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PHARMACOGNOSTICAL, PHYTOCHEMICAL AND ANTIULCER ACTIVITY OF ETHANOLIC EXTRACT OF AEGLE MARMELOS

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ABSTRACT

The objective of present study is to evaluate the antiulcer activity of ethanolic extract of leaves of Aegle marmelos. The cause of ulceration in patients is mainly due to hypersecretion of gastric juice and pepsin. In traditional system of medicine a number of herbal preparations have been used for the treatment of peptic ulcers. The anti-ulcer activity of methanolic extract of Aegle marmelos leaves was investigated by aspirin plus pylorus ligation induced gastric ulcer in rats, Ethanol induced ulcer in rats, water immersion stress test induced ulcer in rats. In aspirin plus pylorus ligation model, Aegle Marmelos at doses of 200 and 400 mg/kg produced significant reduction in gastric volume, free acidity and ulcer index compared to control. In ethanolic extract induced ulcer models both doses (200mg/kg & 400mg/kg) of Aegle marmelos extract significantly reduced severity of ulceration. This present study indicates Aegle marmelos leaves extract have potential antiulcer activity.

KEYWORDS: Aegle marmelos, Ulcers, NSAIDS, Antiulcer.

INTRODUCTION

Pharmacognosy is the objective study of crude drugs of animal, vegetable and mineral origin treated scientifically.

Indian System of Medicine (ISM) has been introduced from time immemorial in the traditional practice to treat various ailmentsand now it's becoming globally accepted with scientific evaluation due to their curative properties (Soumyaprakash etal., 2009).

Herbal medicine is the oldest form of health care known to mankind. Primitive man observed and appreciated the great diversity of plants available to him. The plant provide food, clothing, shelter and medicine. A great variety of plants are used for medicinal treatments. An herb is aplant or plant or specific part root, leaves, fruits, flowers, seeds) is formulated into suitable preparation compressed as tablets or made into pills, used to make infusions (teas), extracts, tinctures etc., or mixed with excipiets to make lotions, ointments, creams etc., herbs produce and contain a variety of chemical substances that act upon the body (Lai PK; 2004) from time to time new drugs are discovered from herbal sources.

Traditional system of medicine whether they are of Indian, China, Tibetan or Thai origins have evolved over several hundreds of thousands of years through transfer of knowledge, and usage practice from generation to generation. From the vast array of the Materia medica of indigenous system it is thought that investigation and research on medicinal plant it might bring to the scientific world many useful remedies for the alleviation of human suffering. Inspite of the remarkable achievement of modern medicine and medical research these ancient systems continue used to be a major component, effectively used in the control or alleviation of disease. Plants and plant-based drugs are less toxic and have acceptable side effect. It is therefore essential to bring the use of these remedies into an existing frame work of rational scientific use of medicine based on the strong traditional knowledge. A rational approach is being developed to use medicinal plants as a lead for the discovery of active molecule, which act as one of the largest reservoirs. It is imperative that India develops a concerned, integrated, structural and modern approach in this area and gain a competitive edge in the international market, and creates a place for the discovery of plants-based drug for a variety of disease for which currently adequate or appropriate remedies are not available.

History of Herbal Medicine

Herbalism is a traditional medicinal or folk medicine practice based on the use of plants and plant extracts. Herbal medicine is called as Herbalism or Botanical Medicine. The scope of herbal medicine is extended to include fungi, bee products as well as minerals, shells and certain animal parts.

Herbal medicine is the oldest form of health care known to mankind. Primitive man observed and appreciated the

great diversity of plants available to him. The term phytotherapy was introduced by the French physician Henri Leclerc (1870 – 1955). He had published numerous essays on the use of medicinal plants, most of them in lapresse medical a leading French medical journal. Leclerc's life and work were described in lively terms in an obituary which appeared in lapresse medicale on 14 May 1955 (Meuss et al.,).

Indian Aryuvedic Medicine has been using herbs such as turmeric and curcumin possibly s early as 1900 BC. Many other herbs and minerals used Ayuveda were later described by ancient Indian herbalists 1st millennium BC. The sustruta samhita attributed to sustruta in the 6th century BC describes 700 medicinal plants, 64 preparations from mineral sources, and 57 preparations based on animal sources (Girish Dwivedi et al., 2008).

