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Evaluation of Anti-ulcerogenic Potential of *Aloe vera* Leaf Gel Extract Studied in Experimental Rats

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Abstract: In the present study, anti-ulcerogenic potential of *Aloe vera* leaf gel was evaluated using two different models of gastric lesions induced in experimental rats; 1) Indomethacin-induced gastric lesions and 2) Ethanol-induced gastric lesions. Pretreatment with oral administration of the extract of *Aloe vera* gel (150 mg kg^{-1}) prevented the formation of acute gastric lesions induced by both the experimental models. Further, treatment with the ethanolic extract of *Aloe vera* leaf gel for a period of 15 days significantly reduced the ulcer index, ulcerated surface and significantly elevated the levels of glycoprotein contents in gastric juice. The histological observations made on the stomach tissue provided further evidence on the anti-ulcerogenic potential of the *Aloe vera* leaf gel extract.

Key words: *Aloe vera*, anti-ulcerogenic effect, indomethacin-induced ulcer, ethanolinduced ulcer

Introduction

The term ulcer was first coined by Quike in 1882 and it is now regarded as one of the most important gastrointestinal disorders (Clinch, 1989). Peptic ulcers are ulcers in the stomach or duodenum. These are the parts of the gut where acid baths the surface. Gastric mucus is a highly hydrated viscoelastic gel that protects the mucosa from the mechanical stress as well as from erosion by pepsin and HCl (Allen *et al*., 1993). The polymer matrix of the gel is provided by large secreted glycoproteins referred to as mucus glycoproteins or mucins which are produced by all cells in the surface mucosa as well as by certain cells in the gastric glands (Nordman *et al*., 1997).

Peptic ulcers are caused when the natural balance between aggressive factors of acid and pepsin and defensive mechanisms of mucus, bicarbonate and mucosal turnover is shifted in favour of the former (Alarcon de la Lastra *et al*., 1994). Gastric ulceration is caused by many factors like non-steroidal anti- inflammatory drugs (NSAIDs), alcohol, smoking, *Helicobacter pylori* infection, stress etc., (McGuigan, 1991). Five to ten percent of populations experience a peptic ulcer at some point in their lives. On rare occasions, a gastric ulcer may be malignant.

A rational therapy for peptic ulcer still remains elusive and search for safer potential drugs is being carried out. Although H_2-receptors (ranitidine, famotidine), proton-pump inhibitors (omeprazole, lansoprazole), antibiotics (metronidazole, amoxicillin, clarithromycin, tetracyclin etc.) and other drugs are currently used for the efficient management of the peptic ulcer disease, they also have some limitations (Shimokawa *et al*., 1996; Martelli *et al*., 1998).

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Use of natural drugs in gastric ulcers is well documented (Goel *et al*., 1986; Sairam *et al*., 2001). Information provided by practitioners of Indian traditional medicine suggests that *Aloe vera* possesses useful antiulcerogenic activity. *Aloe vera* is a perennial, drought-resistant, succulent plant with a whorl of elongated, pointed leaves. Although *Aloe vera* is a member of the Lily family, it is very cactus like in its characteristics. The epidermis of the leaves has a thick cuticle and beneath is a zone of chlorenchyma. The mucilaginous tissue made up of large thin-walled mesophyll cells in the center of the leaf is called *Aloe vera* gel. The peripheral bundle sheath cells contained the bitter yellow sap, commonly termed as *Aloe* juice or *Aloe vera* sap, which exudes from the leaves when they are cut. The nomenclature of Aloe sap and Aloe gel are often ambiguous. Unlike *Aloe vera* sap, *Aloe vera* gel is colorless and contains no anthraquinones and this gel is responsible for many of medicinal properties of *Aloe vera* reported in folk medicine.

Preliminary studies conducted by us using different solvents revealed the presence of appreciable amounts of biologically active compounds in the ethanolic extract of *Aloe vera* gel (Rajasekaran *et al*., 2005a). Further, recently we have reported the hypoglycemic and anti-oxidant properties of *Aloe vera* gel extract in streptozotocin-induced experimental diabetes in rats (Rajasekaran *et al*., 2004; 2005b). The aim of this study was to corroborate the antiulcer effect attributed to *Aloe vera* leaf gel by evaluating the antiulcer activity of an ethanolic extract of this plant.

