ANTIULCER ACTIVITY OF FRESH RHIZOME JUICE OF *CURCUMA AMADA*.

Dissertation work submitted to

The TamilnaduDr.M.G.R. Medical University,

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In partial fulfillment of the requirements for the award of degree of

MASTER OF PHARMACY

IN

PHARMACOLOGY

Submitted by

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OCTOBER 2016

Declaration

I hereby declare with immense pleasure and satisfaction that this dissertation work entitled **'ANTIULCER ACTIVITY OF FRESH RHIZOME JUICE OF CURCUMA AMADA'** was carried out by me under the guidance of **Dr. D. Benito Johnson, M.Pharm ,Ph.D** in the department of Pharmacology, RVS College of Pharmaceutical Sciences, Sulur, Coimbatore.

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SANDEEP.M

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ABSTRACT

In the present study the activity of fresh rhizome juice of *curcuma amada* were administered orally to study the antiulcer effects.

Acute toxicity studies on the albino rats show no morality at a dose of 2ml/kg, during a time period of 14 days. During the study, no noticeable were seen in the rats. This help to predict that it does not contain any type of toxicity and it is full safe. So 2 ml/kg b.w ($1/10^{th}$ dose) of fresh juice were selected of that dose for the further study. The observations indicated that long-term administration of the extract had no adverse effects on the general health of the animals. No significant differences were observed in body weights or food consumption of the animals. Hence this preparation can be utilized clinically. The animals were induced ulcer with ethanol and aspirin and the ulcer animals were treated with fresh juice at a dose of 2ml/kg along with standard drug pantoprazole orally.

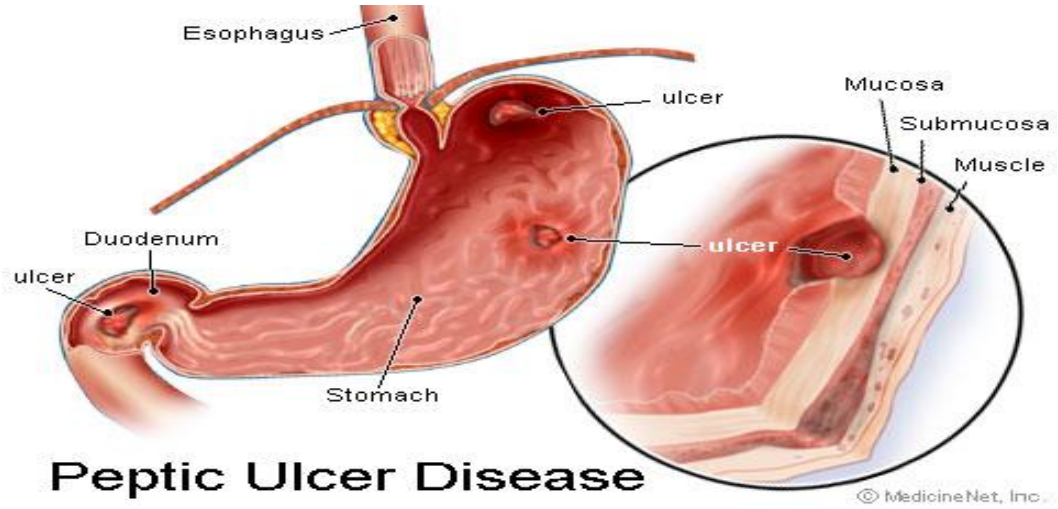
ANTIULCER ACTIVITY OF FRESH RHIZOME JUICE OF CURCUMA AMADA

INTRODUCTION

Peptic ulcer and other acidic symptom affect up to ten percentage of the humans with sufficient severity to prompt victims to seek medical attention. The more significant disease condition requiring medical fuscous is ulcer and gastro esophagealdisease[1].*In the US, approximately 4 million people have peptic ulcer (duodenal and gastric types), and 350 thousand new patient are diagnosed in each year, around 180 thousand peoples are admitted to hospital and treated with drugs yearly, and about five thousand patient from this case die each year as a result of ulcer condition. The lifetime of human being developing a peptic ulcer is about 10 percentages for Americans males and four percentages for female population*[2].

Peptic ulcers is wound in the lesions that are most often affected in younger to older adults population, but this may diagnosed in young adult life. They often appear without obvious sign and symptom, after a period of days to months of active phase of disease,it may heal with or without drug treatment. It also affect because of bacterial infections with H. Pylori.

Figure 1-Diagram of Peptic Ulcer[3]



The following statistics relate to the prevalence of peptic ulcer[4]:

Table 1-prelavance of peptic ulcer

Country/Region	Extrapolated prevalence	Population estimated used
USA	5,398,077	293,655,405
Canada	597,571	32,507,874
India	19,578,503	1,065,070,607
Russia	2,646,581	143,974,059
Australia	366,050	19,913,144

Danger of ulcer[5]:

Bleeding: Upper gastrointestinal (UGI) bleeding is the secondary common medical condition that effect high mortality in peptic ulcer. UGI bleeding commonly present along with hematemesis (vomiting with digested food and blood or coffee-ground like substance) and black, tarry stools (melana). Clinical diagnosis of UGI done by nasogastric tube lavage shows blood or coffee-ground like material presence. However this diagnosis may be negative when the bleeding arises beyond a closed pylorus region. Most of the patient's having bleeding ulcers can be treated with fluid and blood resuscitation, drug therapy, and endoscopic surgery.

Perforation:this ulcer may be spread to small intestine, oesophagus and large intestine ulcers account for 60, 20 and 20 percent of perforations.

Penetration: Ulcer penetration called due to the permeation of the ulcer among the bowel part without free perforation and filtration of whole contents inside the peritoneal cavity. Surgical treatment regimen recommended that permeation affect in twenty percentage of ulcers, but little proportion of penetrating ulcers become clinically important. The commonsymptom these complication include acidic irritation, weight reduction and diarrhoea: watery vomiting is an

uncommon, but diagnostic symptom. No evident clinicaldata is available in thetreatment regimen and guidance for the curing of penetrating ulcers.

Obstruction: Gastric wall obstruction among the frequent ulcer symptoms. Most of the cases are related with duodenal or pyloric part ulceration are 5 percent of the patient populations.

Changes in lifestyle and dietary:

Aspirin and related drugs (non-steroidal anti-inflammatory drugs),[6] alcohol,[7] coffee[8] (even decaf)[9] and tea[10] can interfere with the curing of the peptic ulcers. Smoking may also lowthe ulcer healing process[11]. People with ulcer symptom have been evaluated to had more carbohydrate than people with no ulcers,[12]from this route may occur with a genetic susceptibility for the ulcer pathogenis[13].

Sugar has also been reported to increase stomach pH[14]. Salt may cause the stomach and intestine irritation. Large uptakes of salt have been linked to higher risk of stomach ulcer[15]

One of the amino acid Known as Glutamine, is the important source in the energy in cells which coverthe stomach and intestine[16]. It is also prevent the stress ulcer related by large burns of the preliminary study about the pathogenesis of ulcers[17].

TYPES OF PEPTIC ULCER

1)Gastric ulcer

2)Duodenal ulcer

Gastric ulcer[2]

Gastric ulcers are usually single and less than 20 millimetre in diameters. Ulcers on the small curvature are mainly related for the chronic gastritis condition, whereas those in the larger curvature are often associated to the non-steroidal anti-inflammatory drugs effects

Physiological factors in gastric ulcers:

Gastric ulcers almost invariably arise in the setting of H. pylori gastritis or chemical gastritis that results in injury to epithelium. Most patients with gastric ulcers secrete less acid

than do those with duodenal ulcers and even less than normal persons. The factors implicated include:

(1) back-diffusion of acid into the mucosa,

(2) Decreased parietal cell mass,

(3) Abnormalities of the parietal cells themselves.

A minority of patients with gastric ulcers exhibit acid hypersecretion. In these persons, the ulcers are usually near the pylorus and are considered variants of duodenal ulcers. Interestingly, the intense gastric hypersecretion that occurs in the Zollinger-Ellisonsyndrome is associated with severe ulceration of the duodenum and even the jejunum but rarely with gastric ulcers.

Duodenal ulcer:

Duodenal ulcers are ordinarily located on the walls of the duodenum, on a short distance of the pylorus region.

Physiological factors in duodenal ulcers:

The maximal capacity for acid production by the stomach reflects total parietal cell mass. Both parietal cell mass and maximal acid secretion are increased up to twofold in patients with duodenal ulcers. However, there is a large overlap with normal values and only one third of these patients secrete excess acid.

Accelerated gastric emptying, a condition that might lead to excessive acidification of the duodenum, has been noted in patients with duodenal ulcers. However, as with other factors, there is substantial overlap with normal rates. Normally, acidification of the duodenal bulb inhibits further gastric emptying.

The pH of the duodenal bulb reflects the balance between the delivery of gastric juice and its neutralization by biliary, pancreatic and duodenal secretions. The production of duodenal ulcers requires an acidic pH in the bulb, that is, an excess of acid over neutralizing secretions. In

ulcer patients, the duodenal pH after meal decreases to a lower level and remains depressed for a longer time than that in normal persons.

Impaired mucosal defenses have been invoked as contributing to peptic ulceration. The mucosal factors, including the function of prostaglandins, may or may not be similar to those protecting the gastric mucosa.

Table 2.Distinguishing features of two major forms of peptic ulcer[23]:

Features	Duodenal ulcer	Gastric ulcer
1. Incidence	a. Four times more common than gastric ulcers and b. Usual age 25-50 years.	Less common than duodenal ulcers and Usually beyond 6th decade.
2. Etiology	Most commonly as a result of H.pylori infection and other factors-hypersecretion of acid-pepsin, association with alcoholic cirrhosis, tobacco, hyperparathyroidism, chronic pancreatitis, blood group O, genetic factors.	Gastric colonisation H. pylori asymptomatic but higher chances of development of duodenal ulcer. Disruption of mucus barrier most important factor. Association with gastritis, bile reflux, drugs, alcohol, tobacco.

3. Pathogenesis	Mucosal digestion from hyperacidity most significant factor. Protective mucus barrier may be damaged.	Usually normal to low acid levels Damage to mucus barrier significant factor.
4.Pathologic changes	(a). Most common in the first part of duodenum. (b).1-2.5 cm in size. round to oval.	(a) Most common along the lesser curvature and pyloric antrum. (b) Same to duodenal ulcer.
5.Clinical features	Pain-food-relief pattern Night pain common No vomiting No loss of weight No particular choice of diet Marked seasonal variation Occur more in people at greater stress.	Food-pain pattern No night pain Vomiting common loss of weight Patients choose bland diet devoid of curries No seasonal variation More often in labouring groups

Stomach[24]:

Stomach is a hollow organ situated just below the diaphragm on the left side in the abdominal cavity. When empty, its volume is 50ml and normally it can expand to accommodate 1 to 1.5 liters of solids and liquids. Gastric juice is the mixture of secretions from different glands of the stomach.

Properties: Its volume ranges from 1200 to 1500 ml/day. Gastric juice is highly acidic with pH of 0.9 to 1.2. The acidity of gastric juice is due the HCl. The specific gravity ranges from 1.002 to 1.004.

Composition: It contains 99.5% of water and 0.5% solids. The solids are organic and inorganic substances.

Organic substances:

Gastric enzymes: The enzymes present in gastric juice are pepsin, rennin, lipase and other enzymes.

Pepsin: This is the major protein splitting enzyme in the gastric juice. the precursor of pepsin is pepsinogen.

Rennin: It is a milk curdling enzyme.

Gastric lipase: It is a weak lipid splitting enzyme.

Other gastric juice: The other enzymes of gastric juice are the gelatinase and urase.

Gastric mucus: It is secreted by mucus neck cells of the gastric glands and surface mucus cells in fundus, body and others parts of stomach. It is like a flexible gel covering the gastric mucus membrane. Mucus is a glycoprotein.

Intrinsic Factor: This is necessary for absorption of the extrinsic factor.

Inorganic substances:

The Inorganic substances present in the gastric juice are HCL, sodium, calcium, potassium, chloride, bicarbonate, phosphate and sulfate.

