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Full Length Original Research Paper

Gastroprotective and Anti-ulcer activity of Aloe vera juice, Papaya fruit juice and Aloe vera and Papaya fruit combined juice in Ethanol induced Ulcerated Rats.

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Abstract:
Peptic ulcer is the most prevalent gastrointestinal disease. Even though a wide range of drugs are available for the treatment of peptic ulcer, but many of these do not fulfill all the requirements and have side effects. These factors have attracted researchers to investigate the natural products which have more efficacy, less side effects and less expensive for the treatment of peptic ulcer disease. In the present study the anti ulcer activity of (1) *Aloe vera* juice, (2) papaya fruit juice (3) *Aloe vera* and papaya fruit combined juice were investigated in the ethanol induced ulcerated rats. The administration of plant juices decreased the offensive factors like ulcer index and acid secretion and also reduced the amount of protein and carbohydrates in the stomach fluid. Further, plant juices increased the defensive factors like activity of oxidative enzymes such as superoxide dismutase and reduced glutathione. Activities of alkaline phosphatase and lipid peroxide were higher in the diseased condition and same were reduced after the treatment with plant juices. Content of haemoglobin and RBC and WBC counts were brought back to normalcy after the treatment with plant juices. The efficacy of plant juices was comparable with the reference drug-Ranitidine. The results of the present study reveal that the plant juices are having efficiency in the gastroprotective activity. It is recommended that the above said plant juices can be further studied for their anti ulcer efficacy in human subjects.

Keywords: *Aloe vera* juice, papaya fruit juice, Ranitidine, peptic ulcer, animal study, antiulcer activity.

Introduction

Ulcer is defined as erosion in the lining of the stomach or duodenum and is caused by the disruption of the gastric mucosal defense systems. Ulcer in the stomach is called gastric ulcer and in the duodenum is called duodenal ulcer and together it is named as peptic ulcer. Ulcer incidence varies with the type of ulcer, gender and age. Peptic ulcer has initiated as open craters or sores in the inner lining (mucosa) of the stomach or the duodenum. A coating of mucus and other biochemicals normally shield the stomach and duodenum from digesting themselves. When these protective mechanisms are disturbed, powerful digestive acids can erode into the lining of these organs and cause ulcers. Ulceration is an imbalance between the rate of secretion of gastric juice and the degree of protection afforded by the gastroduodenal mucosal barrier as well as the neutralization of the gastric acid by duodenal juice. Infection by the bacterial pathogen *Helicobacter pylori*, frequent usage of Non-Steroidal Anti-inflammatory Drugs (NSAIDs) and high acid secretion are main reasons for induction of ulcer. Other causes of peptic ulcer are smoking, alcohol consumption, psychological stress and irregularity in diet. Reduction of gastric acid production as well as re-enforcement of gastric mucosal production has been the major

approaches to cure peptic ulcer. As a result, more and more synthetic drugs are introduced and offering newer options for treatment of peptic ulcer. Because of several side effects of synthetic medicines, there is new thought of better natural alternative for the treatment of peptic ulcer.

Medicinal plants are frequently used in traditional medicines to treat various diseases in different parts of the world. The active molecule present in the traditional medicinal herbs is helpful in the exploration of scientific basis for therapeutic uses. Screening of herbs for their potential therapeutic efficacy is still important and might provide a useful source of new antiulcer compounds for developing novel drugs or alternatively, as simple dietary supplements to the existing therapy for faster and efficient remedy. Several herbal plants are reported to have antiulcer activity, few examples are *Cissus quadrangularis* [1]; *Thespesia populnea* [2]; *Bauhinia racemosa* [3]; *Withania somnifera* [4]; *Tephrosia populnea* [5]; *Bambusa arundinacea* [6]; *Ocimum sanctum* [7]; *Emblica officinalis* [8]; *Pterospermum acerifolium* [9]; *Bauhinia variegatea* [10] and *Terminalia chebula*[11].