Ayurveda is the most ancient health care system and is practiced widely in India, Srilanka and other countries. Atharveda (around 1200 BC), Charak Samhita and Sushrut Samhita (100-500 BC) are the main classics that given detailed descriptions of over 700 herbs(Dash et al; 2001). In the western world documentation of use of Natural substances for medicinal purposes can be found as far back as 78 A.D., when Dioscorides wrote "De Materia Medica", describing thousands of medicinal plants(Tyler et al 1988) This treatise include description of many medicinal plants that remain important in modern medicine, not because they continue to be used as crude drug preparations, but because they serve as the source of important pure chemicals that have become mainstays of modern therapy. The term "Material medica" which means "Medical Materials" is no longer utilized routinely in Western medicine, the fact remains that the physicians of today continue to use many substances and products derived from natural sources, usually for the same therapeutic benefit as the crude drug. These single chemical entities, i.e., drugs, form the basis for much of out ability to control disease.(Agarwal 2004) The use of herbs to treat diseases is almost universal among non-industrialized societies. A number of traditionscame to dominate the practice of herbal medicine at the end of 20 century.

In recent times, there have been increased waves of interest in the field of Research in Natural Products Chemistry. This level of interest can be attributed to several factors, including unmet therapeutic needs, the remarkable diversity of both chemical structure and biological activities of naturally occurring secondary metabolites, the utility of novel bioactive natural products as biochemical probes, the development of novel and sensitive techniques to detect biologically active natural products, improved techniques to isolate, purify, and structurally characterize these active constituents, and advances in solving the demand for supply of complex natural products. (Newman et al., 2000). The R & D trust in the pharmaceutical sector is focused on development of new innovative/indigenous plant based drugs through investigation of leads from the traditional system of medicine(Patwardhan et al 2004) The World Health Organization has also recognized the importance of traditional medicine and has created strategies, guidelines and standards for botanical medicines. Proven agro-industrial technologies need to be applied to the cultivation and processing of medicinal plants and the manufacture of herbal medicines (Akerele et al 1993).Over the past decade, there has been a resurgence of interest in the investigation of natural materials as a source of potential drug substance.

Importance of Phytomedicine

Herbal medicines are the synthesis of therapeutic experiences of generations of practicing physicians of indigenous systems of medicine for over hundreds of years while nutraceuticals are nutritionally or medicinally enhanced foods with health benefits of recent origin and marketed in developed countries. The marketing of the former under the category of the latter is unethical. Herbal medicines are also in great demand in the developed world for primary health care because of their efficiency, safety and lesser side effects. They also offer therapeutics for age- related disorders like memory loss, osteoporosis, immune disorders, etc. for which no modern medicine is available. India despite its rich traditional knowledge, heritage of herbal medicine and large biodiversity has a dismal share of the world market due to export of crude extracts and drugs (Dobrin et al., 2006).

The World Health Organization (WHO) has recently defined traditional medicine (including herbal drugs) as comprising therapeutic practices that have been in existence, often for hundreds of years, before the development and spread of modern medicine and are still in use today.Or say, traditional medicine is the synthesis of therapeutic experience of generations of practicing physicians of indigenous systems of medicine. The traditional preparations comprise medicinal plants, minerals, organic matter, etc. Herbal drugs constitute only those traditional medicines which primarily use medicinal plant preparations for therapy.

REVIEW OF LITERATURE

Aegle Marmelos (L) Correa (Rutaceae)

Plant Description

Botanical name: Aegle Marmelos (L)Correa
Family: Rutaceae
Synonyms: Belou Marmelos(L), Crateva Marmelos.L.

Fig. 1: Aegle Marmelos (L) Correa (Rutaceae).

Taxonomical Classification
Domain: Eukaryota
Kingdom: Plantae
Subkingdom: Viridiplantae
Phylum: Tracheophyta
Division: Tracheophyta
Class: Magnoliopsida
Subclass: Rosidae
Superorder: Santalanae
Order: Sapindales
Family: Rutaceae
Genus: Aegle
Species: Aegle Marmelos
Botanical name: - Aegle Marmelos

Common names

The plant is native across the Indian subcontinent and southeast Asiaand is cultivated throughout Sri Lanka, Tamilnadu, Thailand, and Malesia. It was regionally called in various names. Some of them are given below.
Telugu: Maredu
Hindi: Sir Phal
Sanskrit: Shreephal, Bilwa, Bilva
Kannada: Bilva