DIGESTIVE SYSTEM

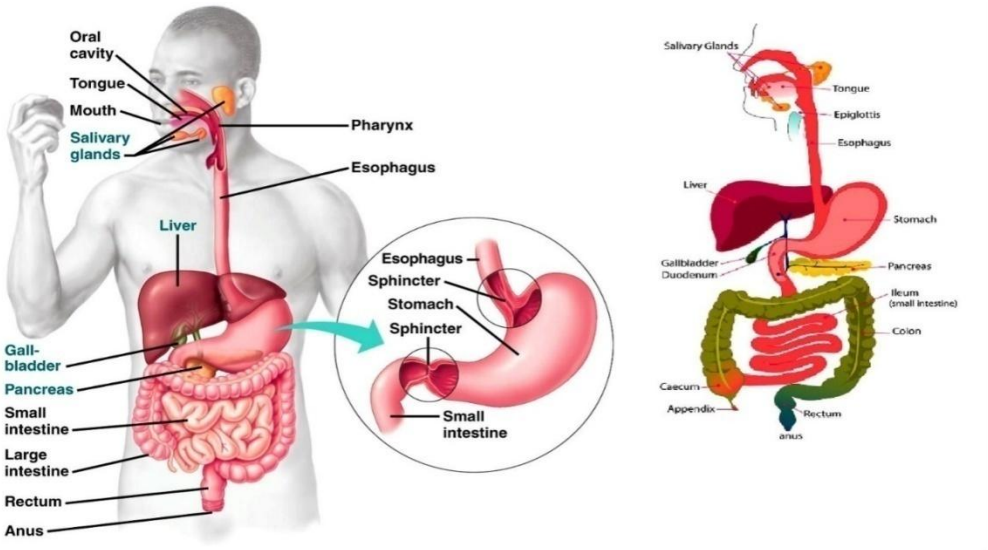
The function of the digestive system is to digest and absorb food. It consists of a tubular gastrointestinal tract and accessory organs that aid in digestion and absorption.

All organisms require food to sustain life. The cells of the body require nutrients for the chemical reactions of enzyme synthesis, cell division, growth and repair and also for the production of heat energy. Most of the food we eat requires considerable processing before it can be used by the cells. It must be broken down mechanically and chemically before it is transported by the blood to the cells[25,26].

The activities that are performed by the digestive system include the following activities:

- ***Ingestion***: the taking of food into the mouth.
- ***Mastication***: chewing food which pulverizes it and mixes it with saliva.
- ***Deglutination***: Swallowing; moving food from the mouth to the pharynx and into the
- esophagus.
- ***Digestion***: The mechanical and chemical breakdown of food to prepare it for absorption.
- ***Absorption***: the passage molecules of food through the mucous membrane of the small intestine and into the blood and lymph for distribution to the cells.
- ***Peristalsis***: the rhythmic wavelike contractions of the smooth muscle of the intestines that move food through the GI tract.
- ***Defecation***: the discharge of indigestible wastes (feces) from the GI tract. Anatomically and functionally the digestive system can be divided into a tubular gastrointestinal(GI) tract and accessory digestive organs. The GI tract which extends from the mouth to the anus is a continuous tube approximately 30 feet (9m) long. It goes through the thoracic cavity and enters the abdominal cavity through the diaphragm. The organs of the digestive system include the oral cavity (mouth), pharynx, esophagus, stomach, small intestine and large intestine. The accessory organs include teeth, salivary glands, liver, gall bladder and pancreas. It usually takes about 24-48 hours for food to travel the length of the GI tract. Food travels in an assembly line manner through the tract where it is broken down to the molecular level and transported to the cells. Each region of the GI tract has a specific function in the process[27,28].

Fig:2 DIGESTIVE SYSTEM



Membranes of the Abdominal Cavity

Most of the digestive organs are located in the abdominal cavity. These organs are covered by serous membranes that line the cavity and cover the organs within. Serous membranes secrete a lubricating serous fluid that continuously moistens the organs. The parietal membrane lines the wall of the abdominal cavity and the visceral membrane covers the internal organs. The membrane that lines the wall of the abdominal cavity is called the parietal peritoneum**.** It comes together to form a double layered peritoneal fold called the mesentery[29]. The mesentery supports the GI tract and at the same time allows the small intestine freedom for peristaltic contractions. It also provides a structure for the passage of blood vessels and nerves. The peritoneal membrane continues around the intestinal organs as the visceral peritoneum. The peritoneal cavity is the space between the parietal and visceral portions of the peritoneum. Certain organs lie posterior to the peritoneal cavity and are said to be retroperitonea**l.** These organs include most of the pancreas, the kidneys, adrenal glands and portions of the duodenum and colon as well as the abdominal aorta[30].

Peritonitis is an inflammation of the peritoneum usually caused by an infection. This can occur due to trauma, rupture of an organ, an ectopic pregnancy or postoperative infection. It is a serious life threatening situation. Treatment usually involves massive doses of antibiotics as well as insertion of a tube to drain excess fluid which accumulates[31].

Extensions of the parietal peritoneum serve to suspend or anchor organs within the peritoneal cavity. The falciform ligament attaches the diaphragm and the anterior abdominal wall to the liver. The greater omentum extends from the stomach to the transverse colon forming an apron like covering over most of the small intestine. Function of the omentum includes storage of fat, cushioning visceral organs, supporting lymph nodes and protection against infection. in cases of infection such as appendicitis the greater omentum may actually compartmentalize the infection, sealing it off from the rest of the peritoneal cavity. The lesser omentumpasses from the lesser curve of the stomach and the upper duodenum to the inferior surface of the liver[32].

Layers of the GI tract[33,34]

The GI tract from the esophagus to the anal canal is comprised of 4 layers or tunics. Each layer performs specific functions in the digestive process.

These layers are :

- ***Mucosa*-** the innermost layer lines the lumen of the GI tract. It is both absorptive and secretory in function.It contains lymph nodes as well as goblet cells which secrete mucous. There is also a thin layer of smooth muscle in this tunid.
- ***Submucosa*-** this is the second layer, much thicker than the mucosa. It is primarily vascular and nerve containing. Absorbed molecules pass through the mucosa to enter blood or lymph vessels here. The submucosa contain glands and a nerve plexus (Meissner's plexus) which provides autonomic innervation to the muscle layer in the mucosa.
- ***Tunica muscularis*-** This is the primary smooth muscle layer of the GI tract which is responsible for peristalsis. It has an inner circle and an outer longitudinal layer of muscle. Contraction of this layer causes the movement of food as well as helping to pulverize and

churn the food with digestive enzymes. There is a large nerve plexus (Aurebach'splexis) located between the 2 muscle layers. It provides both sympathetic and parasympathetic innervation.

- ***Serosa-*** is the outermost layer of the GI tract wall. It is binding an protective in function.

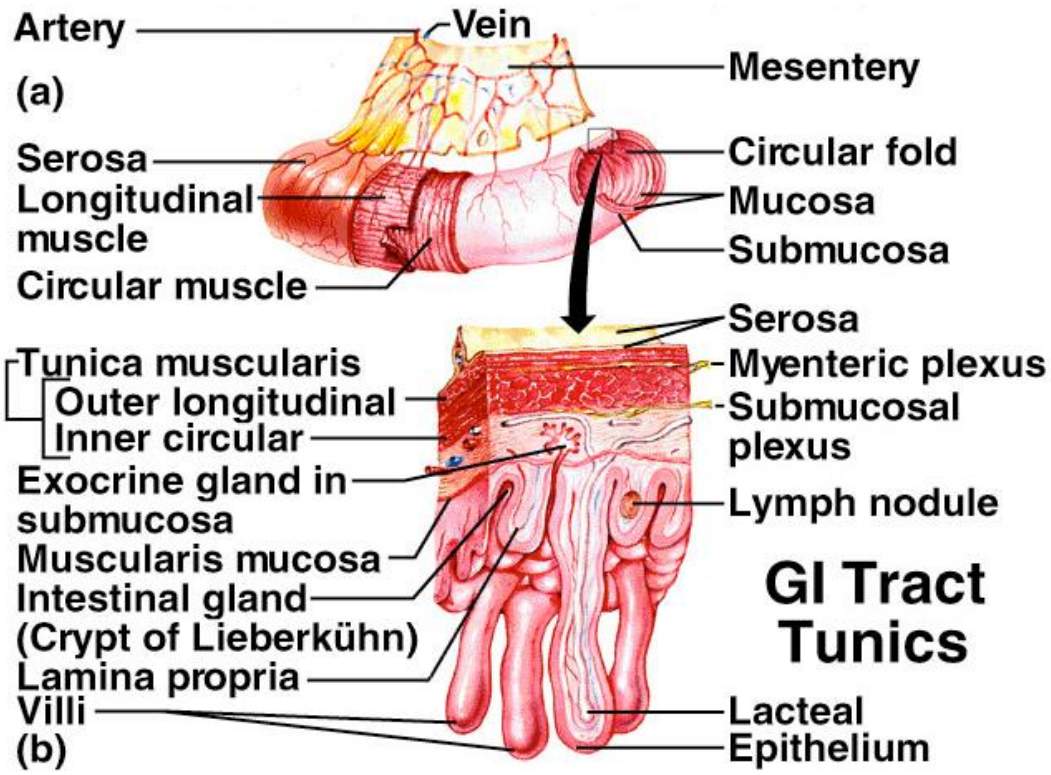


FIG. 3 LAYERS OF GI TRACT

Esophagus

The esophagusis that part of the GI tract that connects the pharynx to the stomach. It is a collapsible tubular organ about 10 inches long originating at the larynx and lying posterior to the trachea. The esophagus lies within the mediastinum of the thorax and passes through the diaphragm just above the opening to the stomach. This opening through the diaphragm is called the esophageal hiatus. The upper third of the esophagus is made up of skeletal muscle, the middle third is a combination of skeletal and smooth muscle. The terminal portion of the esophagus is smooth muscle only[35,36]. The lower esophageal sphincteris a thickening of circular muscle at the junction of theesophagus and stomach. After food or fluid pass into the stomach this constricts to prevent regurgitationinto the esophagus. This occurs normally because thoracic pressure is lower than abdominal pressure. Because this sphincter is not as large or strong as other sphincters of the GI tract backflow can sometimes occur under some conditions. This is what is referred to as heartburn. The acidic stomach contents are coming up into the esophagus. Duringvomiting the contents of the stomach are regurgitated completely to rid thestomach of some perceived toxin or irritant. In babies, this sphincter's function is kind of erraticleading them to spit upfollowing a meal. Some mammals have very strong esophageal sphincters. This is the case with rats and mice; which is why they are killed easily by poisoned bait, they cannot regurgitate the poison. The process of swallowing (deglutination) is a three part process which involves both voluntary and involuntary processes. The first stage which is voluntary involves closing the mouth and interruption of breathing. The tongue is elevated against the roof of the mouth due to contraction of the intrinsic muscles of the tongue and the myohyoid and stylohyoid muscles. The second stage is the passage of the bolus (food) through the pharynx. This is involuntary and is elicited by sensory receptors located at the opening of the oropharynx. Pressure of the tongue against the transverse palatine folds seals off the nasopharynx from the oral cavity and creates pressure that forces the bolus into the oropharynx. The soft palate and uvula are elevated to close off the nasopharynx as the bolus passes. The hyoid bone and larynx are elevated. Elevation of the larynx against the epiglottis seals off the glottis so that food or

fluid are less likely to be aspirated into the trachea. Sequential constriction of the constrictor muscles moves the bolus from pharynx to esophagus. The third and final stage is involuntary as well. The bolus is moved to the stomach by means of peristalsis[37,38].

Stomach

The stomach- the most distensible part of the GI tract- is located in the upper left quadrant, immediately below the diaphragm. It is a J shaped organ that is continuous with the esophagus and empties into the duodenal portion of the small intestine inferiorly.

In the stomach the food is churned mechanically with gastric secretions to form a pasty substance called chyme**.** Once formed it is moved to the small intestine.

The stomach is divided into four regions: the cardia, fundus, body and pylorus[39].

The **cardia**is the narrow upper region immediately below the lower esophageal sphincter.

The **fundus** is the dome shaped portion to the left of and in direct contact with the diaphragm.

The **body** is the large central portion and the **pylorus** is the funnel shaped terminal portion. The pyloric sphincteris the modified circular muscle at the end of the pylorus where it joins the small intestine. *Pylorus* in Greek means gatekeeper and the pyloric sphincter acts to regulate the flow of chyme into the small intestine. The wall of the stomach is composed of the same 4 tunics found in the other regions of the GItract, with 2 principal modifications: an extra oblique muscle layer present in the muscularis, and the mucosa has numerous longitudinal folds called gastric folds or gastric rugae. The mucosa also has microscopic gastric pits and gastric glands[40,41].