The present study evaluates the antiulcer and gastro protective efficacy of (1) *Aloe vera* (*Aloe barbadensis* Mill.) leaf juice, (2) papaya (*Carica papaya* Linn.) fruit juice and (3) combined juice of *Aloe vera* and papaya fruit in alcohol induced ulcerated rats.

Materials and Methods

Collection and preparation of plant juices

Fresh leaves of *Aloe vera* and papaya fruits were collected from the Sri Padhuga Agriculture Farm at Samayapuram village, Tiruchirappalli District, Tamil Nadu State. The plant materials were identified and brought to laboratory. The tip and basal portions of *Aloe vera* leaves were trimmed off and washed in clean water to remove soil and other dirty materials. Finally the leaves were soaked in clean sanitized water (containing 0.1% Gramicid). After removing the rinds from the leaves, the inner gel was collected and ground. The papaya fruit was cleaned in sanitized water and cut into small pieces and again thoroughly washed. They were ground in a mechanical mixer to get the juices and they were filtered through muslin cloth. The juices were stored in air tight container and kept 4°C until further use.

Experimental animals

Healthy adult albino strains of Wister rats, weighing 150-200 g were used as experimental animals. Animals were housed in polypropylene cages at 24±2°C in the college animal house and fed with commercial pellet diet and water *ad libitum*. All the studies were conducted according to the ethical guidelines of CPCSEA after obtaining necessary clearance from the ethical committee (approval No: 790/03/ac/CPCSEA).

Experimental design

Group I : Healthy control animals

Group II : Disease control animals, ulcer was induced with 10.0 ml/kg-bw of 40% alcohol (ethanol).

Group III: Ulcer induced rats treated with the *Aloe vera juice* (20.0 ml/kg-bw) for 22 days.

Group IV: Ulcer induced rats treated with the papaya fruit juice (20.0 ml/kg-bw) for 22 *d*ays.

Group V: Ulcer induced rats treated with the *Aloe vera* and papaya fruit combined juice(20.0 ml/kg-bw) for 22 *d*ays.

Group VI: Drug control animals- alcohol induced ulcerated animals treated with Ranitidine (50mg/kg-bw) for 22 days.

Induction of ulcer

Animals were starved for 12 hours with access only to drinking water *ad libitum*. Gastric ulcer was induced in group II, III, IV, V and VI animals with 10.0 ml/kg-bw of 40% alcohol (ethanol).

Subsequently from the same day of the treatment the group III animals was given *Aloe vera* juice 20.0 ml/kg- body weight (bw). Group IV animals were given papaya fruit juice 20.0 ml/kg-bw. Group V animals were given *Aloe vera* juice + papaya fruit juice 20.0 ml/kg-bw. Group VI animals were given 50 mg/kg-bw of Ranitidine. Ranitidine was dissolved in distilled water and given to the respective animals. After 22 day, the animals were sacrificed. The animals were anaesthetized using ether and the abdomen was opened without causing any damage to its blood supply. Blood samples from each rat were collected. Then passed a thread around the pyloric sphincter and applied a tight knot close to the abdomen wall and the stomach was removed. The stomach fluid was collected in a graduated centrifuge tube. Samples of blood, gastric fluid and stomach tissues were collected from each animal kept in 4°C in refrigerator until further analysis.

Determination of ulcer index in the stomach [11, 12]

The stomach was cut opened and the mucosa was washed slowly with saline. The stomach was pinned on frog board and observed under microscope (10×) for ulcer mean score for each animal. The result is expressed as ulcer index by using following formula.

$$\% \text{ Ulcer index} = \frac{(USc - Ust)}{USc} \times 100$$

USc = Ulcer surface area in control and USt = Ulcer surface area in treated animals.

Determination of total acidity in gastric fluid [13].