Materials and Methods

Preparation of Aloe vera Leaf Gel Extract

Fresh, *Aloe vera* leaves having a length of about 50 cm and about 500-600 g in weight were collected from healthy, five year old plants and the plant was identified in the herbarium of the Centre for Advanced Studies in Botany, University of Madras where a specimen was deposited under accession number (CAS 1070). The rind was selectively removed and the colorless parenchyma was grounded in a blender and centrifuged at 10,000 g to remove the fibers. The supernatant was lyophilized and stored at 4°C (Yagi *et al*., 1998).

Known amount of the lyophilized powder were extracted with 95% ethanol and nearly 85% of the solvent was recovered by distillation over the boiling water bath at atmospheric pressure and the remaiuing under reduced pressure in rotavapor. A known amount of solvent free extract was suspended in water to obtain the desired concentration of the *Aloe vera* leaf gel.

Experimental Animals

Healthy, male albino rats of Wistar strain (150-170 g) were selected for the present study. The rats were procured from Tamil Nadu Veterinary and Animal Sciences University, Chennai. Coprophagy was prevented by keeping the animals in cages with gratings as the floors. The animals were maintained on sterile, standard pellet diet and water *ad libitum*. The experiments were designed and conducted according to the ethical norms approved by Ministry of Social Justice and Empowerment, Government of India and Institutional Animal Ethics Committee Guidelines (IAEC No.01/031/04) for the investigation of experimental pain in conscious animals. Before beginning the experiments, the animals were allowed to acclimatize to animal house condition for a period of one week.

Pretreatment Studies

Six groups of six rats each were pre-treated with single oral administration of *Aloe vera* gel extract at a concentration of 150 mg kg^{-1} body weight 1 h before the ulcerogenic procedures. Gastric

ulceration, was induced in 36 h fasted rats by the oral administration of a ulcerogenic drug, ndomethacin (48 mg kg^{-1} b.w) (Morise *et al*., 1998) and a necrotizing agent, 1 mL of absolute ethanol (Robert *et al*., 1979). The rats were killed 6 h after indomethacin and 1 h after the ethanol administration by an overdose of ether. The stomachs were removed and opened along the greater curvature and the ulcer index was evaluated according to severity and ulcer scores.

Post Treatment Studies

Ethanol-Induced Ulcer Model

Male Wistar rats weighing about 150-170 g were divided into different groups each comprising of a minimum of 6 rats as detailed below.

Group I- Control rats (received 1 mL of water)

Group II- Ethanol-induced ulcer rats (1 mL^{-1} rat)

Group III- Ethanol-induced ulcer rats orally treated with *Aloe vera* gel extract at a dose of 150 mg kg^{-1} b.w., for a period of 15 days.

Group IV- Ethanol induced ulcer rats orally treated with Ranitidine (100 mg kg^{-1} b.w.) for a period of 15 days.

Indomethacin-Induced Ulcer Model

The experimental set up adopted for indomethacin-induced ulcer model was as follows:

Group I- Control rats

Group II- Indomethacin induced ulcer rats (100 mg kg^{-1}. p.o).

Group III- Indomethacin induced ulcer rats orally treated with *Aloe vera* gel extract at a dose of 150 mg kg^{-1} b.w. for a period of 15 days.

Group IV- Indomethacin induced ulcer rats orally treated with Ranitidine (100 mg kg^{-1} b.w.) for a period of 15 days.

The treatment schedule was once a day and the rats were weighed periodically. At the end of the experimental period, all the groups of rats were subjected to pylorus ligation according to the procedure of Shay *et al*. (1945) as modified by Takeuchi *et al*. (1976). Feed was withheld 12 h prior to the operative procedure. The rats were anaesthetized with ether and the abdomen was opened through a mid-line incision. The pylorus was secured and ligated with silk sutures; proper care was taken not to ligate the blood vessels. The abdominal walls were closed and the animals were allowed to recover from anesthesia. After pyloric ligation drinking water was withheld and the gastric juice was allowed to collect for a period of 4 h. The rats were then killed by an overdose of ether and the stomach was removed after clamping the oesophages.