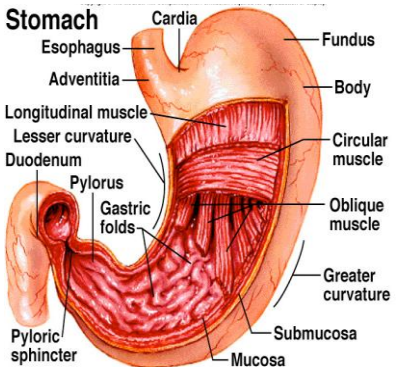


Fig:4 STOMACH

There are 5 types of cells in the gastric glands that secrete specific products:

- **Goblet cells** secrete protective mucous.
- **Parietal cells** secrete hydrochloric acid
- **Principal cells (chief cells)** secrete pepsinoge, an inactive form of the protein digesting enzyme pepsin.
- **Argentaffin cells** secrete serotonin, histamine and autocrine regulators
- **Endocrine cells (G cells)**secrete the hormone gastrin into the blood[42,43].

Small Intestine

The small intestine, consisting of the **duodenum, jejunum and ileum**, is the site where digestion is completed and nutrients are absorbed. The small intestine is the t-portion of the GI tract between the pyloric sphincter of the stomach and the iliocecal valve that opens into the large intestine. It is positioned in the central and lower part of the abdominal cavity and is supported except for the first portion by the mesentary. The fan shaped mesentary permits movement of the small intestine but prevents it from becoming kinked or twisted. Enclosed within the mesentary are blood vessels, nerves and lymphatic vessels that supply the intestinal walls. The small intestine is about 12 feet long (3 m) in a living person but will measure twice that length in a cadaver due to relaxation of the muscular wall. It is called "small" due to its small diameter relative to the large intestine. The small intestine is the body's major digestive organ and the main site of nutrient absorption. It contains digestive enzymes which aid in the final breakdown and absorption of food[44,45].

Regions of the small intestine

- **Duodenum** is a fixed C shaped tube measuring 10 inches from the pyloric sphincter of the stomach to the duodenojejunal flexure. It receives bile secretions from the liver and gall bladder and pancreatic secretions from the pancreatic duct.
- 2. **Jejunum** extends from the duodenum to the ileum, is approximately 3 feet long. It has a larger lumen and more internal folds than the ileum[46].
- 3. **Ileum** (not to be confused with the ilium of the oscoxae) makes up the remaining 6-7 feet of the small intestine. It empties into the cecum of the large intestine through the ileocecal valve. Lymph nodes called mesentary patches are abundant in the walls of the ileum[47,48].

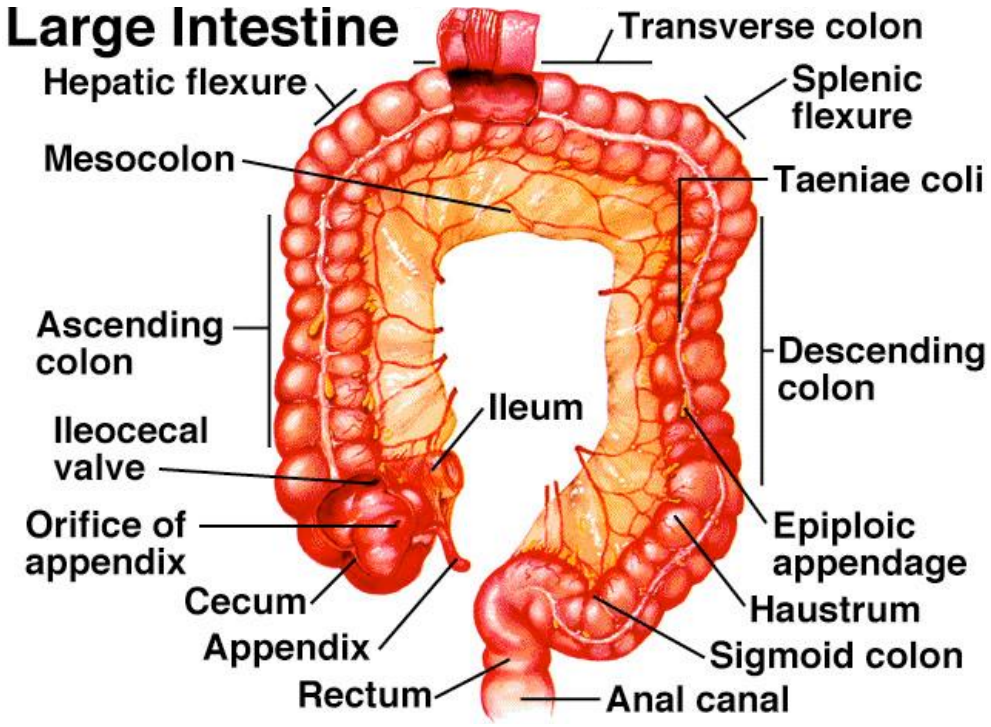
Large Intestine

The large intestine receives food that is undigested or undigestible from the small intestine, absorbs the water and electrolytes from the chyme and passes it as feces out of the GI tract. The large intestine measures about 5 feet in length and 2.5 inches in diameter. The large intestine begins at the end of the ileum in the lower right hand quadrant of the abdomen. From there it leads superiorly on the right side to a point just below the liver; it then crosses to the left, descends into the pelvis and terminates at the anus. A specialized portion of the mesentary**,** the mesocolonsupports the transverse portion of the large intestine along the posterior abdominal wall[49].

The large intestine has little or no digestive function. It absorbs water and electrolytes from the remaining chyme. It also functions to form, store and expel feces from the body.

The large intestine is divided into the cecum, colon rectum and anal canal**.** The cecum is a dilated pouch positioned slightly below the ileocecal valve**.** The ileocecal valve is a fold of mucous membrane at the junction of the small and large intestine that prevents back flow of chyme. A finger like projection of the cecum called the appendixis attached to the inferior margin of the cecum. It contains an abundance of lymphatic tissue but it serves no discernible function. It is thought to be a vestigial remnant of an organ that was functional in our ancestors. Because it is a blind pouch and waste material can accumulate within, inflammation and infection can occur. If not treated, rupture will lead to further infection of the peritoneal cavity, resulting in peritonitis.

Fig:5 LARGE INTESTINE



The superior portion of the cecum is continuous with the colon**,** which consists of the ascending, transverse, descending and sigmoid portions**.** The ascending portion extends superiorly from the cecum along the right abdominal wall to the inferior surface of the liver. The point where the colon bends here is called the hepatic flexure. From this bend it becomes the transverse colon until it reaches another right angle bend on the left side called the splenic flexure**.** From this point it becomes the descending colon as it tranverses inferiorly on the left. At the bottom of the descending colon it angles again in an S shaped bend known as the sigmoid colon.The end of the line, the last 7.5 inches of the tract is the rectum.The final inch (2-3 cm) is the anal canal**.** The anus is the external opening of the anal canal. Two sphincter muscles are found in this opening: the internal anal sphincter which is smooth muscle and the external anal sphincter which is skeletal muscle[50,51].

Mechanical Action of the Large Intestine

Three types of movements occur throughout the large intestine: **peristalsis, haustral churning and mass movement.** In **Haustralchurning**, the relaxed haustrum fills withfood residueuntil a point of distension is reached that stimulates contraction of themuscle. Thismovement churns the food residue and exposes it to the mucosa wherethe waterand electrolytes are absorbed. As this happens food residue becomes solidor semisolid and becomes feces. **Mass movement** is a strong peristaltic wave whichmoves the feces towards the rectum. Mass movement occurs only 2-3 times a day,generally after a meal. In infants this response to eating is called the **gastrocolic reflex** and results in a bowel movement during or shortly after eating[52,53].

The defecation reflex normally occurs when rectal pressure rises to a particular level that is determined by individual habit. At this point the internal anal sphincter relaxes to admit feces

into the anal canal. During defecation , the longitudinal rectal muscles contract to increase rectal pressure and the internal and external anal sphincters relax. This process is aided by contraction of the abdominal muscles which raise intraabdominal pressure and help push the feces through the anal canal and out the anus.

REGULATION OF ACID SECRETION[54]

Parietal cells in the stomach secreteroughly two liters of acid a day in theform of hydrochloric acid . Acid in thestomach functions to kill bacteria, and toaid digestion by solubilizing food. Theacid is also important to establish theoptimal pH (between 1.8-3.5) for thefunction of the digestive enzyme pepsin .

A key protein for acid secretion is the H+ /K + -ATPase (or proton pump). Thisprotein, which is expressed on the apicalmembrane of parietal cells, uses theenergy derived from ATP hydrolysis topump hydrogen ions into the lumen inexchange for potassium ions.

Stimulation of acid secretion involves thetranslocation of H +/K +-ATPases to theapical membrane of the parietal cell.When the cell is resting (not stimulated),H+ /K +-ATPases are located in vesiclesinside the cell. When the cell isstimulated, these vesicles fuse with theplasma membrane, thereby increasingthe surface area of the plasma membraneand the number of proton pumps in themembrane.

There are three regulatory molecules thatstimulate acid secretion (acetylcholine ,histamine, gastrin) and one regulatorymolecule that inhibits acid secretion(somatostatin). Acetylcholine is aneurotransmitter that is released byenteric neurons . Histamine is a paracrinethat is released from ECL(enterochromaffin-like) cells . Gastrin is ahormone that is released by G cells ,endocrine cells that are located in thegastric epithelium. Somatostatin is alsosecreted by endocrine cells of the gastricepithelium; it can act as either aparacrine or a hormone.

The figure (same as on the handout)shows how the positive and negativeregulators interact to stimulate acidsecretion. Acetylcholine and histaminedirectly stimulate parietal cells toincrease acid secretion. Gastrinstimulates acid secretion by stimulatinghistamine release from ECL cells.

(Gastrinalso has a direct effect on parietal cells,which is to stimulate their proliferation).When the pH of the stomach gets toolow, somatostatin secretion isstimulated. Somatostatin inhibits

acidsecretion by direct effects on parietalcells, and also by inhibiting release of thepositive regulators histamine andgastrin. The balance of activity of thedifferent regulators changes as food isconsumed and passes through differentsegments of the upper GI tract.

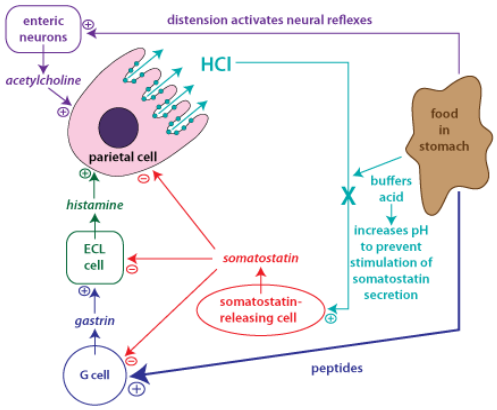


Fig:6 Acid secretion

Cephalic Phase

Cephalic phase stimuli are things like thesight, smell, taste or thought of food.These stimuli, processed by the brain,activate enteric neurons viaparasympathetic preganglionic neuronstraveling in the vagus nerve.

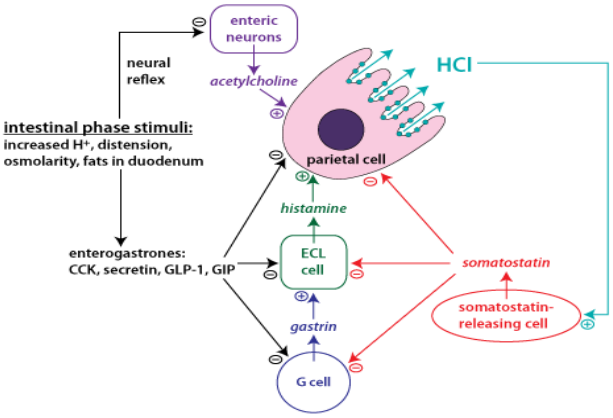


Fig : 7 CEPHALIC PHASE

Gastric Phase

The primary factor during the gastricphase is that there is food in the stomach, which stimulates acidsecretion.There are three different ways that this occurs. Food will stretch thewalls of the stomach; this is sensed bymechanoreceptors, activating a neuralreflex to stimulate acid secretion(purple). Peptides and amino acids infood stimulate G cells to release gastrin(blue). Food also acts as a buffer, raisingthe pH and thus removing thestimulusfor somatostatin secretion (light blue-green).