Centrifuged the gastric fluid at 1000 rpm for 10 min, the volume was noted and pipette out 1ml of supernatant liquid. Diluted it to 10 ml with distilled water and titrated the solution against 0.01N sodium hydroxide (NaOH) using Topfer's reagent as indicator. Titrated up to the end point that the solution turned to yellowish orange colour. Noted the volume of NaOH required for neutralizing the free hydrochloric acid present in the gastric juice. Then 2 to 3 drops of phenolphthalein solution was added and titration was continued until a definite red tinge was reappeared. The difference between the two readings indicated the volume of NaOH required for neutralizing the combined acid present in the gastric fluid. The sum of the two titrations was the total acid present in the gastric fluid.

Acidity was calculated as follow:

$$\text{Acidity} = \frac{\text{Vol. of NaOH} \times \text{Normality of NaOH}}{\text{Vol. of gastric juice used}}$$

The total acidity was expressed as mEq/dl

Estimation of total protein [14].

The content of dissolved proteins in the gastric fluid was estimated in the alcoholic precipitate obtained by adding 90% of alcohol with gastric fluid in 9:1 ratio. Then 0.1 ml of alcoholic precipitate of gastric fluid was dissolved in 1 ml of 0.1 N NaOH and from this solution 0.05 ml was taken in another test tube. To this 4 ml of alkaline copper reagent was added and kept for 10 min. Then 0.5 ml of phenol reagent was added and kept for 10 min and the solution was allowed for colour development. Reading for optical density was taken at 610 nm against blank prepared with distilled water. The protein content was calculated from standard curve prepared with bovine albumin. (Standard Bovine albumin: 20

mg of bovine serum albumin was dissolved in 100 ml of distilled water. Few drops of NaOH were added to it to aid complete dissolution of bovine serum albumin and also to avoid frothing and it was allowed to stand over night in a refrigerator). The result was expressed in terms of µg/ml gastric fluid.

Estimation of carbohydrates [15]

To 0.1 ml of gastric fluid 2 ml of 3N sulphuric acid and 2 ml of sodium tungstate were added and mixed. The content was centrifuged at 3000 rpm for 10 min. From this 0.4 ml of supernatant was taken in test tubes and the blank was prepared without gastric fluid. The volume in all test tubes was made up to 1 ml by adding distilled water. After 10 min of incubation in ice cold water bath, 4 ml of anthrone reagent (freshly prepared by dissolving 0.2 g of anthrone in 100 ml of concentrated sulphuric acid) was added in to all the test tubes. The test tubes were kept in the boiling water bath for 15 min. After cooling down the solution, read the optical density at 540 nm. The carbohydrate content was calculated from standard curve prepared with different strength standard glucose solution (50-200 µg of glucose dissolved in 1ml distilled water) and the results has been expressed in terms of µg/ml of gastric fluid.

Assay of alkaline phosphatase [16]

The reaction mixture was prepared by adding 1.5 ml of 0.1M carbonate buffer (pH 10), 1 ml of 0.1M disodium phenyl phosphate and 0.1 ml of 0.1M magnesium chloride. Finally 0.1 ml of gastric fluid was added to the reaction mixture. The reaction mixture was incubated at 37°C for 15 min. Control tubes were prepared similarly but gastric fluid was not added. The reaction was arrested by the addition of Folin's phenol reagent. 1ml of 15% sodium carbonate was added to the reaction mixture and the colour developed was read at 640 nm after 10 min. The enzyme activity was expressed as IU/ml.

Assay of reduced glutathione [17]

To 0.5 ml of tissue homogenate, 20% TCA was added and the contents were mixed well for complete precipitation of protein and centrifuged. To the clear supernatant solution, 2.0 ml of DTNB reagent (0.6mM DTNB in 0.2 M Phosphate buffer, pH 8.0) was added and then 0.2 M phosphate buffer was added to make a final volume of 4.0 ml. The absorbance was read at 412 nm against a blank without sample. The standard graph was plotted with a series of standard solutions of reduced glutathione (prepared from 1 mg of reduced glutathione dissolved in 100 ml of distilled water) and determines the glutathione in the samples. The amount of glutathione was expressed as nano moles of GSH oxidized/mg protein.