The gastric mucosa was washed with 3 mL of lukewarm distilled water and collected in graduated centrifuge tubes. The gastric juice and washings were homogenized and centrifuged at 5000 rpm for 5 min. The biochemical parameters assayed in gastric juice include gastric volume, total acidity, pH and glycoproteins. Dissolved mucosubstances were estimated in 90% alcoholic precipitate of gastric juice (Shah *et al*., 2003). The precipitate thus obtained was either dissolved in 1 mL: of 0.1 N sodium hydroxide or 1 mL of 0.1 N sulphuric acid. The former was used for the estimation of protein, total hexose, hexosamine and fucose, while the latter was used for the estimation of sialic acid. Hexose was estimated by the method of Niebes, (1972). Hexosamine was estimated by its color reaction with Ehrlich's reagent Wagner (1979). Sialic acid was estimated by the method of Warren (1959). Fucose

was estimated by the method of Dische and Shettles (1948). Total protein was estimated by the method of Lowry *et al.* (1951). Ratio of total carbohydrate (TC = sum of total hexose, hexosamine, fucose and sialic acid) to protein (P) was used as the index of mucin activity.

Determination of Degree of Ulceration

The surface Area (A) mm^2 covered by each lesion was measured (Murakami *et al*., 1992) and the sum of erosion areas per rat stomach was calculated. Percentage Ulcerated Surface (US) was calculated as

$$\%US = \frac{\text{Total area covered by ulcers}}{\text{Total corpus mucosal surface}} \times 100$$

Ulcer index was calculated from percentage ulcerated surface as described by Tan *et al.* (1996). The following score, was used in order to calculate ulcer index: 0. No ulcer; 1. US<0.5; 2. 0.5 = 2.5; 3. 2.5 = 5; 4. 5 = 10; 5. 11 = 15; 6. 15 = 20; 7. 20 = 25; 8. 25 = 30; 9. 30 = 35; 10. US>35.

Histological Studies

A portion of the ulcer region in the stomach tissue was dissected out and fixed in 10% buffered neutral formalin solution for histological observations. After fixation, tissues were embedded in paraffin, solid sections were cut at 5 µm and stained with hematoxylin and eosin (Gordon and Bradburg, 1990). The sections were examined with the help of a qualified pathologist under light microscope and photomicrographs were taken.

Statistical Analysis

The values are expressed as mean±SD for six rats in each group. All the data were analysed with SPSS/7.5 student software. Hypothesis testing method included one way analysis of variance (ANOVA) followed by post hoc performed with Least Significant Difference (LSD) test. The p values of less than 0.05 was considered to indicate statistical significance.

Results

Pretreatment Studies

Table 1 indicates the ulcer index and ulcerated surface in control and experimental groups of both ulcer models. A marked increase was observed in ulcerated surface and ulcer index of both the ulcer-induced groups of rats. In pretreated groups of rats, a significant decrease in ulcer severity was evident by decreased ulcer index.

Post Treatment Studies

Table 2 and 3 show the percentage-ulcerated surface, ulcer index, total gastric volume, gastric acidity and pH of control and experimental groups of rats in both ulcer models. A high degree of ulcer index and ulcerated surface were obtained in both the ulcer-induced groups of rats when compared to control animals. Ulcer index and ulcer severity were found to be comparably higher in indomethacin-induced ulcer rats than ethanol-induced ulcer rats. Treatment with *Aloe vera* leaf gel extract exhibited decrease in both ulcer index and severity of ulcer.

A significant increase was observed in the volume, acidity and a concomitant decrease in pH of gastric juice in both indomethacin and ethanol induced groups of rats. Administration of *Aloe vera* gel

Table1: Effect of pretreatment with *Aloe vera* gel extract on indomethacin-induced and ethanol induced ulcer rats

Groups	Ulcerated surface (%)	Ulcer index
Control	0.0	0
Indomethacin induced ulcer	42.3±3.1[a]*	10
Aloe vera + Indomethacin	2.4±0.16[b]*	2
Ethanol induced ulcer	20.8±0.18[b]*	7
Aloe vera + Ethanol	2.1±0.16[b]*	2

Values are expressed as Mean±SEM of six animals in each group, One way ANOVA followed by post hoc test (LSD). *p<0.05. Comparisons are made between [a] control, [b] indomethacin, Ulcer index: 0. No ulcer; 1. US<0.5; 2. 0.5≤2.5; 3. 2.5≤5; 4. 5≤10; 5. 11≤15; 6. 15≤20; 7. 20≤25; 8. 25≤30; 9. 30≤35; 10. US>35

Table 2: Effect of *Aloe vera* leaf gel extract on the extent of ulceration in control and indomethacin- induced ulcer groups of rats