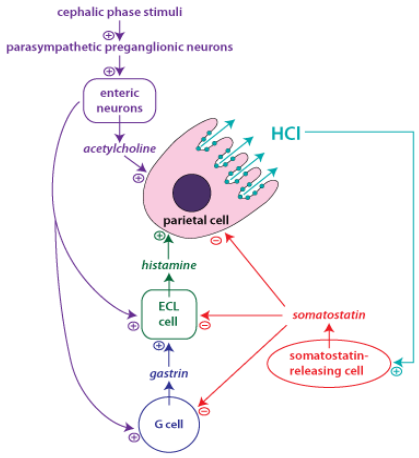


Fig : 8 GASTRIC PHASE

Intestinal Phase

Once chyme enters the duodenum,intestinal phase stimuli activate negativefeedback mechanisms to reduce acidsecretion and prevent the chyme frombecoming too acidic. This occurs byneural reflexes and hormonal reflexes.Enterogastrones are hormones thatinhibit stomach processes (in this case,acid secretion). In addition to their otheractions, CCK ,secretin , GLP-1 , and GIPact as enterogastrones.

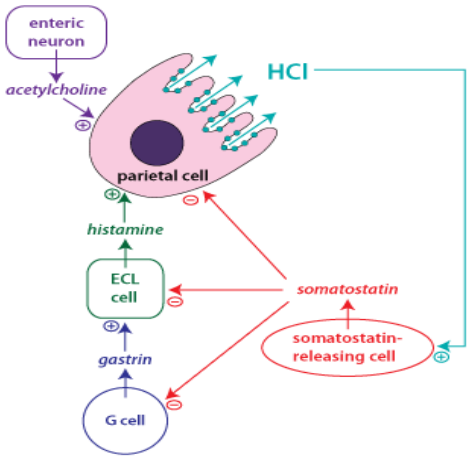


Fig : 9 INTESTINAL PHASE

PEPTIC ULCER

Peptic ulcers are sores thatdevelopin the lining of thestomach, lower esophagus,or small intestine. The most commonsymptom of a peptic ulceris burningabdominal painthat extends from the navel to the chest.Untreated ulcers canbecome worseover timeand lead to other health conditions.

Peptic ulcers are sores that develop inthe lining of the stomach, loweresophagus, or small intestine (theduodenum)usually as a result ofinflammation caused by the bacteria H.pylori, as well as from erosion fromstomach acids. Peptic ulcers are a fairlycommon health problem

There are three types of peptic ulcers:

Gastric ulcers: ulcers that developinside the stomach.

Esophageal ulcers: ulcers thatdevelop inside the esophagus.

Duodenal ulcers: ulcers thatdevelop in the upper section of thesmall intestines, called theduodenum.

Causes of Peptic Ulcers[55]

Different factors can cause the lining ofthe stomach, the esophagus, and thesmall intestine to break down. TheseInclude:

- Helicobacter pylori (H. pylori): abacteria that can cause a stomachinfection and inflammation.
- Frequent use of aspirin, ibuprofen,and other anti-inflammatory drugs(risk associated with this behaviorincreases in women and peopleover the age of 60)
- Smoking
- Drinking too much alcohol
- Radiation therapy
- Stomach cancer

Symptoms of Peptic Ulcers

The most common symptom of a pepticulcer is burning abdominal pain thatextends from the navel to the chest,which can range from mild to severe. Insome cases, the pain may wake you upat night. Small peptic ulcers may notproduce any symptoms in the earlyphases[56].

Other common signs of a peptic ulcerinclude:

- Changes in appetite
- Nausea
- Bloody or dark stools (melena)
- Unexplained weight loss
- Indigestion
- Vomiting

- Chest pain

SCREENING METHODS FOR ANTIULCER ACTIVITY[57]

1) Pylorus ligation in rat (SHAY rat):

This model is a simple and convention method for induction of gastric ulceration in the rat through ligature in the pylorus region, the ulceration is affected by accumulation of acidic juice inside the stomach. Ulcer index & pH of gastric content of treated animals are compared with control groups. Different cumulative group administration followed by dose - response curves establishment for ulcer formation can be measured in these method.

Procedure: Female Wistar rats weighing 150-170 g are starved for 48 hours having access to drinking water ad libitum. During this time they are housed single in cages in prevent coprophagy. Six animals are used per dose and as control groups. Under mild ether anaesthesia an incision is made at the abdominal midline. The pylorus is closed by using small nylon the higher supervision is required to avoid he damage of blood vessels inside the pylorus region. Grasping the stomach with instruments is to be meticulously avoided; else ulceration will invariably develop at such points. The abdominal wall are sutured through surgical procedure. The test sample are administrated through oral ingestion or injected subcutaneous route. The animals are placed for 19 hours in a suitable plastic container. Afterwards, these animals are sacrificed in CO_2 anaesthesia. The abdomen is re ligated and a ligature is placed above the esophagus region and closer to the diaphragm area. The stomach is replaced to a watch glass and the materials are collected in to a centrifugal tube. Above the longer curvature the stomach fully opened and pinned between a cork plates. The mucosal layer is observed with the help of a stereomicroscope.

2) Stress ulcer through immobilization stress:

Psychogenic factors, such as stress, produce a major role in etiology of gastric ulcers in human beings and animals. Hence not only antacids ingestion, anticholinergics, H_2– antagonists, proton pump inhibitors treatment, and also psychotropic agentssuch as neuroleptics have also effective for the treatment.

Procedure: Groups of 6 female Wister rats per dose of test drug and for controls weighing 150-170 g are used. Food and water are removed 24 hours before the experimental procedure. After oral or subcutaneous ingestion of the test substance or the placebo drug in animal's extremities are fixed combine and the animals are tied in wire gauze. These animals are horizontally suspended in a dark room at 20^{o}C for one day and last animals are sacrificed in CO_2 anaesthesia method. The stomach has been cut, fixed in a cork plate and the count and score the severity of ulcers by the help of video recorded stereo-microscope.

3) Stress ulcers by cold water immersion:

Cold water treatment of rats in during the restraint duration boost the appearance of gastric ulcers and reduce the time necessary immobilization process.

Procedure: Groups of 8-10 Wistar rats weighing 150-200 g are used. After oral administration of the test compound, the rats are placed vertically individual restraint cages in water at 22^{o}C for 1 hour. These are removed, allowed to dry and injectevans blue (30mg/Kg) intravenously through tail vein.After ten minutes, these animals are sacrificed by CO_2 anesthesia, stomachs was collected in Formol - saline (2%v/v) overnight storage about 24 hours. After that the stomachs are opened the greater curvature, washed via warm water and examined through 3-fold magnifier.

4) Indomethacin induced ulcers in rats:

Nonsteroidal anti- inflammatory agents, like indomethacin and acetyl-salicylic acid, produce a gastric lesions in human beings and in rodents by the inhibition of gastric cyclo-oxygenase leading for the formation of prostacyclin.

Procedure: Groups of 5-6 Wistar rats weighing 150 - 200 g are used. The test drugs are administered orally in 0.1 % tween 80 solution 10 minutes before the oral indomethacin at a dose about 20 mg/kg (4 mg/ml dissolved in 0.1 % tween 80 solution). Six hours later, the rats are euthanatized through CO_2 anaesthesia, these animals stomach was removed and inject with Formol-saline (2%v/v) for storage about one days.After that the stomachs are opened the greater curvature, washed via warm water and examined through 3-fold magnifier.

5) Ethanol induced mucosal damage in rats

(Cytopotective activity)

Intragastric application of absolute ethanol is a reproducible method to produce gastric lesions in experimental animals. The lesions may be blocked by some drugs (ex:- prostaglandins). These protective activity opposite to the irritants are known as cytoprotective activity.

Procedure: Male Wistar rats weighing 250 - 300 g are deprived of food 18 hours prior to the experiment but are allowed free access to water. During this time they are kept in restraining cages to prevent coprophagy. The rats are administered either are appropriate vehicle or the cytoprotective drugs, for example a prostanoid, intragastrically 30 minutes prior to administration of 1 ml absolute ethanol. Untreated animals are included as controls. One hour after administration of ethanol, the animals are sacrificed in CO_2 anaesthesia and their stomachs exercised, cut along the greater curvature and gently rinsed under tap water. The stomachs are stretched on a piece of foam core mat, mucosal site up. The subjective scores of the treated tissues are recorded.

6) Subacute gastric ulcer in rats

This is a method for producing standard subacute gastric ulcers in rats and for the quantitative evaluation of the healing process.

Procedure: Female Wistar rats weighing 120-150 g are fasted for 24 hours having access to water ad libitum in cages with wire sieves at the bottom. The rats are anesthetized with ether and a polyethylene catheter including a fine steel wire with a needle tip (1.2 mm diameter) at the lower end is orally inserted into the stomach. After the cannula reaches the gastric wall, the upper end of the steel wire is pressed in a definitive manner, so as to puncture the gastric wall. Each rat is kept in the same position during the intervention in order to localize the puncture at nearly the same region of the glandular part of the stomach. The test substances are administered orally, 30 minutes prior or 24 hours after puncture. Free access to food and water is provided from 2 hours up to the end of the experiment. Each group consists of 8 - 15 rats. The animals are sacrificed by overdose of ether at definitive time intervals after puncture. The stomach is dissected and opened along the lesser curvature, extensively rinsed in tap water and fixed to the end of a polyethylene tube of 10 mm diameter (plastic tip of an automatic pipette) in a position

with the punched ulcer in the center. The end of the tube with the gastric wall is suspended in a beaker containing physiological saline, and the pressure in the tube is gradually increased with a valved rubber ball connected to the other end of the tube. The third part of the system is a tonometer calibrated up to 1 bar. The value of tension at which bubbles appear at the ulcerous gastric wall is noted. This value is termed as tensile strength and can be expressed in mm Hg.

Tests and Exams for Peptic Ulcers[58]

Two types of tests are available todiagnose a peptic ulcer. They are calledupper endoscopy and upper gastrointestinal (GI) series.

Upper Endoscopy : In this procedure, your doctor inserts along tube with a camera down yourthroat and into your stomach and smallintestine to examine the area for ulcers.This instrument also allows your doctorto remove tissue samples forexamination.

Not all cases require an upperendoscopy. However, this procedure isrecommended for people with a higherrisk of stomach cancer. This includespeople over the age of 45, as well asthose who experience:

- Anemia (a low number of red bloodcells)
- Weight loss
- Gastrointestinal bleeding
- Difficulty swallowing

Upper GI

If you don't have difficulty swallowingand have a low risk of stomach cancer,your doctor may recommend an upperGI test instead. For this procedure, you'lldrink a thick liquid called barium, andthen a technician will take an X-ray ofyour stomach, esophagus, and smallintestine. The liquid will make it possiblefor your doctor to view and treat theulcer.Because H. pylori is a cause

of pepticulcers, your doctor will also run a test tocheck for this infection in your stomach[59].

How to Treat a Peptic Ulcer

Treatment will depend on the underlyingcause of your ulcer. If tests show thatyou have an H. pylori infection, yourdoctor will prescribe a combination ofmedication, which you will have to takefor up to two weeks. The medicationinclude antibiotics to help kill infections,and proton pump inhibitors (PPIs) tohelp reduce stomach acid.You may experience minor side effectslike diarrhea or upset stomach fromantibiotic regimens. If these side effectscause significant discomfort or don't getbetter over time, talk to your doctor.If your doctor determines that you don'thave an H. pylori infection, they mayrecommend a prescription or over-the-counter PPI (such as Prilosec orPrevacid) for up to eight weeks toreduce stomach acid and help your ulcerheal.Acid blockers (like Zantac or Pepcid) canalso reduce stomach acid and ulcerpain. These medications are available asa prescription and also over the counterin lower doses[60].

NATURAL REMEDIES

Bari ilayachi (Elettaria cardamomum and Amomum subulatum): Both drugs has gastro protective effect may be due to a decrease in gastric motility. They cause relaxation of circular muscles which may protect gastric mucosa through flattening of the folds. This will increase the mucosal area exposed to narcotizing agents and release the volume of gastric agents on rugal crest. Such action has been postulated to play a role in cytoprotective effect of prostaglandins.

Black berry: One of the most interesting substances that has been obtained from chilly peppers and present in spicy plants such as ginger or black pepper is capsaicin. This substance acts on sensory neurons to stimulate their membrane receptors, predominantly vaniloid (VR)-1 receptors, and release various kinins such as substance P. When applied in large dose capsaicin destroys selectively C-fiber neuronal endings leading to inactivation of sensory nerves and the loss of all reflexes in which these nerves are involved. In smaller dose, capsaicin is the potent gastroprotective agent and stimulant of gastric microcirculation[61].

Chamomile (Matricaria recutita): Chamomile is an herb that has been used traditionally as a mild sedative to relieve anxiety and in treating digestive disorders including peptic ulcers.

