total acidity (mg HCl/100g)	Free acidity (mg HCl/100g)	Ulcer Index
1	2.2	6.58	1.53	12.4
2	2.4	6.60	1.55	12.3
3	2.2	6.61	1.56	12.1
average	2.2	6.60	1.55	12.3

**FIG. 2: COMPARISON OF ULCER ACTIVITY OF VARIOUS EXTRACTS OF CARDIOSPERMUM HALICACABUM WITH RANITIDINE**

- I- Blank
- II- Ranitidine 12.5 mg/2ml
- III- Pet ether extract 18.75 mg/2ml
- IV- Chloroform extract 18.75 mg/2ml
- V- Ethylacetate extract 18.75 mg/2ml
- VI- Ethanol extract 18.75 mg/2ml

REFERENCES:

- Dictionary of Indian Medicinal plant, 105.
- The wealth of India, Raw materials, Revised edition Vol.3, 1982, p.269-271..
- Journal of American oil and chemical society, 60(5) : 949-950.
- Aogya (Manipal, India) 10(1). 1984: 56-60.
- Plant foods and Human Nutrients (Dordrecht, Netherland), 1988; 38(3): 235-241.
- Indian drugs 1990; 27(4):257-258.
- Bulletin of faculty of pharmacy (Cario University Egypt) 1990; 28(2):79-83.
- Investigation on Anti feedant and antihelmentic potential of Adothoda vasica Nees, Indian journal of Natural products 1988; 14(1):26.
- Paul .L, Schiff J.R: Bis benzyl iso quinoline alkaloids, Journal of Natural products 1987; 50(4):620-622.
- Johg Hwan Kwak, Kyung Bok Lee, Francis J Sschmitz: Four new coumarin derivatives from Artemisia keiskeana, Indian journal of Natural products 1989; 5(2):8-10.
- Spitzer .V: Fatty acid composition of some seed oils of the Sapindaceae, Phytochemistry, 1996; 42(5):1357-1360.
- An Asoc.Quim.Argentina, 1986; 74(5):571-574.
- Biochemistry and syn Ecol (Cardoba Univ, Argentina) 1992;20(5):469-471
- Kokate C.K.: *Practical pharmacognosy*, 4th edn. (Vallabh Prakashan Pune) 1996, 107.
- Harbone J.B: *Phytochemical methods*.1973.
- Plaisted, Philip. H: *Contributions from Boyee Thompron Institute*1958; 9: 231-44.
- Sethi P.D: *HPTLC Quantitative Analysis of Pharmaceutical Formulations*, 1st Ed.CBS Publishers and Distributors, New Delhi. 1996; 3-73.
- An Asoc.Quim.Argentina, 1986; 74(5):571-574.
- Ghosh M .N: *Fundamentals of experimental pharmacology*, 2nd Edition 1984,144.
- Robert A: Turner, *Screening methods in pharmacology*, Academic press, New York, 1965, 104.
- Kulkarni S .K: *Handbook of Experimental pharmacology* p. 63-65.
- Eddy N. B: Studies of morphine and codeine and their derivatives. *J. Pharmacol.* 1932; 45: 339.
- Kamant J.V and Rana A .C: *Indian Drugs*. 2003; 40:292.

24. Akthar M.S and Munir M: Evaluation of gastric antiulcerogenic effects of *Solanum nigrum*, *Brazsica oleracea* and *Ocimum basilicum* in rats. J Ethano Pharmacol, 1989; 27:163-176.
25. Panda P.K and Panda D.P: Methods used for testing of Antiulcer drugs, Pharma times, 1993: 9-11.
26. Parmar N.S: Effect of Nalaxone and Morphine on the experimentally induced gastric ulcer in rats. Indian Drugs. 1991; 29 (7): 299-302.
27. Shay H, Komavoro S.A, Fele S.E, Meraze D, Grusetin M and Sipler H.A: A simple method for the uniform production of gastric ulceration in the rat. Gastroenterology. 1945; 5: 43-61.
28. Raj Kapoor B, Anandhan R and Jayakar B, Antiulcer effect of *Nigella sativa* Linn Against gastric ulcers in rats. Current Science. 2002; 82: 177-179.
29. Pandit S, Sur T.K, Jana U, Bhattacharya D and Debnath P.K: Antiulcer effect of Shanka bhasma in rats, a preliminary study. Indian J Pharmacol.2000; 32: 378-380.
30. Amritage P, Eds., In; Stastical Methods in Medical Research, Blackwell Scientific Publications, London, 1971. 217.
31. Piper D.W and Stiel D.D: Pathogens of chronic peptic ulcer, current thinking and clinical implications. Medical Progress.1986; 2; 7-10.
32. Ra A and Tobe S.W: Annals of Pharmacotherapy .2004; 38:41.
33. Zlabek J.A and Anderson C.G: Annals of Pharmacotherapy, 2002; 36:809.
34. Gonalez P, Sorinao V, Lopez P and Nivero e, Allergic immunopathaology. 2002; 30:342.
35. Fisher A.A, Lecounter D.G:Drug safety, 2001;24: 39.
36. Brown G.G. An introduction to Histotechnology, I st edition. (Appleton century crofts, Newyork, 1978) 293-308.
37. Jainu M, Mohan K.V and Devi C.S.S. Gastro protective effect of *Cissus quadragularis* extract in rats with experimentally induced ulcer. Indian J Med Res.2006; 123:799-806.
38. Goel R.K and Sairam K. Antiulcer drugs from indigenou sources with emphasis on *Musa sapiteum*, *Tamrabhasma*, *Asparagus racemosus* and *Zingeber officinale*. Indian J Pharmacol .2002; 34:100-110.