Parameters	Control	Indomethacin induced ulcer	Indomethacin+ *Aloe vera*	Indomethacin + Ranitidine
Ulcerated surface (%)	0.0	81.3± 6.2[a]*	1.2±0.09[b]*	1.4±0.10[b]*
Ulcer index	0	10	2	2
Total gastric volume (mL)	2.24±0.16	4.34±0.21[a]*	2.89±0.42[b]*	3.01±0.33[b]*
Gastric acidity (mEq L^{-1})	3.78±0.42	6.92±0.56[a]*	3.97±0.33[b]*	4.21±0.43[b]*
pH	4.23±0.32	2.3±0.23[a]*	4.01±0.35[b]*	3.98±0.36[b]*

Values are expressed as Mean±SEM of six animals in each group, One way ANOVA followed by post hoc test (LSD). *p<0.05. Comparisons are made between [a] control, [b] indomethacin, Ulcer index: 0. No. ulcer; 1. US<0.5; 2. 0.5≤2.5; 3. 2.5≤5; 4. 5≤10; 5. 11≤15; 6. 15≤20; 7. 20≤25; 8. 25≤30; 9. 30≤35; 10. US>35

Table 3: Effect of *Aloe vera* leaf gel extract on the extent of ulceration in control and ethanol-induced ulcer groups of rats

Parameters	Control	Ethanol induced ulcer	Ethanol+ *Aloe vera*	Ethanol + Ranitidine
Ulcerated surface (%)	0.0	59.6±4.8[a]*	1.5±0.10[b]*	2.76±1.9[b]*
Ulcer index	0	10	2	8
Total gastric volume (mL)	2.53±0.24	4.45±0.43[a]*	2.72±0.22[b]*	4.40±0.41[b]*
Gastric acidity (mEq L^{-1})	3.45±0.31	6.57±0.44[a]*	3.93±0.23[b]*	6.42±0.52[b]*
pH	4.35±0.52	2.21±0.20[a]*	4.12±0.70[b]*	2.16±0.21[b]*

Values are expressed as Mean±SEM of six animals in each group, One way ANOVA followed by post hoc test (LSD). *p<0.05. Comparisons are made between [a] control, [b] indomethacin. Ulcer index: 0. No. ulcer; 1. US<0.5; 2. 0.5≤2.5; 3. 2.5≤5; 4. 5≤10; 5. 11≤15; 6. 15≤20; 7. 20≤25; 8. 25≤30; 9. 30≤35; 10. US>35

Table 4: Levels of glycoprotein contents and TC: P ratio in the gastric juice of control and experimental groups on indomethacin-induced ulcer rats

Parameters	Control	Indomethacin induced ulcer	Indomethacin+ *Aloe vera*	Indomethacin + Ranitidine
Hexose (μg mL^{-1})	402.4±28.6	312.3±21.2[a]*	396.7±26.1[b]*	401.3±27.6[b]*
Hexosamine (μg mL^{-1})	181.3±13.6	114.8±10.1[a]*	170.3±11.6[b]*	167.6±12.1[b]*
Sialic acid (μg mL^{-1})	37.3±2.7	24.6±2.0[a]*	35.7±2.9[b]*	36.0±3.1[b]*
Fucose (μg mL^{-1})	38.1±3.2	27.3±2.8[a]*	36.8±3.7[b]*	37.2±3.6[b]*
Protein (μg mL^{-1})	236.4±13.5	332.0±32.0[a]*	245.0±18.5[b]*	252.0±17.5[b]*
TC:P ratio	3.70±0.35	2.30±0.15[a]*	3.53±0.31[b]*	3.46±0.27[b]*

Values are expressed as Mean± SD for six animals in eacg group.One way ANOVA followed by post hoc test (LSD). *p<0.05. Comparisons are made between [a] control, [b] indomethacin

extract was observed to significantly decrease the acidity, volume and increases the pH in the gastric juice of both the ulcer-induced rats. The beneficial effect of ranitidine was more pronounced in indomethacin-induced ulcer when compared ethanol-induced ulcer group.