Distribution and Morphology

Aegle marmelos is a subtropical plant which can grow up to an altitudeof 1200 m from the sea level. It grows well in the dry forests of hilly and plain areas. A. marmelos can adapt a wide range of habitat and can be cultivated worldwide. It is native to India and has its origin from Eastern Ghats and central India. This tree is mentioned in the pre-historic writings dating back to 800 B.C. The Chinese Buddhist pilgrim, Hiuen Tsiang, when came to India (1629 A.D.), noticed the presence of this tree in India. It is cultivated throughout India and due to mythological importance; it is mainly grown near the temples. It grows wild in dry forests on hills and plains of central and southern India, Sub-Himalayan tracts from Jhelum eastwards to West Bengal, The Deccan Plateau, the East coast, and also found in Andaman Islands. It found almost in all the states of India such as in Andhra Pradesh, Bihar, Himachal Pradesh, Jammu and Kashmir, Karnataka, Kerala, Madhya Pradesh, Maharashtra, Punjab, Rajasthan, Tamil Nadu, Uttar Pradesh and West Bengal. In West Bengal, there are 13 types of fruits in Aegle marmelos based on the fruits morphology.The fruits were grouped under five categories; oval, flat, spherical, oblong and pear shaped and in each group three subgroups (small, medium, big) were separated. It is also cultivated in Nepal, Myanmar, Tibet, Ceylon, Vietnam, Laos, Cambodia, Sri Lanka, Bangladesh, Thailand, Indonesia, Malaysia, the drier areas of Java, Fiji and to a limited extent on Northern Luzon of Philippine Islands where it first fruited in 1914. It is grown in Surinam and Trinidad, and some gardens of Egypt. In the 1500's this fruit was resorted to by the Portuguese in the East Indies and later by British colonials as a means of remedy to treat diarrhea and dysentery. It has grown well and fruited on the oolitic limestone of Southern Florida. Bael fruit was introduced in Europe in 1959.

Habit: This plant is a medium sized deciduous tree, upto 15m tall. Older branches spiny, spines solitary or paired,1-2 cm long, straight, sharp.

Bark: Bark grey or brownish in colour, and it bears a number of long, straight spines. It includes gums, which form from wounded branchesesd and harden overtime. The easiest way to describe these gums is as transparent, sticky sap.

Leaves: Leaves has trifoliate leaves with a circular base and a pointed apex, the adult dark green, while the youngest leaves are pale green.

Flowers: The flowers are bisexual and greenish or yellowish in colour. It is usally evident with fresh leaves.

Fruit: The beal fruit has a tougher outer jacket with a diameter of around 5- 12cm. It is green while unripe and

turns yellowish brown when ripe, it's interior includes upto 20 orange pulp.

Seed: They're small (almost 1cm) hard, hairs, flattened oblong and each is surrounded by adhesive sac.

Pharmacognostical Studies of leaves of aegle marmelos (rutacea)

Introduction

Most of the plants and their parts have been used to cure and treatment ofmany diseases since ancient time. In current scenario, synthetic drugs are easy available and more effective in treatment of various diseases butcaused some side effect in human body. Most of the person still prefers using traditional phytomedicines because of their minute side effects for health. Phytomedicinal plants are precious items for getting novel drugs that forms the constituent in conventional systems of medicine, nutraceuticals, modern medicines, folk medicines, food supplements, bioactive principles, pharmaceutical intermediates, and lead compounds in synthetic drugs.

There is a wide diversity of compounds, especially secondary metabolites like an alkaloid, phenols and flavonoid found and isolated by plants. Studies have shown that these compounds have analgesic, anticancer, anti- bacterial, antitumor, anti-inflammatory, antiviral and many other activities to a greater or lesser extent. Eminent examples of these phyto-chemical compounds include phenols, flavonoids, and saponins, phenolic glycosides, cyanogenic glycosides, stilbenes, nitrogen compounds (alkaloids, amines, betalains), terpenoids, tannins and some other endogenous metabolites. This drives the need to screen medicinal plants for novel bioactive compounds as they are safe, less side effects and have biodegradable . Aegle marmelos (L.) Corr., golden apple belongs to the family Rutaceae and also known as Bael tree. It is native to India and is used in traditional medicines. A. marmelos is a slow growing tree of a medium size (up to 12-15 m tall) throughout the deciduas forest of India of height up to 1200 meters with flaking, soft, short trunk, thick bark and spreading spiny branches. It occurs all over India, especially in dry forest on hilly slopes and plains of Eastern Central, sub-Himalayan forest, Bengal and south India.From Homoeopathic point of view, the unripe fruit and ripe fruit are being used as digestive, astringent and stomachic problems and it is prescribed for diarrhoea and dysentery treatment . The fresh juice of the leaves is taken with honey as a febrifuge and laxative; it is also used in asthmatic complaints. The ripe fruit is used as a remedy for diarrhoea. Beverages prepared with ripe fruit pulp are used to relive body heat. Cologne is also obtained by distillation from flowers. All parts of Aegle marmelos (L.) tree such as pulp, bark, flower, root, leaf, fruit, trunk and seed are useful inmany ailments. The unripe fruit is also said to be an excellent remedy for diarrhoea and is mainly useful in case of chronic diarrhoea. In the present study, an attempt for morphology, physicochemicalstandards, fluorescence analysis, preliminary phytochemical screening and high performance thin layer chromatography were performed.