Chamomile also may be effective in relieving inflamed or irritated mucous membranes of the digestive tract and in promoting digestion. Chamomile has a soothing action on the digestive system. Its gentle soothing action is beneficial in digestive disorders like indigestion, acidity and peptic ulcers. It is also high in the flavonoid apigenin-another flavonoid that has inhibited growth of H. pylori in test tubes[62].

Dong quai (Angelica sinensis): Animal studies suggest that dong quai may soothe ulcers, but studies in people are needed before a definitive conclusion can be drawn.

Licorice (Glycyrrhiza glabra): Licorice root has a high background in effect of soothing effect in the inflamed and damaged mucous membranes of the digestive tract. Licorice also protect the stomach and intestinal parts by increased production of mucin, which protects the lining of the HCl and other substances. According to Preclinical research, Flavonoids of licorice may also supressed the growth of H. Pylori[63].

Marshmallow root (Althaea officinalis): For decades, marshmallow has been used in folk medicine to help cure gastric ulcers. The roots of the marshmallow contain mucilage, a gelatinous substance found in plants. When it comes into contact with water, this mucilage swells, forming a soft, protective gel. This is believed to provide a protective barrier against irritating substances that may aggravate ulcers.

Tea root extract (Camellia sinensis): Tea root extract might primarly decrease the leakage of plasma proteins into the gastric juice with strengthening of the mucosal barrier and increase in its resistance to the damaging effect of ethanol induced ulcer[64].

Turmeric (Curcuma longa): Constituents of Curcuma longa exert several protective effects on the gastrointestinal tract. A salt of curcumin, sodium curcuminate, was found to inhibit intestinal spasm, and p-tolymethylcarbinol, a turmeric component, was found capable of increasing gastrin, secretin, bicarbonate, and pancreatic enzyme secretion. Turmeric has also been shown in rats to inhibit ulcer formation caused by stress, alcohol, indomethacin, pyloric ligation, and reserpine. This study demonstrated turmeric extract significantly increased the gastric wall mucus in rats subjected to these gastrointestinal insults[65]

Complications of a Peptic Ulcer

Untreated ulcers can become worseover time and lead to other, moreserious health complications, such as:

Perforation: A hole develops in thelining of the stomach or smallintestine and causes an infection.A sign of a perforated ulcer issudden, severe abdominal pain.

Internal bleeding: Bleeding ulcerscan result in significant blood lossand thus require hospitalization.Signs of a bleeding ulcer includelightheadedness, dizziness, andblack stools.

Scar tissue: This is thick tissuethat develops after an injury. Thistissue makes it difficult for food topass through your digestive tract.Signs of scar tissue includevomiting and weight loss.

All three complications are medicalemergencies that require surgery. Callyour doctor if you feel dizzy or ifsymptoms return. Seek urgent medicalattention if you experience the followingsymptoms:

- Sudden, sharp abdominal pain.
- Fainting, excessive sweating, orconfusion, as these may be signsof shock.
- Blood in vomit or stool.
- Abdomen that's hard to the touch[66].

Outlook for Peptic Ulcers

With proper treatment, most pepticulcers heal. However, you may not healif you stop taking your medication early or continue to use tobacco and painrelievers during treatment. Your doctorwill schedule a follow-up appointmentafter your initial treatment to evaluateyour recovery.Some ulcers, called refractory ulcers,don't heal with treatment. If your ulcerdoesn't heal with the initial treatment,this can indicate:

- An excessive production ofstomach acid
- Presence of bacteria other than H.pylori in the stomach
- Another disease, such as stomachcancer or Crohn's disease

Your doctor may offer a different methodof treatment or run additional tests torule out stomach

cancer and othergastrointestinal diseases[67].

How to Prevent Peptic Ulcers

Certain lifestyle choices and habits canreduce your risk of developing pepticulcers. These include:

- Not drinking more than twoalcoholic beverages a day.
- Not mixing alcohol with medicationwashing your hands frequently toavoid infections.
- Limiting your use of ibuprofen,aspirin, and naproxen sodium.

Maintaining a healthy lifestyle through abalanced diet rich in fruits, vegetables,and whole grains, and quitting smokingand other tobacco use will also help youprevent developing a peptic ulcer[68].

LITERATURE REVIEW

G.Vinothapooshan etal2010[69] evaluated the anti-ulcer activity of methanolic,choloroform,diethel ether extract of *mimosa pudica* investigated in rats using three models, i.e. Aspirin, Alcohol and pyloric ligation models experimentally induced gastric ulcer. The parameters taken to assess anti-ulcer activity were volume of gastric secretion, PH, free acidity, total acidity and ulcer index. The results indicate that the alcoholic extract significantly ($P < 0.001$) decreases the volume of gastric acid secretion, PH, free acidity, total acidity and ulcer index with respect to control.

N. L. Dashputre et al 2011[70] investigate antiulcer activity of methanolextract of *Abutilon indicum*L. (Family: Malvaceae) leaves in pylorus ligated and ethanol induced ulceration in the albino rats. Preliminary methanol extract of *A. indicum*was subjected to the acute oral toxicity study according to the OECD guideline no. 425. Based on which, two dose levels i.e. 250 and 500 mg/kg were selected for the further study. It showed also significant (*P<0.05*) decrease in number of ulcers and ulcer score index in pylorus ligation and ethanol induced ulceration models. The result of this was antiulcer properties of the extract may be attributed to the presence of phytochemicals like flavonoids (quercetin), alkaloids and tannins present in the plant extract with various biological activities.

P. Thirunavukkarasu et al 2009[71] investigated the gastro protective effect of *E. agallocha*in a model of NSAID induced ulcer rat. Lyophilized extract was given by oral gavages (125 and 62.5mg/kg) three times at 12 h intervals beforeadministering dicolofenac 100mg/kg. Pretreatment with the extract resulted in a significant decreased of the ulcerated area. The *E. agallocha*was able to decrease the acidity and increase the mucosal defense in the gastric areas, there by its use as an antiulcerogenic agent.

Amandeep Kaur et al 2012[72] evaluated the antioxidant and antiulcer potential of ethanolic extract

of rhizomes of *R. emodi*on Pylorus ligation ulcers. Both doses (50 mg/kg/*p.o.*and 100 mg/kg/*p.o.*) was found to reduce the ulcer index along with the reduction in volume and total acidity, and an increase in the pH of gastric fluid in pylorus ligated rats. The study validates scientifically the use of *R. emodi*as an ethnomedicine to treat ulcers.

Mohsen Minaiyan et al 2006[73]. Here he studied , the effects of this ginger on an acute model of experimental duodenal ulcer induced by cysteamine was evaluated. Ginger is a widespread herbal medicine mainly used for the treatment of gastrointestinal (GI) disorders including dyspepsia, nausea and diarrhea. Aromatic, spasmolytic, carminative and absorbent properties of ginger suggest that it has direct effects on the GI tract and anti-ulcerogenic potential. Larger doses of extract given p.o. (350 and 700 mg/kg) were effective to reduce both the ulcer area and index but the lowest dose of extract (100 mg/kg) was not effective.they conclude that ginger hydroalcoholic extract was effective to protect against duodenal ulceration and for i.p. injection as well as chronic administration, the efficacy was comparable with ranitidine as reference drug.

O. J. Ode et al 2011[74] studied antiulcer effects of the methanolic extract of *Cassia singueana*leaves were investigated using ethanol-induced gastric ulcer model in rats. *Cassia singueana*extract (CSE) exhibited a more gastro-protective effect against ethanol-induced stomach ulcers at 250 and 750 mg/kg than omeprazole (20 mg/kg) and solvent treated (control) rats. CSE had 59% while omeprazole and distilled water produced 55% and 0% respectively. *C. singueana*extract was found to be significantly protective against ethanol-induced gastric ulcers in the experimental rats.

Swarnamoni Das et al 2012[75] investigated the anti-ulcer activity of the ethanolic extract of the rhizome of *Caurcumacaesia* on experimental animal models. stomachs of the sacrificed rats were removed and (1)volume of gastric juice (2)ulcer index (3)pepsin activity(4)free acidity(5)total acidity (6)gastric mucus secretion were studied. The ulcer index, pepsin activity, free and total acidity and volume of gastric juice in group test and standard showed significant

decrease in comparison to group experimental control whereas there was increase in gastric mucus secretion ($p<.01$).

YaraCavalcante Fortes Goulart et al 2005[76] evaluated antiulcer activity of a hydro-ethanolic extract prepared from the stems of *Kielmeyeracoriacea Mart*.(Guttiferae) in rats employing the ethanol-acid, acute stress and Indomethacin induced gastric ulcers. Treatment with *K coriacea* hydro-ethanolic extract provided significant antiulcer protection in the ethanol-acid and Indomethacin models, but not in the acute stress model.

N Venkat Rao et al 2011[77] studied antiulcer activity of fruit of the plant *Momordicacharantia* with the alcoholic and aqueous extracts. Ld50 studies for both (alcoholic and aqueous) extracts were conducted upto the dose level of 2 g/kg by following OECD up and down method of guidelines No.425. Anti ulcer activity was evaluated in various animal models like Pylorus ligation , aspirin, Stress induced ulcer models in rats. No mortality was observed with any of the 2 extracts up to the maximum dose level of 2 g/kg. Further alcoholic and aqueous extracts at 200 and 400 mg/kg, p.o but not with 100 mg/kg p.o doses significantly ($P < 0.01$) reduced the ulcer score, ulcer number, ulcer index, free acidity and total acidity in Pylorus ligation , aspirin, Stress induced ulcer models in rats.

Samaresh Pal Roy et al 2013[78] investigated the antiulcer activity by ethanolic extract of the different doses (100mg/kg, 200mg,kg & 400mg/kg) of the flower of Delonixregia (EEDRF) on ethanol induced ulcer model in experimental rat.The plant contain the chemical constitutent like tannin, saponin, flavonoid, so it have a good antioxidant property. It has been found that the extract shows significant antiulcer activity in a dose dependent manner. The protection of ulcer may due to the presence of antioxidant principles present in the plant.

Abirami J et al 2012[79] evaluated the gastro protective effect of administration of *Musa paradisiaca*L (Rhizome) juice in Aspirin induced peptic ulcer rats. Biochemical evaluation of ulcer induced rats revealed significant reduction in serum protein level. It is noted that *Musa paradisiaca*L (Rhizome) juice treated rats showed reduced ulcer congestion, haemorrhage and

ulceration. The result of the present study substantiated the use of *Musa paradisiaca*L (Rhizome) juice in ulcer incidences.

JyothibasuTammu et al 2013[80] studied the anti-ulcer activity of methanolic extract of *Physalis minima* leaves was investigated on ethanol induced ulcer models and pylorus ligation in wistar rats. In both models the common parameter determined was ulcer-index. The study indicates that *Physalis minima* leaves extract have potential anti ulcer activity in both models. This results may further suggests that methanolic extract was found to posses anti-ulcerogenic as well as ulcer healing property, which might be anti-secretory activity.

M.C. Ubaka et al 2010[81] investigated the antiulcer activity of leaves of *Aspiliaafricana*C.D. Adams (Compositae) in ratsThe ulcer inhibitory effects of the extract were comparable with those of standard drugs especially in the drug-induced ulcers. Oral LD50 value greater than 5000 mg/kg was obtained indicating the safety of the plant for consumption. Results of the study suggest the aqueous extract of *A. africana*possesses antiulcer activity as claimed by its folkloric use.

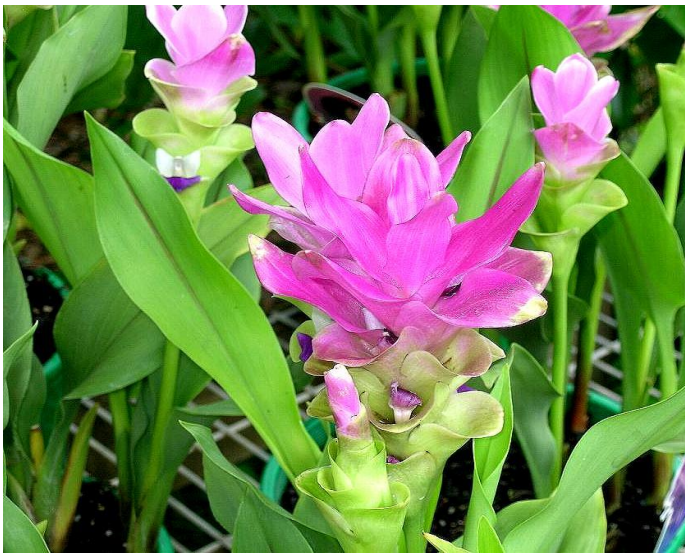
Shakeel Ahmad Jatoi et al 2010[82] studiedgenetic structure of mango ginger (*Curcuma amada*) acquired from farmers and *ex situ* genebank in Myanmar using neutral (rice SSR based RAPDs) and functional genomic (P450 based analog) markers. The major fraction of the molecular variance (neutral-markers = 85%, functional-markers = 93%) was explained within germplasm acquisition sources and this tendency was also supported by the estimate of gene diversity. The genebank accessions have shown comparatively more genetic variability than farmers' accessions. As the target sites of these markers are different, therefore, the variability detected is believed to cover diverse part of the genome together with neutral and functional regions

P. Venugopalan et al 2014[83] investigated the antioxidant activity of dried rhizomes extract of the spice *Curcuma amada* (Mango ginger), a unique spicehaving morphological resemblance

with ginger but imparts a raw mango flavouris studied by the inhibition of auto oxidation of linoleic acid in aqueous alcohol system and by DPPH method along with antibacterial activity against selected organisms studied by disc diffusion method were reported.