Levels of Glycoproteins

The levels of glycoprotein contents and TC:P ratio in the gastric juice of control and experimental groups of rats on indomethacin induced and rats induced with ethanol are presented in Table 4 and 5,

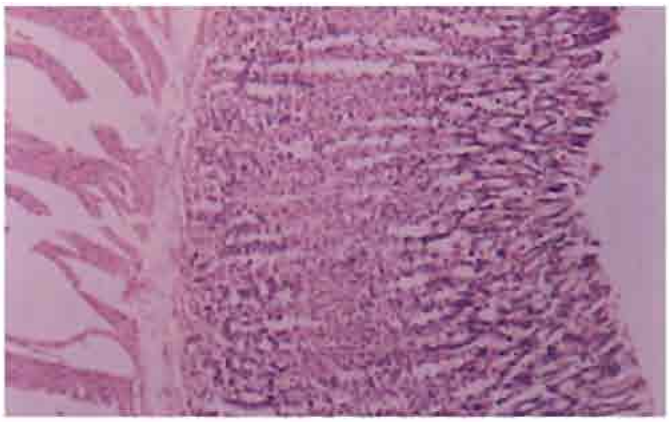

Fig 1a Section of control rat showing normal architecture of the gastric mucosa

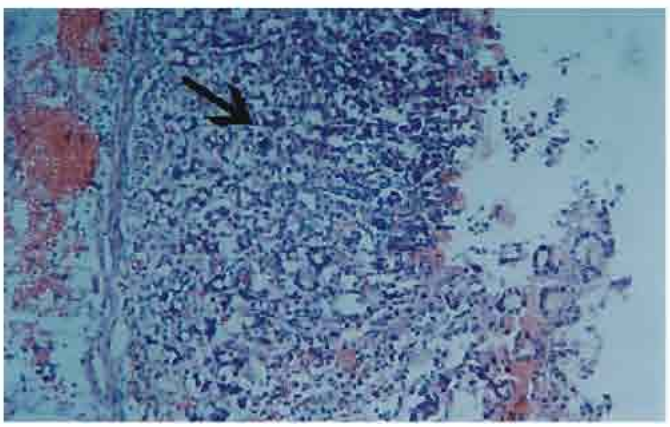

Fig 1b Section of indomethacin induced ulcer rat showing gastric lesions

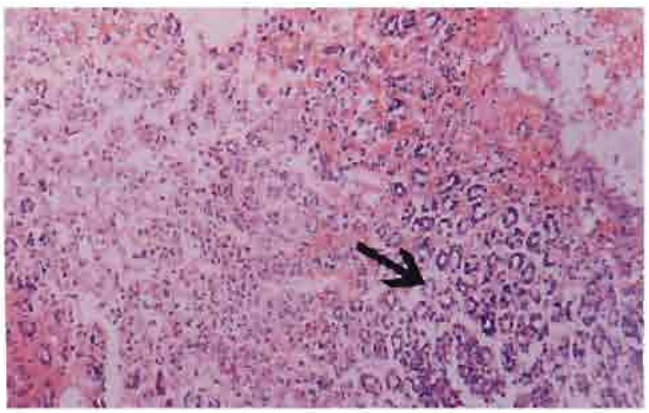

Fig 1c Section of ethanol induced ulcer rat showing gastric lesions

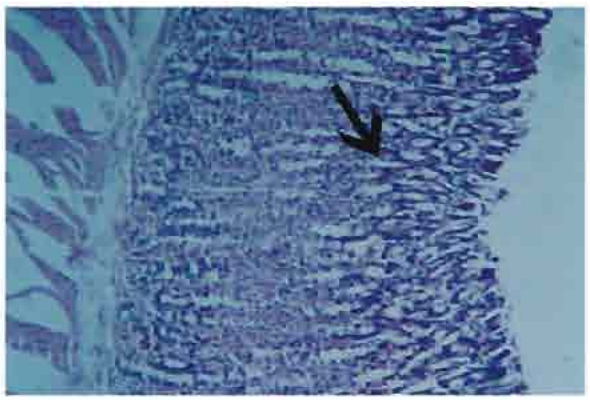

Fig 1d Section of indomethacin-induced ulcer rat treated with *Aloe vera* gel extract showing apparently normal architecture