Assay of lipid peroxide [18]

To 0.1ml of tissue homogenate, 4 ml of 0.85N H_2SO_4 and 0.5 ml of 10% phosphotungstic acid were added and stirred well. The content was centrifuged at 5000 rpm for 10 min. The supernatant was discarded and the sediment was mixed with 2.0 ml of H_2SO_4 and 0.3 ml of 10% phosphotungstic acid. The mixture was centrifuged for 10 min. The sediment was suspended in 4.0 ml of distilled water and 1 ml of TBA reagent (mixture of equal volume of 0.67% TBA aqueous solution and glacial acetic acid). The tube was kept in a boiling water bath for 1 hr, after cooling, 5 ml of butanol was added. The butanol phase was separated out and read at 532 nm. The reaction mixture without tissue homogenate was used as blank. The enzyme activity was expressed as nano moles/mg tissue protein.

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Assay of superoxide dismutase [19]

To 0.1ml of tissue homogenate 0.75 ml of ethanol and 0.15 ml of ice cold chloroform were added and centrifuged. The supernatant was taken and 0.5 ml of 0.6nM EDTA solution and 1 ml of potassium phosphate buffer (0.1 M; pH 10.2) were added and mixed well. The reaction was initiated by the addition of 0.5 ml of fresh epinephrine (1.8nM) and the increase in absorbance was measured at 480 nm. The reaction mixture without tissue homogenate was used as blank. The enzyme activity was expressed as U/ml.

Studies on haematological parameters [20]

Determination of haemoglobin

20µl blood is added to 4 ml of diluent (Drabkin's Solution) and mixed well by inverting the tube several times. It is allowed to stand at room temperature for 5-10 minutes so that all haemoglobin is converted to HiCN. The absorbance is then measured in the spectrophotometer at 540 nm and the reading is noted. Absorbance of a known standard is also read in spectrophotometer with each batch of tests and Hb is calculated by the following formula:

$$\text{Hb(g/dl)} = \frac{\text{bsorbance of test X Concentration of Standard}}{\text{Absorbance of Standard}}$$

Enumeration of RBC count

The anticoagulated blood was sucked into pipette up to the mark of 0.5. It was diluted with RBC diluting fluid (Hayem's diluting fluid) by sucking up to 100 mark (dilution of 1 to 200). The pipette was shaken for a min and wiped away the excess of blood by using blotting paper. Placed a drop of blood at the edge of haemocytometer and placed a cover slip on it, which covered the counting chamber. The RBCs were counted under microscope in each of five fields (each with 16 smallest squares).

Enumeration of WBC count

The anticoagulated blood was sucked into pipette up to the mark of 0.5. It was diluted with WBC diluting fluid (Turkey's fluid) by sucking up to 10 mark. The pipette was shaken for a min and wiped away the excess of blood by using blotting paper. Placed a drop of blood at the edge of the haemocytometer and placed a cover slip on it, which covered the counting chamber. WBCs are counted in the four outside large squares of counting chamber.

Statistical analysis

The data of results obtained were subjected to statistical analysis and expressed as mean ± SD. The data were statically analyzed by one way analysis of various (ANOVA) and $p<0.05$ was considered to be significant.