Collection and Authentication

The leaves of Aegle marmelos L. belonging to family Rutaceae was collected from our institution medicinal garden and it was identified and authenticated. The taxonomical identification of leaves was done by Mrs. K. Vanitha Kumari., HOD of Botany,St. Joseph Degree college, Kurnool. The vochure specimen was preserved in our laboratory for further reference.

Macroscopical Studies of Leaf

Macroscopical characters: A small to medium – sized aromatic tree, deciduous stem branches, light brown to green ; strong auxiliar spines present on the branches the average of tree 8.5metres Leaves : are alternate, pale green trifoliate; terminal lraflet, 5.7 cm long, 2.8cm broad, having a long petiol the two lateral leaflets, almost sessile, 4.1 cm long ,2.2 cm wide, ovate to lanceolate having reticulate pinnate venation petiol 3.2 cm long.

Leaflets : Ovate or ovate -lanceolate, glabrous and densely minutely glandular - punchulate on both surfaces lateral leaflets to 7cm long and 4.2 cm wide ,petiolules 0-3mm long

Microscopic Study of Leaf (Transverse Section): The Bael (Aegle marmelos L.) Leaf is 3 leaflets in nature. Transverse section (T.S.) of the leaf showed the upper arched epidermal cells with stomata. The fibers were extent beneath the epidermis. Mesophyll cells include sclerenchyma and collenchymas fibers that proliferate from the sheath around the vein. Small acicular crystals, xylem, phloem, pith and trichom were formed in idioblasts of mesophyll and lower epidermis was showed Fig. 2.

Fig. 2: Microscopic Study of Leaf.

Powder Analysis

The powder character of a drug are mainly used in the identification of thedrug in the powder form. The leaf powder the powder the pale green in colour, aromatic, astringent and papery in texture. The microscopic

examination of the leaf peel showed paracytic stomata with absence of trichomes in the epidermal cells. Resin globules and parenchyma cells filled with evidence. Shakyawar etal.reported the presence of prismatic calcium oxalate crystals and starch grains in the leaf powder.

Fluorescence Analysis
Under white light

Dry powder	Hcl acid	NaoH &Methanol	NaoH & Water	Nitric acid	Sulphuric acid
green	Yellowish dark green	Green	Yellowish green	Dark orange	Deep reddish brown

Physico Chemical Parameters
Table 1 Physico chemical parameters.

S.no	Name of Experiment	Leaf
1	PH %	6.11
2	Solubility test %	-
3	Aqueous extract	39.43
4	Methanol erxtract	15.74
5	Total Ash value	19.18+0.01
6	Acid insoluble ash	3.43+0.13
7	Water soluble	16.29+0.06
8	LOD(loss of drying)%	6.10
9	Acidity as citric acid%	137.36
10	Foreign matter	<0.2)%
11	Dry powder particle size	0.159 um
12	Wet powder particle size	0.163 um
13	Foaming index	337.5 U
14	Swelling index	3.5%

Phytochemical analysis of leaf Aegle marmelos (rutacea)

Introduction
Phytochemical constituents have played a major role as basic source for the establishment of several pharmaceutical industries. Many medicinal plants occurring in India are yet to be subjected to various chemical investigations, which may help in the discovery of several new drugs. To investigate such chemical constituents from plants, phytochemical screening is required. Broadly, chemical constituents in plants may be divided into major groups viz., primary and secondary chemical constituents. Primary constituents are the basic metabolites of plants such as carbohydrates, proteins, lipids, cellulose and chlorophyll which are distributed in almost all the plants. Secondary chemical constituents are selective and vary considerably from plant to plant and even within the species or varieties of same genus. Secondary chemical constituents are chiefly responsible for the biological activities of plants or drugs.
Materials and Methods

Collection and Identification of Plant Material: The fresh leaves of Aegle marmelos from 3 varieties/accessions were collected from the medicinal garden of K.V.Subba reddy institute of pharmacy,Dupadu,Kurnool,India.The taxonomy of the plant was authenticated.

Extract Preparation: The leaves of the plant were properly washed in tap water and rinsed in distilled water. The rinsed leaves were hot air-dried for 3 days. The dried leaves of plant were pulverized using pestle mortar to obtain a powdered form which was stored in airtight glass containers at 4∘ C until used.About 1 kg of the leaf material was successively extracted with methanol as a solvent in a Soxhelt apparatus. The extract was concentrated and traces of the solvent were completely removed under reduced pressure and stored in vacuum desiccator for further use.

Fig. 3: Extraction through Soxhlet apparatus.

Phytochemical analysis
The concentrated extracts were subjected to chemical tests as per the methods mentioned below for the identification of the various constituents as per the standard procedures given by Kokate and Treaseand Evans.