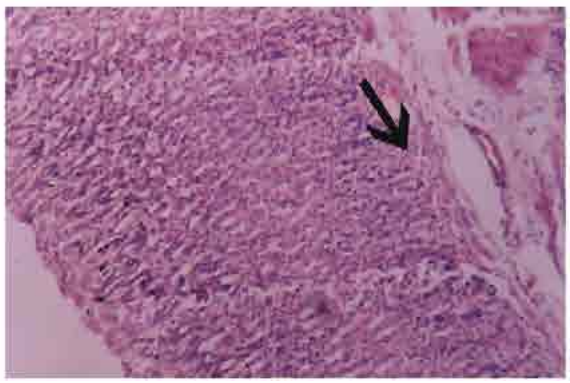

Fig 1e Section of ethanol induced ulcer rat treated with *Aloe vera* gel extract showing egression ulceration

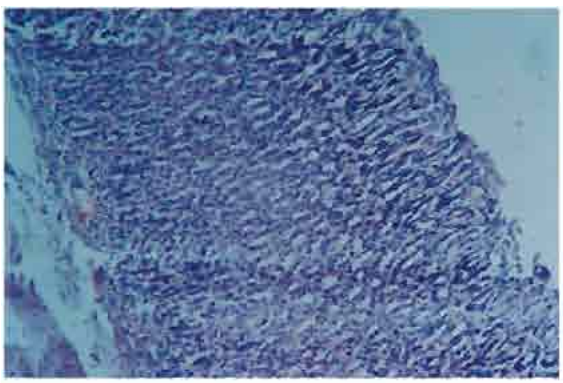

Fig 1f Section of indomethacin induced ulcer rat treated with ranitidine showing apparently normal gastric mucosa

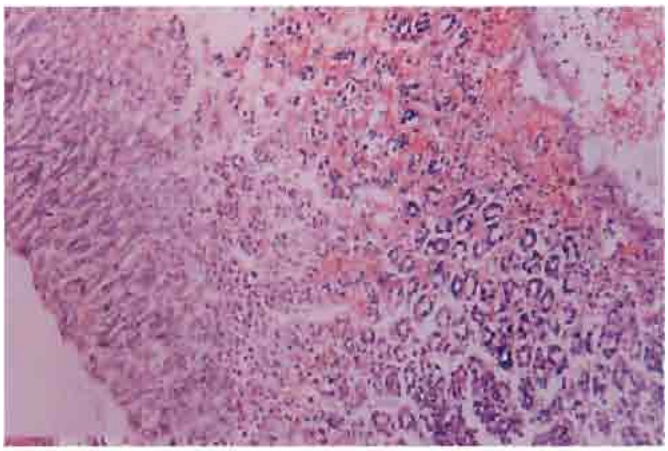

Fig. 1g: Section of ethanol-induced ulcer rat treated with ranitidine showing moderate ulceration

Fig. 1 (a-g): Histopathological observations made on the gastic mucosa of control and experimental groups of rats

Table 5 Levels of glycoprotein contents and TC P ratio in the gastric juice of control and experimental groups on ethanol-induced ulcer rats

Parameters	Control	Ethanol induced ulcer	Ethanol+ *Aloe vera*	Ethanol + Ranitidine
Hexose ($\mu g\ mL^{-1}$)	421 4±31 8	344 6±28 6^{a*}	411 1±32 0^{b*}	354 7±28 6^{b*}
Hexosamine ($\mu g\ mL^{-1}$ l)	191 1±13 1	128 6±10 7^{a*}	183 4±12 8^{b*}	131 7±12 5^{b*}
Sialic acid ($\mu g\ mL^{-1}$)	38 7±2 8	26 1±2 1^{a*}	37 3±2 9^{b*}	27 1±2 0^{b*}
Fucose ($\mu g\ mL^{-1}$)	33 1±2 4	25 6±2 0^{a*}	32 5±2 5^{b*}	24 8±1 9^{b*}
Protein ($\mu g\ mL^{-1}$)	254 1±20 1	320 6±21 4^{a*}	263 6±21 3^{b*}	300 9±22 6^{b*}
TC P ratio	3 29±0 22	1 64±0 12^{a*}	2 52±0 23^{b*}	1 58±0 12^{b*}

Values are expressed as Mean±SD for six animals in eacg group One way ANOVA followed by post hoc test (LSD)
*p<0 05 Comparisons are made between ^{a}control, ^{b}indomethacin

respectively. From the results it is evident that the levels of hexose, hexosamine, sialic acid, fucose and TC: P ratio in both the ulcer models were considerably lowered when compared to control group of rats. Oral administration of *Aloe vera* gel extract significantly elevated ($p<0.05$) the levels of glycoprotein contents after 15 days of treatment in both the ulcer-induced groups.