Values are ± SEM. n=6

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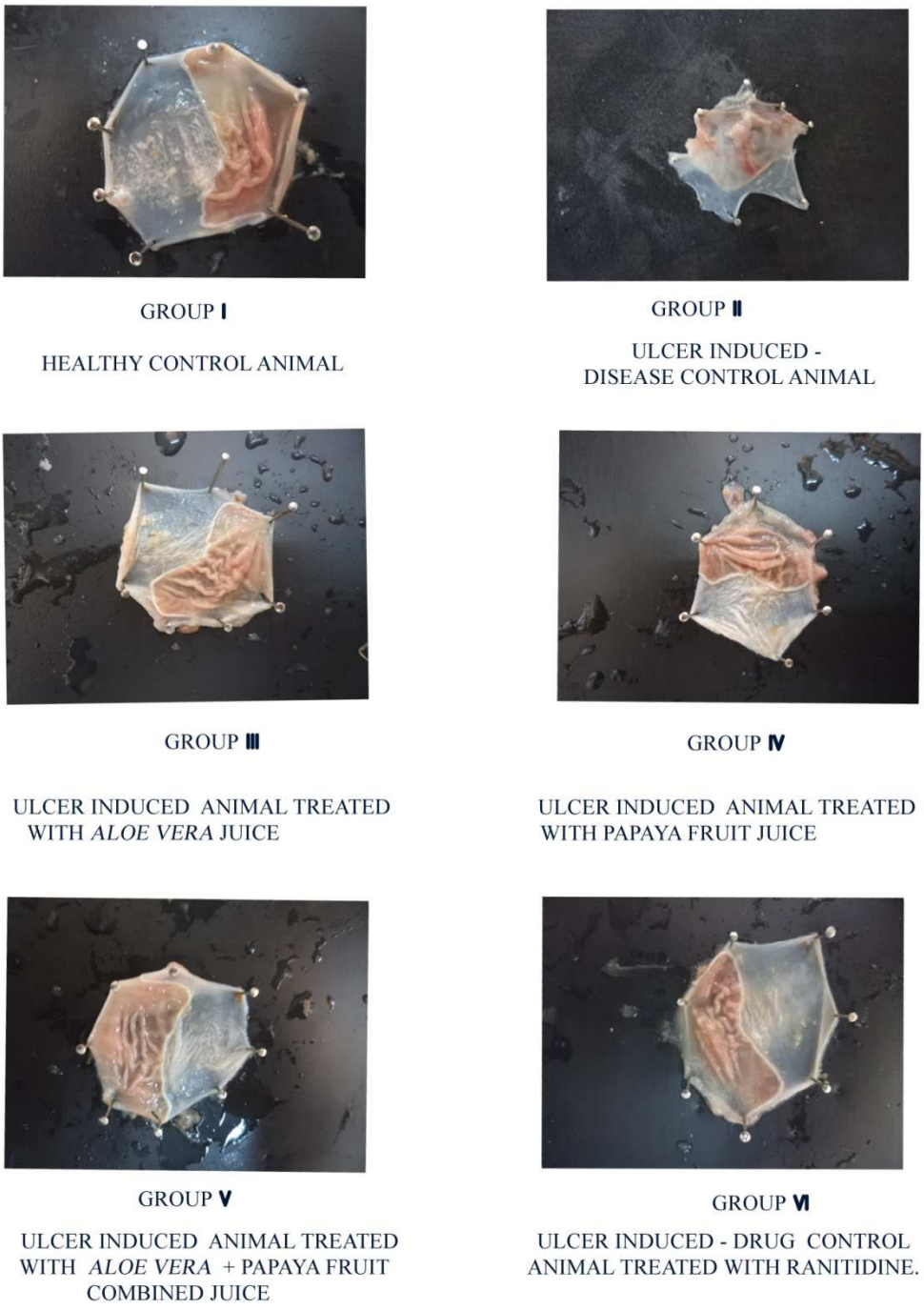

PLATE : 1- PHOTOGRAPHS SHOWING ULCERATION IN THE MUSCOSA OF EXPERIMENTAL ANIMALS.

Results

The results on the effect of *Aloe vera* juice, papaya fruit juice and combined juice of *Aloe vera* and papaya fruit reveals that the plant juices (plant drugs) have significantly ($p < 0.001$) reduced the ulcer index (PLATE 1). Ulcer index was severe (3.23 ± 0.21) in the disease control (ulcer induced animals) and the same was decreased in other group of animals which were treated with plant juices. Maximum inhibition of ulcer index was observed in the animals treated with combined juice of *Aloe vera* and papaya fruit (Table 1).