Table 2: Extract characteristics of aegle marmelos leaves in successive extraction

Solvent	Extraction value %w/w	Colour	Odour	Consistency
Ethanol	4.16	Dark green	Characteristic	Sticky

Table 3: Phytochemical analysis of aegle marmelos extract.

Phytoconstituent	Experiments name	Result
Tannins	a.Ferric chloride test b.Gelatin test c.Lead test d.Aqueous bromine est	+
Alkaloids	Mayer's test Dragondroff's test Wagner's test Hager's test	+
Carbohydrates and Glycosides	Molisch's test Fehling's test Benedict's test Liebermann- Burchard's test Legal's test	Crbh(+) Gly(-)
Saponins	Frothing test	+
Steroids	Liebermann - Burchard reaction	+
Terpenoids	Salkowski test	+

Antiulcer Activity Of Ethanolic Extracts Of Aegle Marmelos (Rutaceae) Leaves

Peptic/Gastric Ulcer

A peptic ulcer, also known as PUD or peptic ulcer disease, is an ulcer (defined as mucosal erosions equal to or greater than 0.5 cm) of an area of the gastrointestinal tract that is usually acidic and thus extremely painful (web 4). As many as 70-90% of ulcers are associated with Helicobacter pylori, a spiral-shaped bacterium that lives in the acidic environment of the stomach; however, only 40% of those cases go to a doctor. Ulcers can also be caused or worsened by drugs such as aspirin, Plavix (clopidogrel), ibuprofen, and other NSAIDs. Contrary to general belief, more peptic ulcers arise in the duodenum (first part of the small intestine, just after the stomach) rather than in the stomach. About 4% of stomach ulcers are caused by a malignant tumor, so multiple biopsies are needed to exclude cancer. Duodenal ulcers are generally benign.

Classification

By Region/Location: • Stomach (called gastric ulcer)
Duodenum (called duodenal ulcer)
Esophagus (called Esophageal ulcer)
Meckel's Diverticulum (called Meckel's Diverticulum ulcer)
Modified Johnson Classification of peptic ulcers

Type I: Ulcer along the body of the stomach, most often along the lesser curve at incisura angularis along the locus minoris resistentiae.
Type II: Ulcer in the body in combination with duodenal ulcers. Associated with acid oversecretion.
Type III: In the pyloric channel within 3 cm of pylorus. Associated with acid oversecretion.
Type IV: Proximal gastroesophageal ulcer
Type V: Can occur throughout the stomach. Associated with chronic NSAID use (such as aspirin).

History

John Lykoudis, a general practitioner in Greece, treated patients for peptic ulcer disease with antibiotics, beginning in 1958, long before it was commonly recognized that bacteria were a dominant cause for the disease. Helicobacter pylori was rediscovered in 1982 by two Australian scientists, Robin Warren and Barry J. Marshall as a causative factor for ulcers. In their original paper, Warren and Marshall contended that most stomach ulcers and gastritis were caused by colonization with this bacterium, not by stress or spicy food as had been assumed before. The H. pylori hypothesis was poorly received so in an act of self- experimentation Marshall drank a Petri dish containing a culture of organisms extracted from a patient and five days later developed gastritis. His symptoms disappeared after two weeks, but he took antibiotics to kill the remaining bacteria at the urging of his wife, since halitosis is one of the symptoms of infection.

This experiment was published in 1984 in the Australian Medical Journal and is among the most cited articles from the journal. In 1997, the Centers for Disease Control and Prevention, with other government agencies, academic institutions, and industry, launched a national education campaign to inform health care providers and consumers about the link between H. pylori and ulcers. This campaign reinforced the news that ulcers are a curable infection, and that health can be greatly improved and money saved by disseminating information about H. pylori.

Signs and symptoms

Symptoms of a peptic ulcer can be

abdominal pain, classically epigastric with severity relating to mealtimes, after around 3 hours of taking a meal (duodenal ulcers are classically relieved by food, while gastric ulcers are exacerbated by it); bloating and

abdominal fullness; waterbrash (rush of saliva after an episode of regurgitation to dilute the acid in esophagus); nausea, and copious vomiting; loss of appetite and weight loss; hematemesis (vomiting of blood); this can occur due to bleeding directly from a gastric ulcer, or from damage to the esophagus from severe/continuing vomiting. melena (tarry, foul-smelling feces due to oxidized iron from hemoglobin); rarely, an ulcer can lead to a gastric or duodenal perforation, which leads to acute peritonitis. This is extremely painful and requires immediate surgery. A history of heartburn, gastroesophageal reflux disease (GERD) and use of certain forms of medication can raise the suspicion for peptic ulcer. Medicines associated with peptic ulcer include NSAID (non-steroid anti-inflammatory drugs) that inhibit cyclooxygenase, and most glucocorticoids (e.g. dexamethasone and prednisolone).In patients over 45 with more than two weeks of the above symptoms, the odds for peptic ulceration are high enough to warrant rapid investigation by EGD. The timing of the symptoms in relation to the meal may differentiate between gastric and duodenal ulcers: A gastric ulcer would give epigastric pain during the meal, as gastric acid is secreted, or after the meal, as the alkaline duodenal contents reflux into the stomach. Symptoms of duodenal ulcers would manifest mostly before the meal when acid (production stimulated by hunger) is passed into the duodenum. However, this is not a reliable sign in clinical practice.