Ankita Joshi et al 2013[84] investigated the anticancer properties of *curcuma amada*in BHK-21 cells. Acetone, Methanol, Ethanol and aqueous extracts of the rhizomes of *Curcuma amada*were screened for their anticancer properties. The cytopathology observed were included rounding and clumping of cells, detachment of cells, flagging of cells and apoptosis. The concentration of 10 mg/ml of ethanolic extract inhibited the cancerous cell growth.

PLANT PROFILE



CURCUMA AMADA

Classification[85]

Kingdom :plantea

Division :magnoliophyta

Class :monocotyledonea

Order :zingeberales

Family :zingiberaceae

ANTIULCER ACTIVITY OF FRESH RHIZOME JUICE OF CURCUMA AMADA

Genus : curcuma

Species :c.amada

VERNACULAR NAMES[86]

Sanskrit: Amradrakam,Amragandha-haridra, KarpuraHaridra

Bengali: AamaaAadaa

English: Mango-ginger

Gujrati: Aambaahaldhar

Hindi: Aamaa-haldi, Amiyaahaldi

Kannada: Ambarasini, HuliArsin

Malayalam: Mangayinji

Marathi: Aambehalad, Ambaahalad

Punjabi: Ambiyahaladi

Tamil: Mankayyinji

Telugu: MamidiAllamu

Unani: AambaHaldi, Daarchob

DESCRIPTION

Mango-ginger looks exactly likecommon ginger but it has flavour ofraw mango. It is the rhizome ofplant Curcuma amada and belongsto family Zingiberaceae, genusCurcuma. In Genus Curcuma, thereare more than eighty species ofrhizomatous herbs. IndianArrowroot (starch used), Wildturmeric, turmeric, Karchura aresome of the medicinal plantsbelonging to genus curcuma. In India, Mango-ginger is mainlycultivated in Gujarat, wild in parts ofWest Bengal, Uttar Pradesh,Karnataka and Tamil Nadu[87].

Ayurvedic Propertiesand Action on body

In Ayurveda, Mango-ginger is usedin treatment of skin itching,wounds, cough, respiratory illness,hiccups, fever, inflammations, earpain and in vitiation of all tri-dosha.

Rasa (Taste): Tikta/Bitter, Madhura/Sweet

Guna (Characteristics): Laghu/Light

Virya (Potency): Sheet/ Cool

Vipaka (Post Digestive Effect): Katu/Pungent

Action: Improves digestion andappetite, Kapha-har, Pitta-har,increase virility; aphrodisiac[88]

Medicinal uses of Mango-ginger

Mango-ginger is known as AmraHaridra or KarpuraHaridra, inAyurveda. It is used as spice andalso for pickling. Similar to othermembers of genus curcuma, it hasalso many therapeutic propertiesand is especially useful in digestivecomplaints. Its use gives relief inabdominal gas. It promotes appetiteand improves digestive strength.Similar to ginger it is expectorantand gives relief in cold and cough.Its use is also recommended in liver inflammation, joint pain,rheumatism and inflammation dueto injuries. The rhizomes are madeinto paste and applied on sprains,bruise, and skin diseases[89,90].

In arthritis, Mango-ginger is usedalong with Moringa (Moringaoleifera). For this purpose, 200gbark of Moringa is ground andboiled with water. Due toevaporation of water a paste isprepared which is collected andmixed with 100g Mango-ginger and100g Maricha powder orblack pepperpowder. This paste is applied on thejoints.In scientific study, mango gingerexhibits decrease in liver total lipidsand serum triglycerides. For medicinal purpose, the driedrhizomes powder should be taken indose of 3-5 grams or 10-20 ml offresh juice[91,92].

AIM AND OBJECTIVE

AIM

To evaluate the antiulcer activity of *curcuma amada*.

OBJECTIVES

- Evaluation of antiulcer activity of *curcuma amada.*
- Determination of the extract of *curcuma amada.*
- Dose dependent studies.
- Time dependent studies.
- To find out the effect of *curcuma amada* extract on different parameters.

PLAN OF WORK

Proposed plane of work was carried out in the following stages:

Phase I

- Literature survey

Phase II

- Collection of herbal ingredients and raw materials.

Phase III

- Preliminary phyto chemical screening.
- Toxicological assessment
    - Acute toxicology

Phase IV

- Pharmacological evaluation
    - Antiulcer Effect

Phase V

- Compilation of data and conclusion

MATERIALS & METHODS

CHEMICALS

All the chemicals and reagents used in the study were of analytical grade and procured from reputed Indian manufacturers.

COLLECTION AND AUTHENTICATION OF PLANT

Curcuma amada was produced from the Botany Central council for Research in Ayurvedia and Siddha Govt of India.

The dried whole plant powder of Curcuma amada was supplied and authenticated by Chelladurai.v research officer Botany Central council for Research in Ayurvedia and Siddha Govt of India.

II-PHYTO CHEMICAL SCREENING[93].

The plant may be containing the following compound such as carbohydrate, protein, and lipids. That is utilized as food by man. It also contains the compound like. Tannins, glycosides, alkaloids. Volatiles oils. The compound that is responsible for lots of medicinal properties

TEST FOR CARBOHYDRATES

Molish test

The sample powdered was added with 1 ml of alpha napthol solution along with conc Sulphuric acid solution in the test tube reddish colour was produced at the junction between 2 liquid this is shows the presence of carbohydrate.

Fehling test.

To the sample powder was added with both Fehling A and Fehling B solution and placed in the water bath for a sufficient time. This shows the brick red colour. It shows the presence of carbohydrate.

Benedicts test.

To the sample powder add 8 drops of benedicts reagents and boil the sample vigorously for 5 min it shows the red ppt. this shows the presents of carbohydrate.

TEST FOR ALKALOIDS

To the small of stored powder (sample) was taken and add few drops of hydrochloric acid and filtered. The filtered was tested with various alkaloid agents.,

Mayer's reagents:

To a small of above filter add small quantity of Mayer's reagent to form cream precipitate. This shows the presence of alkaloids.

Dragendorffs reagents

From the above filter add small amount of Dragendorffs reagents it forms a orange brown precipitate. This shows the presents of alkaloids.

TEST FOR FLAVONOIDS

To the filter of the plant extract add 5 ml of dilute ammonia solution and followed by the addition of concentrated sulphuric acid. It forms a yellow colour. It shows extract indicated the presence of flavonoids.

TEST FOR STEROIDS.

Salkowaski test

Few amount of plant extract was mixed with chloroform and the same volume of sulphuric acid is added on it. Cherry red colour was obtain in the chloroform layer. This shows the sample contain steroids.

Libbbermann burchatd test:

The extract is dissolved in 2 ml of chloroform 10 drops of acetic acid and conc. Sulphuric acid were added. Now the solution becomes reddish colour then it turns to bluish green colour. This shows the plant extraction indicates the presents of steroids.

TEST FOR TANNINS.

From few amount of plant extract is treated with vanillin hydrochloric acid reagent. It forms, pink or red colour due to the formation of phloroglucinol, it indicate the presence of tannins.

TEST FOR PROTEIN.

Mellon's reagents.

Mellon's reagents (mercuric nitrate in nitric acid containing a trace of nitrous acid) usually yields a white precipitate on addition to a protein solution which turns red on heating.

Ninhydrin Test.

From the sample solution add 2 drops a freshly prepared 0.2% ninhydrine reagent was added to the extract and heating. Development of blue colour may indicate the presence of peptide, amino acid (PROTEIN).

TEST FOR GLYCOSIDES:

Keller- killani test.

From the small quantity of small powder acetic acid was dissolved and adds few drops of ferric chloride and transferred to the surface of conc Sulphuric acid. At the junction, reddish brown colour was formed, which gradually becomes blue indicates the presents of cardiac glycosides.

TEST FOR SAPONINS.

Foam test:

1 ml of extract solution is diluted separately with distilled water to 20 ml and shaken in a graduated cylinder for 15 minutes. A 1 cm layer of foam indicates the presence of Saponins.

III-PHARMACOLOGICAL SCREENING

ANIMALS

The albino rat (average body weight 200-300g),used from in house laboratory. The animals were maintained under standardized environmental conditions (22-28^{o}C , 60-70% relative humidity, 12 hr dark/light cycle) in animal house, Department of pharmacology,RVS College of Pharmaceutical Sciences, sulur,Coimbatore. The animals were provided with standard mouse chow (Sai Durga Feeds and Foods, Bangalore, India) and water *ad libitum*. All animal experiments were conducted during the present study got prior permission from Institutional Animal Ethics Committee (IAEC approved) and following the guidelines of Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA) constituted by the Animal Welfare Division, Government of India (No:- IAE 1012/c/07/ CPCSEA-Corres-2013-2014).

ACUTE TOXICITY STUDIES (Dose Fixation[94])

Experimental Protocol

Guideline	:	OECD – 420-fixed dose method
CPCSEA Reg. No	:	1012/c/06/CPCSEA
Test	:	Limit test
Species	:	*Rattus norvegicus*
Strain	:	Albino Wistar rats
Number of animals	:	05
Sex	:	Male/female
Initial dose	:	2ml/kg
Route of administration	:	Oral
Duration	:	3hr close observation, followed by 14 days observation
	:	Body weight, water intake, mortality status

Parameters : CNS, ANS and behavioral changes

Blood collection : Not needed

Sacrifice : On day 14 after oral administration

TABLE: 03

EXPERIMENTAL DESIGN FOR ACUTE TOXICITY STUDIES

Group	**Dose(mg/kg)**
Group I	5
Group II	50
Group III	300
Group IV	2000

STUDY DESIGN

Test animal – 6-8weeks old Adult Wistar rats of male and female, nulliparous and non-pregnant animals were obtained from centralized animal house from RVS College of Pharmaceutical Sciences, Sulur and acclimatized to holding for 1 week prior dosing.

Housing conditions

Temperature – The experimental animal room temperature maintained at 22°C±3°C OECD guideline-425, 2001. These ranges are designed to allow homeotherms to maintain metabolic rate or to be within their thermo neutral zones. Because, temperature below the recommended range leads to increased food intake, increased energy expenditure but decrease in efficiency. In contrast, temperature above the recommended range leads to decreased food

intake, decreased weight and decreased energy expenditure. Toxicity can vary with temperature might increase with linearity with temperature.

Humidity – The relative humidity maintained at 40%-60% preferably not exceeds 70% (OECD-425, 2001).The relative humidity below the recommended range can develop lesions such as ring tail and food consumption may be increased.

Light – 12-12 hours, Light/dark cycle. Appropriate lighting and light cycle play a key role in maintaining the physiology and the behavior rat. Light provided for adequate vision and for neuroendocrine regulation of diurnal and circadian cycles (CPCSEA guidelines for laboratory animal facility 2003).

Light intensity – The light intensity maintained at 325 lux approximately 1m above the floor. Consideration of variations in light intensity, for the arrangement of animals on cage rack for toxicology study is necessary.

Caging – Polypropylene cages with solid bottom and walls. Lids made up of stainless steel grill capable of holding of both feed and water.**Feeding condition** – Sterile laboratory feed (*ad libitum*) and RO water bottles daily.

Feed – Brown colored chow diet

Drug administration – Animals were fasted for 12hour prior to dosing on day 0. Treatment rats were dosed by oral gavages, using a curved and ball tipped stainless steel feeding needle, with 20% gum acacia solution.