Histological Studies

The results of histological observations made on stomach of control and experimental rats are presented in Fig. 1(a-g). Fig. 1a shows the histological observations made on the gastric mucosa of control rats showing normal architecture. Fig. 1b represents stomach tissue of indomethacin induced ulcer rats with severe ulcer lesions on the gastric mucosa. Fig. 1c illustrates alcohol induced ulcer rats with prominent lesions and ulcerated surface on the gastric mucosa. Figure 1d and e represent *Aloe vera* gel extract (150 mg kg^{-1} b.w) treated indomethacin and ethanol-induced ulcer rats, respectively. Administration of *Aloe vera* gel was found to protect the gastric surface against ulceration, which is evident, by decreased/absence of lesions in both the ulcerinduced models. The apparently normal architecture of gastric mucosa in *Aloe vera* treated ulcer rats confirms the gastroprotective effect of *Aloe vera* gel. Figure 1f and g represent ranitidine treated indomethacin and ethanol-induced ulcer rats, respectively, showing intact mucosa when compared with Fig. 1b and c (indomethacin and alcohol induced ulcer, respectively).

Discussion

In most cases, the stable incidence of ulcer in rat models provides a powerful and convenient tool for the investigaton of therapeutic modalities for the disease and for its complications. Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) like indomethacin and aspirin are known to induce numerous punctiform and filiform gastric ulcers during the course of anti-inflammatory therapy and hence indomethacin induced ulcer model was used in the present study. Although the mechanisms underlying the ulcerogenicity of indomethacin are not completely understood, inhibition of prostaglandin synthesis may be an important (Vane, 1971). This view is supported by the fact that prostaglandins normally have a protective function in the stomach by maintaining gastric microcirculation (Ferreira *et al*., 1974) and cause gastric secretion of bicarbonate (Garner *et al*., 1979) and mucus (Menguy and Desbaillets, 1967).

Consumption of alcohol produce severe hemorrhagic lesions in the gastric mucosa and hence ethanol induced ulcer model was included in the present study. Ethanol-induced lesion formation may be multifactor. The factors involved in the formation of ulcer using ethanol have been described (Lange *et al*., 1985). Further, Koo *et al*. (1986) have suggested that the gastric wall mucus depletion induced by ethanol is one of the pathogenic mechanisms responsible for gastric lesion. The numbers of lesions present on the gastric mucosa are indicative of the severity of ulcer disease (West, 1982). The diameters of the lesion are used for the determination of ulcer index, a measure of ulcer in the gastric mucosa.

The observed decrease in ulcer index in *Aloe vera* gel extract pretreated groups of rats may be due to its antisecretory or cytoprotective properties or both. Though, the mechanism of ulcer formation by indomethacin and ethanol is quite different, the efficacy of the drug was found to be the same in controlling the gastric ulceration.

Although there is considerable controversy about the role of mucus in the prevention of gastric mucosal injury (Henagan *et al*., 1986), the gastric mucus coat is considered to be important both in preventing damage to the gastric epithelium as well as in facilitating its repair (Wallace and Whittle, 1986). The incidence of ethanol-induced ulcers, which is predominant in the glandular part of the stomach, has been reported to stimulate the formation of leukotriene C_4 (LTC_4) resulting in the damage of rat gastric mucosa (Cho *et al*., 1985).

Administration of *Aloe vera* gel enhanced the mucosal resistance and thus resulted in decrease in ulcer index and ulcerated surface. The antisecretory drug ranitidine, also markedly inhibited the indomethacin-induced gastric lesions. These results suggest that the antiulcer activity of the *Aloe vera* gel extract against indomethacin-induced ulcer might also be related to its antisecretory effect.

Ranitidine did not overcome the mucus depletion induced by ethanol, since it acts via blocking of H_2-receptors. This is in accordance with previous reports (Palacios *et al*., 1998). On contrary, *Aloe vera* gel extract administration resulted in decreased ulcer index. The mucus depletion by ethanol was overcome by *Aloe vera* extract which underlines its cytoprotective nature.

It may also be proposed that the decrease in ulcer severity by *Aloe vera* may be attributed to its active ingredients with gastric-protective nature. The phytochemical analysis revealed the presence of tannins, saponins and flavanoids (Rajasekaran *et al*., 2005a). These substances known to affect the integrity of mucous membranes (Oliver, 1960). Tannins are known to protect the outermost layer of mucosa and to render it less permeable and more resistant to chemicals and mechanical injury or irritation and thus prevent ulcer development (Asuzu and Onu, 1990). Flavanoids have also been reported to offer some protection in ulcer development by increasing capillary resistance and improving microcirculation (Hashizume *et al*., 1978).