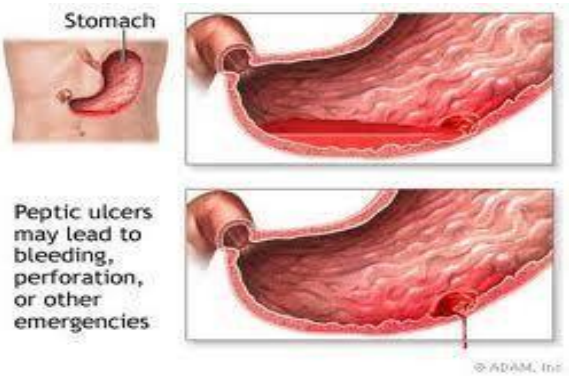

Fig. 4: Gastric ulcer.

Complications

Gastrointestinal bleeding is the most common complication. Sudden large bleeding can be life-threatening. It occurs when the ulcer erodes one of the blood vessels, such as the gastroduodenal artery.

Perforation (a hole in the wall) often leads to catastrophic consequences. Erosion of the gastro-intestinal wall by the ulcer leads to spillage of stomach or intestinal content into the abdominal cavity. Perforation at the anterior surface of the stomach leads to acute peritonitis, initially chemical and later bacterial peritonitis. The first sign is often sudden intense abdominal pain. Posterior wall perforation leads to pancreatitis; pain in this situation often radiates to the back.

Penetration is when the ulcer continues into adjacent organs such as the liver and pancreas.

Scarring and swelling due to ulcers causes narrowing in the duodenum and gastric outlet obstruction. Patient often presents with severe vomiting.

Cancer is included in the differential diagnosis (elucidated by biopsy), Helicobacter pylori as the etiological factor making it 3 to 6 times more likely to develop stomach cancer from the ulcer.

Cause

A major causative factor (60% of gastric and up to 90% of duodenal ulcers) is chronic inflammation due to Helicobacter pylori that colonizes the antral mucosa. The immune system is unable to clear the infection, despite the appearance of antibodies. Thus, the bacterium can cause a chronic active gastritis (type B gastritis), resulting in a defect in the regulation of gastrin production by that part of the stomach, and gastrin secretion can either be decreased (most cases) resulting in hypo- or achlorhydria or increased. Gastrin stimulates the production of gastric acid by parietal cells and, in H. pylori colonization responses that increase gastrin, the increase in acid can contribute to the erosion of the mucosa and therefore ulcer formation.

Another major cause is the use of NSAIDs (see above). The gastric mucosa protects itself from gastric acid with a layer of mucus, the secretion of which is stimulated by certain prostaglandins. NSAIDs block the function of cyclooxygenase 1 (cox-1), which is essential for the production of these prostaglandins. COX-2 selective anti-inflammatories (such as celecoxib or the since withdrawn rofecoxib) preferentially inhibit cox-2, which is less essential in the gastric mucosa, and roughly halve the risk of NSAID-related gastric ulceration. As the prevalence of H. pylori-caused ulceration declines in the Western world due to increased medical treatment, a greater proportion of ulcers will be due to increasing NSAID use among individuals with pain syndromes as well as the growth of aging populations that develop arthritis. The incidence of duodenal ulcers has dropped significantly during the last 30 years, while the incidence of gastric ulcers has shown a small increase, mainly caused by the widespread use of NSAIDs. The drop in incidence is considered to be a cohort-phenomenon independent of the progress in treatment of the disease.

Diagnosis

Endoscopic image of gastric ulcer, biopsy proven to be gastric cancer. The diagnosis is mainly established based on the characteristic symptoms. The stomach pain is usually the first to signal a peptic ulcer. In some cases, doctors may treat ulcers without diagnosing them with specific tests and observe if the symptoms resolve, meaning their primary diagnosis was accurate. Confirming the diagnosis is made with the help of tests such as endoscopies or barium contrast x-rays. The tests

are typically ordered if the symptoms do not resolve after a few weeks of treatment, or when they first appear in a person who is over age 45 or who has other symptoms such as weight loss, because stomach cancer can cause similar symptoms. Also, when severe ulcers resist treatment, particularly if a person has several ulcers or the ulcers are in unusual places, a doctor may suspect an underlying condition that causes the stomach to overproduce acid.