Clinical observations – All rats were monitored continuously for 4 hour after dosing for signs of toxicity. For the remainder of the 14 days study period, animals were monitored and any additional behavioral or clinical signs of toxicity. Animal's body weight was measured prior to dosing and on days 7 and 14.On all animals were killed and at the end of the study LD_{50} value was established. Clinical observations and gross pathological examination was carried out.

Ethanol induced gastric ulcer

Albino Wistar rats of both sex having (150-200g) are divided in to 5 groups of 6 animals each. They are housed in individual cages and fasted for 24hrs allowing free access to drinking

water. Care being taken to avoid coprophagy. Ulceration was induced in 36 hours without feeding the rats by the administration of 80% ethanol orally in a dose of 1ml for each rat. Test and Standard is given each dose level of rat, one hour before the ethanol administration. After two hours of ethanol administration, animals will be sacrificed by CO_2 poisoning. The stomach is dissected out, opened along the greater curvature and the contents are drained in a centrifuge tube and were centrifuged at 1000rpm for 10 minutes and the volume is noted. The p^H of the gastric juice is recorded by using a p^H meter. Then the contents are subjected to analysis for free and total acidity. The stomachs are then washed with running water to see for ulcers in the glandular portion of the stomach. The numbers of ulcers per stomach are noted and severity of the ulcers scored microscopically with the help of 10x lens.

ASPIRIN INDUCED ULCER[96]

Table 4- Time dependent studies:

SI NO.	DRUG	DOSE	NO. OF ANIMALS	DURATION	PARAMETERS FOR STUDY
1.	Control (water)	----------	6	15days	1.Ulcer index 2.Total acidity 3.Acid volume 4.pH 5.Glutathione 6.Total protein
2.	Standard (pantoprazole)	1.5mg/kg	6	15days	
3.	Fresh juice	2 ml/kg	6	15days	
4	Control (water)	----------	6	30 days	

5.	Standard (pantoprazole)	1.5mg/kg	6	30 days	
6	Fresh juice	2ml/kg	6	30 days	

1) Ulcer index[97]

Procedure:

1. Animals in the group of ethanol induced ulcer were starved for 36 hours having access to drinking water ad libitum.

2. 1ml of 80% ethanol would be administered orally. Pantoprazole is given to one group and fresh juice to the other groups 1 hour before the administration of ethanol.

3. After 2 hours of ethanol administration, animals will be sacrificed by overdose of ether.

4. The stomach was removed and fixed on a cork plate and the number of and severity of ulcers was registered with a stereo-microscope using the following scores.

Severity score:

0 = Normal coloured stomach

0.5 = Red colouration

1 = Spot ulcer

1.5 = Hemorrhagic streaks

2 = Ulcers $\geq$ 3 but $\leq$5

3 = ulcers > 5

Calculation:

Ulcer index is determined by using following formula;

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

Where,

UI = ulcer index

UN = average of number of ulcers per animal

US = average of severity score

UP = percentage of animal suffered ulcer

2) Determination of total acidity[98]

Principle:

A known amount of gastric residue was titrated with 0.1 N sodium hydroxide to a pH of 3.5. If pH meter is not available, add two drops of Topfer's reagent which changes to a salmon colour when all the free hydrochloric acid is neutralized. The total acidity however was determined by titration using phenolphthalein as indicator.

Reagents:

(a) **Sodium hydroxide solution (0.1N NaOH):** Stock Sodium hydroxide solution (0.1N NaOH) was diluted ten-folds. Alternatively, 4g of NaOH was dissolved in fresh distilled water and made up to 1000 ml.

(b) **Phenolphthalein solution (1% alcoholic):** 1 g of phenolphthalein was dissolved in 100 ml of 95% alcohol.

(c) **Topfer's reagent (Dimethylaminoazobenzene), 0.5% alcoholic solution:** 0.5 g of Topfer's reagent was dissolved in 100 ml of 95% alcohol.

Procedure:

1. 10ml of gastric juice specimen was transferred in a porcelain evaporating dish.

2. 1-2 drops of Topfer's reagent is added.

3. A colour change was observed; a bright red colour appears if free hydrochloric acid is present. 1-2 drops of phenolphthalein was added to the gastric juice with Topfer's reagent.

4. Titrated with 0.1 NaOH from a burette, mixing was done after each addition until the last trace of red colour disappeared and was replaced by a canary yellow colour.

5. The numbers of millilitres of NaOH used was read from the burette. This represents the amount of free hydrochloric acid.

6. The titration was continued until the red colour of phenolphthalein appeared (deep pink), titrated to the point at which the further addition of alkali did not deepen the colour.

7. Reading was taken (ml NaOH) for total acidity.

Calculation:

Y = ml of 0.1 N NaOH x 10

Where,

Y= Total acidity (mEq/L)

3) Acid volume[99, 100]

Procedure

1. Animals in the group of ethanol induced ulcer were starved for 36 hours having access to drinking water ad libitum.

2. 1ml of 80% ethanol would be administered orally. Pantoprazole is given to one group and fresh juice to the other groups 1 hour before the administration of ethanol.

3. After 2 hours of ethanol treatment, animals will be killed by overdose of ether.

4. The stomach was removed and the contents were drained into a graduated centrifuge tube through a small nick along the greater curvature.

5. The volume of the juice was measured.

4) pH

Procedure:

1. Animals in the group of ethanol induced ulcer were starved for 36 hours having access to drinking water ad libitum.

2. 1ml of 80% ethanol would be administered orally. Pantoprazole is given to one group and *curcuma amada* juice to the other groups 1 hour before the administration of ethanol.

3. After 2 hours of ethanol administration, animals will be sacrificed by overdose of ether.

4. The stomach was removed and the contents were drained into a graduated centrifuge tube through a small nick along the greater curvature.

5. The tubes were centrifuged at 3000 rpm for 10 minutes and the centrifuged samples were decanted and analyzed for pH (using digital pH meter, Type DPH – 100- Data instruments).

5) Estimation of glutathione[101]

Reagents

DTNB reagent (5-5 dithiobis-2 nitrobenzoic acid): 39.6 mg of DNTB dissolved in 100 ml of 1 % of sodium citrate solution.

Trichloroacetic acid (TCA).

Procedure:

The mucosa of glandular stomach was removed by scraping with a blunt knife and 10% homogenate was prepared. The homogenate was precipitated with 25% trichloro acetic acid (TCA) and centrifuged. The supernatant was taken for GSH estimation using freshly prepared DTNB solution. The supernatant was taken for GSH estimation using freshly prepared DTNB solution. The intensity of the yellow color formed was read at 412 nm parallel blank for each sample without reagent was run.

Calculation:

The amount of Glutathione was determined using molar extinction coefficient.

Calculate the enzyme activity by the following formula:

$$A = Є. b. c$$

Where,

A = Absorbance of the solution.

Є = molar extinction coefficient.

b = path length of the light.

c = Concentration of absorbing solute.

6) Estimation of total protein[102]

Biuret method: This method is easy to follow and provide accurate results.

Principle:

Proteins and peptides react with alkaline copper tartrate solution to give a violet coloured complex. The intensity of the final colour complex is measured colorimetrically at 540 nm and is proportional to the concentration of the total protein in the specimen under test. Under carefully controlled conditions this method can prove to be very useful but the reagents must be prepared carefully.

Reagents:

a) Working biuret solution.

(b) Saline (NaCl, 0.85%w/v in water): 8.5 g of sodium chloride was dissolved in about 800 ml of water and placed in a one liter volumetric flask. The solution was brought up to the 1000 ml mark with water and mixed by inversion. The solution was kept in a stoppered glass bottle.

(c) Standard protein solution: The value of the protein concentration was in the range of 6 to 8 g protein per 100 ml.

Procedure:

1. Three test tubes were set up marked as T, S and B for test, standard and blank respectively.

2. 5 ml of working Biuret reagent was pipetted out into the above test tubes.

3. 100µL of undiluted specimen and standard was added in T and S tubes respectively, and 100µL of water in tube B.

4. Contents were mixed thoroughly and incubated for 15 minutes at 37^0C in a water bath or alternatively for 30 minutes at room temperature.

5. Absorbance of the test and standard was measured against the blank at 540nm. The readings were completed within one hour.

Calculation:

Total protein concentration in test specimen (g/dL) = $(A_t/A_s) \times 6$

Where,

A_t = Absorbance of test

A_s = Absorbance of standard

RESULT AND DISCUSSION

PRELIMINARY PHYTO CHEMICAL SCREENING.

Curcuma amada rhizome juice was subjected various chemical tested as per the standard methods for the identification of the various constituents. The result if this phyto chemical analysis is listed below.

Table 5- Qualitative phyto chemical screening of *curcuma amada* rhizome juice

PLANT CONSTITUENT	INFERENCE			
	Acetone	**Methanol**	**Ethanol**	**Chloroform**
Carbohydrate	+	+	+	+
Alkaloids	+	+	+	-
Flavonoids	-	+	-	+
Proteins and amino acids	-	-	-	-
Glycosides	+	+	+	+
fixed oil	+	+	+	-
Tannins	+	+	+	-

PHARMACOLOGICAL STUDY

ACCUTE TOXICITY STUDIES

Table 6 shows dose dependent effect of FJCA. The antiulcer effect of fresh juice of curcuma amada (FJCA) was found to have increased with increasing doses. The maximum effect was

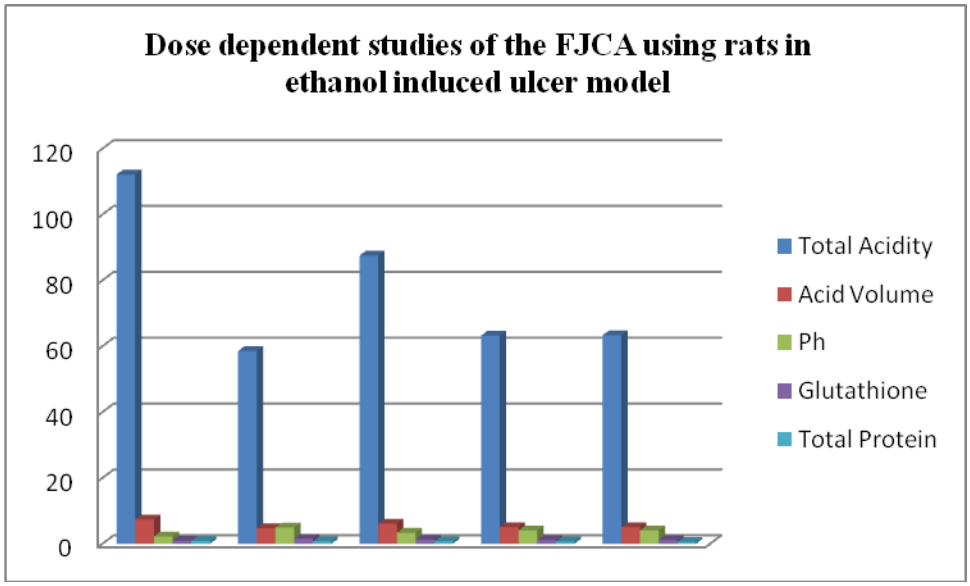
observed at 2ml/kg body weight for. Administration of ethanol resulted in severe erosions.

Table 6- Dose dependent studies of FJCA using ethanol induced ulcer model rat model

S.No	**Treatment**	**No of animal**	**Dose**	**Ulcer Index**	**Total Acidity (m Eq/L)**	**Acid Volume (ml)**	**Ph**
1	Control (water)	6	-	11.85±0.30	112.1±1.13	7.33±0.21	2.2±0.10
2	Pantoprazole	6	1.5mg/kg	4.80±0.42**	58.5±0.84**	4.73±0.33**	4.9±0.16**
3	FJCA	6	1.5ml/Kg	8.55.00±0.28	87.5±0.22*	6.05±0.11*	3.32±3.05
4	FJCA	6	2ml/Kg	4.91±0.004*	63.2±0.516*	5.05±0.09*	4.05±4.77**
5	FJCA	6	4ml/Kg	4.65±0.11**	63.3±0.21**	5.02±0.04**	4.02±3.33**

However, the FJCA decreases the severity and incidence of gastric erosions in ethanol treated animals. The ulcer index of group I animals which served as control (water) was 11.85±0.30. The ulcer index for group III (100mg/kg), group IV (200mg/kg) and group V (400mg/kg) was 8.55±0.28, 5.39±0.21, 1.84±0.11 respectively. Pantoprazole, the reference standard (group II) had ulcer index 4.80±0.42 as shown in Table

Figure 11- Dose dependent studies of the FJCA using rats in ethanol induced ulcer model



FJCA showed reduction in total acidity at all doses tested when compared with control as reflected by the total acidity values. The total acidity of group I which served as control (water) was 112.1±1.13. The total acidity of group III (1.5ml/kg), group IV (2ml/kg) and group V (4ml/kg) was 87.5±0.22, 63.2±0.516, 63.3±0.21respectively, as shown in Table 6.pantoprzole, the reference standard (group II) had total acidity 58.5±0.84, as shown in Table 1.