Total acidity was increased in the ethanol induced ulcerated rats (disease control animals)

and the same was decreased in the rats after the administration plant drugs and ranitidine (group III, group IV, group V, group VI) (Table 1)

The levels of protein and carbohydrate in the gastric fluid were increased in the ulcer induced animals, when compared to healthy control animals. But the intake of plant juices significantly decreased the protein and carbohydrate levels. (Table 1).

The activities of antioxidant enzymes such as alkaline phosphatase and lipid peroxide increased in the ulcerated animals and the treatment with plant juices and ranitidine decreased the activities (Table 2). The activities of reduced glutathione and superoxide dismutase were drastically decreased in the ulcer induced group of rats. But the activities of all the enzymes were increased in the animals treated with plant juices. The activities were comparable with standard drug ranitidine. (Table 2).

The haemoglobin level and Red Blood Cells (RBC) count were reduced in the ulceration condition. But both them were significantly ($p < 0.01$) increased in animals which were treated with plant juices. Further the effect was comparable with healthy control animals. White Blood Cells (WBC) count was higher in the disease control rats (Group II) than healthy control animals (Group I). But the administration of plant juices and ranitidine brought down the WBC count in group III, IV and V animals. The amount of WBC was almost comparable to the healthy control animals (Table 3).

Table 1: Effect of *Aloe vera* juice, papaya fruit juice and *Aloe vera* + papaya fruit combined juice on ulcer index, total acidity, protein, and carbohydrate levels in alcohol induced ulcerogenic rats.

Parameters	Group I	Group II	Group III	Group IV	Group V	Group VI
Ulcer index	00.00	3.23±0.21***	0.66±0.13*	0.43±0.23**	0.31±0.22	0.18±0.11
Total Acidity (mEq/dl/mg)	41.5±0.42	88.2±0.31**	48.9±0.46*	46.3±0.34	37.7±0.42**	37.5±0.52*
Protein (µg/ml)	310.65±1.4	495.13±1.2**	341.6±0.71*	314.36±0.51*	216.56±0.41	255.80±0.52
Carbohydrate (µg/ml)	165.00±8.2	192.66±6.3**	170.66±7.1	168.33±6.2*	169.66±8.2*	176.00±5.2

Values are expressed as mean±S.E.M (n=6) *p<0.05, **p<0.01, ***p<0.001 Compared with control group

Table 2: Effect of *Aloe vera* juice, papaya fruit juice and *Aloe vera* + papaya fruit combined juice on alkaline phosphatase, lipid peroxide, reduced glutathione and superoxide dismutase activity in alcohol induced ulcerogenic rats.

Parameters	Group I	Group II	Group III	Group IV	Group V	Group VI
Alkaline phosphatase (IU/ml)	35.13±5.2	81.16±2.3*	35.13±5.4**	45.20±6.1*	28.83±6.2	28.90±7.2*
Lipid peroxide (nmoles/ mg)	36.03±3.4	39.50±2.1*	20.43±3.2***	29.56±6.2**	20.10±5.7*	21.76±3.3
Reduced glutathione (nmoles/ml)	82.26±5.2	52.56±3.4*	81.10±4.2**	94.96±5.5*	97.80±6.7*	83.56±4.8*
Superoxide dismutase (U/ml)	51.76±4.3	29.23±3.1**	61.70±5.5*	63.03±8.2*	67.30±4.9*	57.50±7.6*

Values are expressed as mean±S.E.M (n=6) *p<0.05, **p<0.01, ***p<0.001 Compared with control group

Table 3: Effect of *Aloe vera* juice, papaya fruit juice and *Aloe vera* + papaya fruit combined juice on haemoglobin content, Red Blood Cells (RBC) and White Blood Cells (WBC) counts in alcohol induced ulcerogenic rats.