An esophago gastro duodenoscopy (EGD), a form of endoscopy, also known as a gastroscopy, is carried out on patients in whom a peptic ulcer is suspected. By direct visual identification, the location and severity of an ulcer can be described. Moreover, if no ulcer is present, EGD can often provide an alternative diagnosis. One of the reasons why blood tests are not reliable on establishing an accurate peptic ulcer diagnosis on their own is their inability to differentiate between past exposure to the bacteria and current infection. Additionally, a false-negative is possible with a blood test if the patient has recently been taking certain drugs, such as antibiotics or proton pump inhibitors.

Macroscopic appearance

A benign gastric ulcer (from the antrum) of a gastrectomy specimen. Gastric ulcers are most often localized on the lesser curvature of the stomach. The ulcer is a round to oval parietal defect ("hole"), 2 to 4 cm diameter, with a smooth base and perpendicular borders. These borders are not elevated or irregular in the acute form of peptic ulcer, regular but with elevated borders and inflammatory surrounding in the chronic form. In the ulcerative form of gastric cancer the borders are irregular. Surrounding mucosa may present radial folds, as a consequence of the parietal scarring.

Microscopic appearance

A gastric peptic ulcer is a mucosal defect which penetrates the muscularis mucosae and muscularis propria, produced by acid-pepsin aggression. Ulcer margins are perpendicular and present chronic gastritis. During the active phase, the base of the ulcer shows 4 zones: Inflammatory exudate, fibrinoid necrosis, granulation tissue and fibrous tissue. The fibrous base of the ulcer may contain vessels with thickened wall or with thrombosis.

Differential diagnosis of epigastric pain
Peptic ulcer
Gastritis
Stomach cancer
Gastroesophageal reflux disease
Pancreatitis
Hepatic congestion
Cholecystitis
Biliary colic
Inferior myocardial infarction
Referred pain (pleurisy, pericarditis)
Superior mesenteric artery syndrome

Treatment

The best way to stop any further growth of your stomach ulcer is to follow a healthy diet. It must contain non-acidic meals along with liquid meals. Sour agents like lemon should be strictly avoided in the diet. Younger patients with ulcer-like symptoms are often treated with antacids or H2 antagonists before EGD is undertaken. Bismuth compounds may actually reduce or even clear organisms, though the warning labels of some bismuth subsalicylate products indicate that the product should not be used by someone with an ulcer. Patients who are taking nonsteroidal anti-inflammatories (NSAIDs) may also be prescribed a prostaglandin analogue (Misoprostol) in order to help prevent peptic ulcers, which may be a side-effect of the NSAIDs.

Perforated peptic ulcer is a surgical emergency and requires surgical repair of the perforation. Most bleeding ulcers require endoscopy urgently to stop bleeding with cautery, injection, or clipping. Ranitidine provides relief of peptic ulcers, heartburn, indigestion and excess stomach acid and prevention of these symptoms associated with excessive consumption of food and drink. Ranitidine is available over the counter from a pharmacy and works by decreasing the amount of acid the stomach produces allowing healing of ulcers. Zantac tablets contain Ranitidine 150mg as the active ingredient which can also be bought generically.

Epidemiology

The lifetime risk for developing a peptic ulcer is approximately 10%. In Western countries the prevalence of Helicobacter pylori infections roughly matches age (i.e., 20% at age 20, 30% at age30, 80% at age 80 etc.). Prevalence is higher in third world countries. Transmission is by food, contaminated groundwater, and through human saliva (such as from kissing or sharing food utensils.) A minority of cases of Helicobacter infection will eventually lead to an ulcer and a larger proportion of people will get non-specific discomfort, abdominal pain or gastritis. Peptic ulcer disease had a tremendous effect on morbidity and mortality until the last decades of the 20th century, when epidemiological trends started to point to an impressive fall in its incidence.

The reason why the rates of peptic ulcer disease decreased is thought to be the development of new effective medication and acid suppressants and the discovery of the cause of the condition, H. pylori. In the United States about 4 million people have active peptic ulcers and about 350,000 new cases are diagnosed each year. Four times as many duodenal ulcers as gastric ulcers are diagnosed. Approximately 3,000 deaths per year in the United States are due to duodenal ulcer and 3,000 to gastric ulcer.