The acid volume of gastric secretion of group I animals which served as control (water) was 7.33±0.21 and in group III (1.5ml/kg), group IV (2ml/kg), group V (4ml/kg) was 6.05±0.11, 5.05±0.09, 5.02±0.04 respectively. Group II standard (pantoprzole) treated had acid volume 4.73±0.33, as shown in Table 7.

pH of gastric secretion of group I animals which served as control(water) was 2.2±0.10 and in group III (1.5ml/kg), group IV (2ml/kg), group V (4ml/kg) was 3.32±3.07, 4.05±4.77, 4.02±3.33 observed respectively. Group II standard (pantoprazole) treated had pH 4.9±0.16, as shown in Table 6.

Since glutathione is intimately associated with the prevention of gastric erosions. It was thought worthwhile to measure glutathione level in control and treated rats, group I animals which served as control had gutathione level 0.92±0.012. In group III (1.5ml/kg), group IV (2ml/kg), group V (1.5ml/kg) the glutathione level was 1.20±0.012, 1.10±0.094, 1.11±0.024 respectively. The level of glutathione of Group II standard (pantoprazole) treated was 1.53±0.19.

FJCA was also studied for its effect on total protein content of the gastric juice. It showed rise in protein content in the control group where as pretreatment with FJCA at different dose levels was observed as declining the protein content. Simultaneously, there was a fall in the protein content in pantoprazole treated group. The total protein content of the group I which served control was 0.853±0.02. Group III (100mg/kg 0.5ml/100gm), group IV (100mg/kg 1.0ml/100gm), group V (100mg/kg 2.0ml/100gm) was having the total protein content 0.721±0.09, 0.532±0.05 and 0.555±0.02 respectively. pantoprazole which was used as standard (Group II) had total protein content 0.700±0.03.

Aspirin Induced Model

Table 7 shows dose dependent effect of FJCA. The antiulcer effect of fresh juice of curcuma amada (FJCA) was found to have increased with increasing doses. The maximum effect was observed at 200mg/kg body weight for. Administration of aspirin resulted in severe erosions. However, the FJCA decreases the severity and incidence of gastric erosions in ethanol treated animals. The ulcer index of group I animals which served as control (water) was 10.80±0.30. The ulcer index for group III (100mg/kg), group IV (200mg/kg) and group V

(400mg/kg) was 6.10±0.24, 2.09±0.25, 2.15±0.11 respectively.pantoprazole the reference standard (group II) had ulcer index 4.30±0.42 as shown in Table 7.

S. No	Treatment	No of animals	Dose	Treatment Duration (days)	Ulcer Index	Total Acidity (mEq/)	Acid Volume (ml)	pH
1	Control	6	-	15	11.3±0.42	105.00±3.13	8.01±0.421	2±0.06
2	pantoprazole	6	1.5ml/kg	15	4.75±0.48	55.00±0.95**	4.18±0.22**	4.3±0.02**
3	FJCA	6	2ml/kg	15	3.49±0.11	45±0.45*	4.08±0.08	4.09±0.05#
4	Control	6	-	30	11.8±0.30	102±0.44**	7.53±0.06	2.1±0.09
5	pantoprazole	6	1.5ml/kg	30	2.74±0.02	54.5±0.22**	3.70±0.02	4.5±0.06**
6	FJCA	6	2ml/kg	30	0.50±0.12	49±0.22	3.55±0.02*	6.2±0.02**

Time dependent studies:

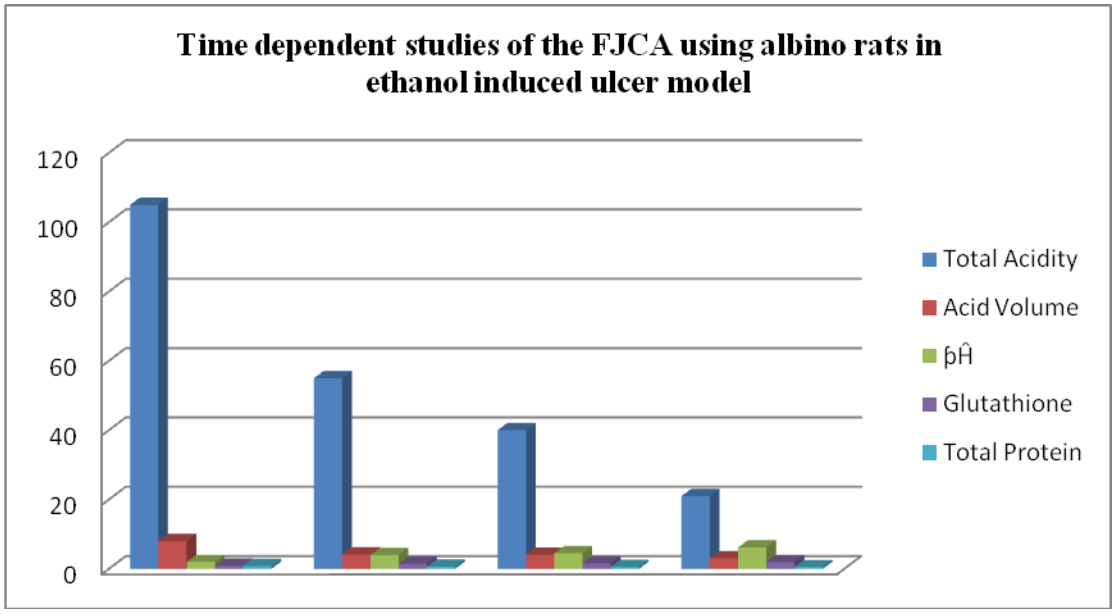
Ethanol Induced Model

Table 7-Time dependent studies of the FJCA using albino rats in ethanol induced ulcermodels

FJCA-fresh juice of curcuma amada

**P<0.001, *P<0.05, compared with control.

Figure 12- Time dependent studies of the FJCA using albino rats in ethanol induced ulcer model



Time dependent effect (15 days) of FJCA is shown in table 7 At dose of 2ml/kg body weight it had shown that time dependent administration decreases the ulcer index. The ulcer index of group I animals which served as control (water) was 11.3±0.42. pantoprazole, the reference standard (group II) had ulcer index of 4.75±0.48. The ulcer index values in group III was 1.99±0.11

The total acidity of group I animals which served as control was 105.00±3.13. The total acidity of group III was 59±0.45. pantoprazole, the reference standard had total acidity 55±0.365.

The acid volume of gastric secretion of group I animals which served as control was 8.01±0.41 and in group III was 4.08±0.08. pantoprazole treated had acid volume of 4.18±0.23.

The pH of gastric secretion of group I animals which served as control was 2±0.06 and in group III was 4±0.05. The standard reference (pantoprazole treated) had pH 4.19±0.02.

The glutathione content of group I animals which served as control was 0.89±0.01. The glutathione level of group III was 1.60±0.03. The reference standard (pantoprazole treated) was 1.45±0.66.

The total protein content of the group I which served as control was 0.809±0.08. The total protein content of group III was 0.532±0.02. pantoprazole which is used as standard had total protein content of 0.615±0.06.

At dose of 200mg/kgbody weight it had shown that (30 days) time dependent administration decreases the ulcer index more then (15 days) time dependent administration. The ulcer index of group IV animals which served as control (water) was 11.6±0.30. The ulcer index values in group VI was 2.74±0.18. pantoprazole, the reference standard (group V) had ulcer index of 0.50±0.08.

The total acidity of group IV animals which served as control (water) was 102.44. The total acidity values in group VI was 54.5±0.22. pantoprazole, the reference standard (group V) had ulcer index of 49±0.22.

The acid volume of group IV animals which served as control (water) was 4.53±0.06. The acid volume values in group VI was 3.55±0.02. pantoprazole, the reference standard (group V) had ulcer index of 4.72±0.02.

The pH of group IV animals which served as control (water) was 1.9±0.09. The pH values in group VI was 4.32±0.02 . pantoprazole, the reference standard (group V) had ulcer index of 4.50±0.06.

The glutathione of group IV animals which served as control (water) was 0.93±0.01. The glutathione values in group VI was 1.80±0.09. pantoprazole, the reference standard (group V) had ulcer index of 1.50±0.02.

The total protein of group IV animals which served as control (water) was 0.818±0.14. The total protein values in group VI was 0.510±0.002. pantoprazole the reference standard (group V) had ulcer index of 0.541±0.27.

SUMMARY AND CONCLUSION

The plant curcuma amada is widely distributed in india and srilanka.the leafes of the plant have been studied its antiulcer activity but the antiulcer effect of rhizomes fresh juice have been never studied. Hence the objective of the study is determining this effect from the fresh juice of rhizomes of curcuma amada.

The preliminary phytochemical screening of whole plant extracts indicate in presence of flavonoid, alkaloid, tannins, terpenoids and glycosides may accounts antioxidant and anti-ulcer potential.

The antiulcer effect is screened in fresh juice of rhizome of curcuma amada on ethanol and aspirin induced time and dose dependent ulcer study. The results get from these study have been shown that fresh juice of rhizome of curcuma amada produce antiulcer effect in ethanol and aspirin induced ulcer models. In ethanol and aspirin induced model, there is reduction in ulcer index, total acidity, total volume of gastric contents, total protein concentration and higher concentration of glutathione content and pH of gastric secretion they compared with control treated group.

pantoprazole used as a standard comparison agents. pantoprazole used as proton pump inhibitors blocker, is significantly reduce about 90% of basal, food induced and hormonal mediated gastric acid, which again induced by , gastrin, parasympathomimetic drugs and [103]

Total acidity responsible quantification acid is present in the gastric secretion. It has a important aggressive factor which induced the ulcer. Gastric release is maintained by vagal control and higher activity of vagus stimulation also contributes to ulcer formation[106].

On ethanol administration, the mucosal mast cells mediate to secretion of vasoactive mediators containing histamine. Histamine is mediated to stimulate the synthesis of cyclic AMP through activation of the enzyme adenyl cyclase which mediate the activation of gastric proton pump and secrete of hydrogen ions. The treatment of fresh juice showed reduce the total acidity of the gastric contents.

Serum protein including albumin and globulin. In the peptic ulcer the total protein concentration of serum or gastric secretion are increased. This may be due to leakage of plasma protein in to the gastric secretion or serum with lower mucosal resistance/barrier of the gastric mucosal layer[107].After treatment with FJCA there was a significant reduction in protein concentration of gastric juice which enhancing leakage of plasma proteins.

Acid volume is amount (in ml) of acid release in the gastric content release contain HCl, pepsinogen enzyme, mucus secretion, bicarbonates concentration, intrinsic factor and proteins. Amount of acid release is an important factor responsible for the production of ulcer mediated by exposure of the unprotected lumen of stomach by concentrated acids[107]. FJCA treatment showed decrease in the acid volume of the gastric secretion.

Increased pH shows a lower concentration of the hydrogen ion. The hydrogen ion is a major triggering factor responsible for the etiologic factor for ulcer and gastric damage[108]. FJCA treatment indicate higher concentration of pH of the gastric juices. This values directly shown the FJCA reduce possibility of ulcer and has a protective effect of surface of the gastric mucosa.

In gastric ulcer tissues, Glutathione (g-glutamylcysteinylglycine, GSH) levels were found to be decreased[109]. Ethanol-induced genesis of free radical concentration reduces the cysteine concentration which mediated for GSH released. Values from this study responsible for depletion of gastric GSH is related with induction of gastric lesion in the rats. GSH is a tripeptide and having a superoxide radical scavenger and it protect thiol protein contents essential for release the integrity of tissue against oxidation reaction[110, 111]. In my present study, FJCA treatment showed increase in the glutathione content.

The present study is evaluated the antioxidant potential and antiulcer effect of FJCA. The results analysed from the present study have indicate that FJCA possesses antioxidant and antiulcer effect on ethanol induced ulcers.

Pre-treatment with FJCA particularly at a dose of 2ml/kg in a single schedule and 0.5ml/100gm for 15 and 30 days treatment reduce the ulcer index value, total acidity concentration, total volume of acid release and total protein and increase value pH and glutathione content when compared with control groups.

All these data indicate that the FJCA could be regarded as a favourable antioxidant and anti ulerogenic effect.

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