Parameters	Group I	Group II	Group III	Group IV	Group V	Group VI
Haemoglobin (g/dL)	12.83±3.4	7.25±4.2**	12.46±4.2*	13.33±6.6*	13.00±4.3*	13.33±3.9*
Red Blood Cells (RBC) (million cells/mm^3)	6.73±0.8	4.54±0.4*	7.82±0.8**	7.25±0.4*	7.81±0.5*	7.93±0.4*
White Blood Cells (WBC) (thousand cells/mm^3)	7.75±0.8	9.43±1.5**	7.62±1.2*	7.85±1.5*	7.61±1.4**	7.33±0.6*

Values are expressed as mean±S.E.M (n=6) *p<0.05, **p<0.01, ***p<0.001 Compared with control

Discussion

The experimental animals were divided into 6 groups and each group consisting of 6 animals.

Animals in group I were maintained as healthy control where as animals in the group II were administered with 40% ethanol and ulcer was induced. An animal in the group II was sacrificed after 48 hrs of ulcer induction and checked the stomach for ulceration. Ulcer was noticed and the observation confirmed that the group II animals were ulcerative. The plant juices, such as (1) *Aloe vera* juice, (2) papaya fruit juice (3) combined juice of *Aloe vera* juice and papaya fruit and ranitidine (standard drug) were started administered after 48 hrs. On 22nd day after treatment the animals were sacrificed and analyzed for the curative effect of plant juices.

The administration of alcohol has induced the peptic ulcer in the experimental animals and the ulcerated condition increased the levels of offensive factors such as ulcer index and total acidity. Administration of plant drugs significantly decreased the levels of offensive factors.

Protein and carbohydrate levels in the stomach fluid were increased during ulcerogenesis. It is reported that ethanol has the ability to damage the gastric mucosa by mechanical injury [21]. Further, ethanol induced gastric lesion formation may be due to stress in the gastric blood flow which contributes to the development of hemorrhage and tissue damage due to necrosis. Hydrochloric acid present in the gastric fluid further deepens the necrosis and increase the tissue damage. Because of the tissue damage the protein and carbohydrate levels were increased in the stomach fluid of ulcerated animals. Administration of plant juices has decreased the levels of protein and carbohydrate in animals. This indicates that plant juices healed the ulcer wounds in the stomach, so that disintegration of protein and carbohydrate from tissues was prevented and the dissolution of protein and carbohydrate in the stomach fluid was reduced. The treatment with *Aloe vera* juice and papaya fruit juices may enhance the gastric mucosal defensive factors. Therefore the protection afforded by plant juices against ethanol induced gastric ulceration may be due to inhibition of the 5- lipoxygenase pathway or to the antagonistic activity of leukotrienes. Flavonoids are implicated in the protection of the gastric mucosa from necrotizing substances[22].

Rivera-Pastrana et al.[23] reported that flavonoids like β-carotene, rutin (quercetin 3-o-rutinoside), lutein, zea-xanthin and cryptoxanthin are reported in the papaya fruit. Flavonoids have been reported as highly useful in the therapy of acute and chronic gastric ulceration [24,25,26]. The antiulcer and gastroprotective effects of quercetin and its glucosides are reported by

many researchers. Martin *et al.,* [27] and Kahraman *et al.,* [28] reported the antioxidant mechanisms involved in gastroprotective effects of quercetin in ethanol induced ulcerative rats. Antiulcer activity of flavonoids by stimulating Platelet Activator Factor (PAF) in acid –ethanol induced ulcerative animal model was reported by Izzo *et al.*,[29]. Effects of quercetin and other flavonoids on the reserpine induced ulcerogenic mice was recorded by Barnaulov *et al.,*[30]. Motilva *et al.,*[31] recorded the effects of naringenin and quercetin on the acetic acid induced ulcercerogenic rats.

Further, papaya fruit is also an excellent source of Vitamin-A and vitamin C. Vitamin A is required for maintaining healthy mucus membrane. Vitamin C has many important functions like scavenger of free radicals, immune booster, and anti-inflammatory agent. The wound healing efficacy may be further attributed to the availability of micro and macro nutrients and other nutraceutical constituents from the plant juices.