Acidity plays an important role in the pathogenesis of indomethacin induced gastropathy. Gastric mucosal damage induced by indomethacin is augmented by the presence of high concentration of acid into the gastric lumen (Yeomans *et al*., 1992). Indomethacin induced damage to rat gastric mucosa is markedly dependent on luminal pH (Elliott *et al*., 1996). Gastric acidity may potentially facilitate indomethacin induced mucosal damage by two mechanisms: (i) by enhancing gastric absorption of these drugs or (ii) by amplifying mucosal injury once mucosal defenses have been impaired by the decrease in prostaglandin synthesis (Yeomans *et al*., 1992). Stimulation of mucus secretions such as glycoproteins and mucin by *Aloe vera* gel helps in decreasing the volume and acidity of gastric juice. Further, hyposecretory nature of *Aloe vera* gel in ulcer-induced rats may further help in decreasing the volume, pH and acidity of gastric juice towards near normal levels. Thus normalization of gastric juice acidity may indirectly help in healing of ulcer lesions in *Aloe vera* treated ulcer rats.

Glycoproteins are the important constituents of plasma membrane and specific intracellular organelles such as golgi complexes, lysosomes and secretory granules. Surface mucus cells and mucus neck cells of gastric mucosa secrete mucus by exocytosis (Zalewsky and Moody, 1979). The main components of gastric mucus are the acidic glycoprotein, sialic acid and neutral mucopolysaccharides like total hexoses, hexosamine and fucose. These glycoproteins are of importance for their specific properties such as gel formation and viscosity. Glycoproteins are obligatory components of mucus and their quantitative determination has been used as a measure of mucus formation (Lukie and Frostner, 1972). A decrease in the synthesis of sulphated mucus glycoprotein has been implicated in the etiology of peptic ulcer (Younan *et al*., 1982).

The observed decrease in the level of glycoprotein moieties both in gastric juice of ulcerated groups of rats may be attributed to two factors namely, (a) decreased activity of defense mechanisms as a result of damage to the gastric mucosa and (b) disintegration and degradation of glycoprotein moieties into their simpler components in the process of ulceration induced by ulcerogens. The histopathological observations made on the stomach tissue support this view.

Two main features of the mucus layer are its thickness and turnover rate. These two processes are of great value in protecting the mucosal layers from the offensive factors (Allen, 1978). The mucosal layer is a dynamic entity in which the surface cells are continuously renewed (Bickel and Kauffmen, 1981). The observed decrease in the levels of sialic acid and hexosamine levels may be attributed to the decreased production or turnover of mucus. The mucus possessing less amount of sialic acid and hexosamine is prone for easy degradation (Kerss *et al*., 1982).

Treatment with *Aloe vera* gel extract antagonizes the aggressive factors, which play a crucial role in the pathogenesis of gastric lesions and augment defensive factors to protect the gastric mucosa from ulceration. The increase in the levels of glycoproteins, particularly sialic acid and hexosamine in the extract treated groups indicate the increase in the production of mucus, thereby possibly protecting the gastric mucosa in both ulcer models. The efficacy of the extract was more or less same in both the models and showed promising antiulcer activity more than that of ranitidine.

Tannins, one of the constituents of *Aloe vera* extract, form a pellicle over the lining of gastric mucosa to resist the attack of proteolytic enzymes (John and Onabanjo, 1990). Thus resistance to proteolysis may help in the restoration of glycoprotein moiety of gastric mucosa in *Aloe vera* treated ulcer rats. Further, flavanoids have been reported to be present in *Aloe vera* gel (Davis *et al*., 1989). Flavonoids might play a role in stabilizing the antioxidant status of the gastric mucosa, which may have maintained its glycoprotein moiety. Thus, *Aloe vera* gel may have ameliorated glycoprotein abnormalities through its action on pepsin-mediated proteolysis.

Thus, the present investigation establishes the gastro-protective nature of *Aloe vera* gel extract and the protective effect may be mediated by defensive mucosal factors. The histological studies further established the ulcer curative properties of *Aloe vera* leaf gel extract.

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