Alkaline phosphatase and lipid peroxide were found higher in the ulcer induced animals. The release of more amount of alkaline phosphatase has been suggested to play a role in the tissue necrosis process and the increasing trend of alkaline phosphatase was observed with various other animal models of gastrointestinal ulceration [32]. In the present study the activities of alkaline phosphatase, and lipid peroxide were higher in the diseased condition and the same were decreased after the treatment of plant juices. Further, the activities were comparable with healthy control animals, which reveal the plant juices brought normalcy in the activities of these enzymes. Augustine [33] observed that the aqueous extract of papaya fruit significantly decreased the activities of alkaline phosphatase and lipid peroxide in aspirin induced ulcerated rats.

Reduced glutathione and superoxide dismutase are considered as antioxidant enzymes which are responsible for the antioxidant activities (scavenging and disposal of free radicals from the tissues). In the present study activities of reduced glutathione and superoxide dismutase enzymes were decreased in the ulcerated animals, where as the activities of these enzymes were increased in the animals which were treated with plant juices. Further, the animals treated with standard drug (ranitidine) showed lesser enzyme activity than the animals treated with plant juices. This observation clearly indicates that the plant juices are more capable of enhancing the antioxidant activity. This action may be due to the availability of antioxidant phytochemicals in the plant juices. Lot of phenolic compounds like ferulic acid, caffeic acid, gallic acid and protocatechuic acid and their glucosides are reported from papaya fruit [23]. These phenolic compounds may be responsible for the enhanced antioxidant activity of papaya fruit juice. There are evidences that consumption of antioxidant phenolic compounds is associated with prevention chronic diseases such as cancer, diabetes and cardiovascular disease. The present study proves that phenolic compounds are beneficial in gastroprotection and antiulcer activity.

It is reported that papaya fruit juice contains beta- carotene and other flavonoids and *Aloe vera* juice contains glucomannans, amino acids, lipids, sterols and vitamins. Roa *et al.,* [34] reported that bioflavonoid protects against oxidative stress related to ulcers in rats. Further, Russo *et al.,* [35] reported that flavonoids act as antiradical and

antioxidant agents and protect cell/tissue damage.

Anti-inflammatory action of *Aloe vera* gel is well documented. *Aloe vera* gel inhibits the cyclooxygenase pathway and reduces prostaglandin E_2 production from arachidonic acid. Recently, the novel anti-inflammatory compound called C-glucosyl chromone was isolated from *Aloe vera* gel extracts. This may be the possible explanation for ulcer curative property of *Aloe vera* juice [36].

The hematological parameters such as haemoglobin, RBC, and WBC are the indicators of healthy physiological function of the circulatory system. It is well documented that biosynthesis of haemoglobin and RBC were decreased during ulcer disease condition. The same observation was made in the present study also. Both haemoglobin and RBC contents were lesser in the ulcerated rats when compared to the healthy rats. Treatment with *Aloe vera* juice alone and combined juice of *Aloe vera* and papaya fruit enhanced the haemoglobin content and RBC counts. Gopinathan [37] and Gopinathan *et al.* [38] reported that reduction in the haemoglobin contents and RBC counts were increased by the treatment with *Aloe vera* juice and *Aloe vera* juice in combination with banana stem juice and banana flower juice in the alcohol induced ulcerated rats.

Ulcerogenesis drastically enhanced the production of white blood cells (WBC) in the rats. This may be due to the over production WBCs during disease condition to combat the pathogens which were infected in the ulcerated tissues. Further, it was observed that WBCs count was brought to normal after the treatment with plant juices and count was comparable to healthy control animals.

From the present study, it is well evidenced that *Aloe vera* juice, papaya fruit juice and *Aloe vera* and papaya fruit combined juice have the efficacy in curing peptic ulcer. But *Aloe vera* juice in combination with papaya fruit juice showed better performance in all parameters studied. This may be attributable because of the phyto-nutrients and phyto-chemicals present the combined juice.

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