Antiulcer Activity

Ethanol induced gastric ulceration

Animals

Adult Albino Wistar rats of both sexes weighing 140–190g were used in the experiments. They were housed in standard cages at room temperature (25°C) and provided with food and water ad libitum. Twenty four hours before each experiment (except for the subchronic toxicity test), the animals were deprived of food but not of water.
Grouping
Group 1: control (Saline water)
Group 2: standard (Standard drug, Sucralfate)
Group 3: EEAM 200mg/kg
Group 4: EEAM400mg/kg
Ethanol induced gastric ulceration

Principle
Alcohol causes secretion of gastric juice and decrease mucosal resistance due to which protein content of gastric juice is significantly increased by ethanol. This could be leakage because of plasma protein in the gastric juice with weakening of mucosal resistance barrier of gastric mucosa, this leading to peptic ulcer.

Method
Adult Albino Wistar rats, 6 per group, were tested according to the method of Mizui and Doteuchi (1983) (Biswaas 2003). Thirty minutes after drugs administration, each rat was given orally 1.0 ml of a 0.3 M solution of HCl in 60% (v/v) ethanol. The animals were sacrificed one hour later. The stomach was then excised and cut along the greater curvature, washed carefully with 5.0 ml of 0.9% NaCl and ulcer score was determined. EEEAM and EEEAM were suspended in distilled water and administered at the doses of 200 and 400 mg/kg, respectively. Control groups received saline water. Sucralfate suspension (100 mg/kg) and Quercetin (50 mg/kg) were given orally as reference drugs. . Ulcer index was calculated as per the formula given below. The numbers of ulcers per stomach are noted and severity of the ulcers scored microscopically with the help of hand lens (10x) and scoring was done.
0 = Normal stomach
0.5 = Red coloration 1 = Spot ulcers
1.5 = Haemorrhagic streaks
2 = Ulcer > 3 mm but > 5 mm 3 = ulcers > 5 mm.
Ulcer index=UA+US+UP/10.,
Where, UA=Average number of ulcers per animal, US=Ulcer severity score, UP=Percentage of animals with ulcers. UP=Total ulcers in a group/total number of animals x 100.
Percentage ulcer inhibition was calculated by the formula, Percentage inhibition=UIC-UIT/UIC X 100.
Where UIC=Ulcer index of control group, UIT= Ulcer index of test group.

Statistical analysis
The results are reported as Mean±SEM. Sequential differences among means were calculated at the level of P≥0.05, 0.01, 0.001 using Dunnet's analysis.

RESULTS AND DISCUSSION

The extracts showed the antiulcer activity dose dependently in ethanol induced gastric ulceration, but it was found lesser compared to the standard that is sucrolfate. Before the results been discussed the actual ulcerative causative mechanism of ethanol should be prior known.

Table Ulcer index and Percentage inhibition in Ethanol induced gastric ulceration model.

Sl.no.	Group	Ulcer index	% inhibition
1.	Control	51.24±0.0425	
2.	Standard	22.24±0.1417*	56.5855
3.	EEAM 200mg/kg	35.9±0.1949*^	29.938
4.	EEAM400mg/kg	25.74±0.08612*^	49.762

EEAM - ethanolic extract of aegle marmelos *p<0.001 compared to control; a not significant at p<0.05, bp<0.001 compared to standard.

Concerning this mechanism sucrolfate, a synthetic E1 prostaglandin analogue was selected as standard.sucrolfate inhibits peptic ulcers by lowering the gastric acid secretion and protecting the tissue from oxidation (Watkinson 1988) leading to tissue damage. Observing the results, the antiulcer acitivity of aegle maemelos extracts was less potent than standard in indomethacin induced ulceration, suggesting the actual antiulcer mechanism of the extract is certainly is not the prostaglandin mechanism yet it is clear the extracts pocess some antiulcer activity. This might be due to wound healing activity and antioxidant activity of the Polyphenols in extract that was responsible for the antiulcer activity. This might be by scavenging the reactive oxygen free radicals or by preventing the lipid peroxidation by which quercetin acts to inhibit gastric ulcers.

EEAM showed antiulcer activity in Ethanol induced ulceration in a dose dependant manner with the results similar to that of quercetin. In contrast to indomethacin model, the percentage inhibition of the EEAM at 400 mg/kg was better than that of the standard and the lesser doses of 200mg/kg were also seemed to be pocessing the similar activity with that of the standard.

Sucralfate antiulcer mechanism was found to be the protection of mucosal area from the direct exposure to

acid in stomach and also helps in the wound healing. Actual mechanism being it forms complexes with proteins and buffers gastric acid (Susumu Okabe 1983; Bauer 1986). Results suggest that the wound healing with that of the extracts was much better and the antioxidant capacity of the polyphenols present in the extract might have helped in the activity. The mechanism still can be supported through the ulcer causative mechanism of ethanol. As discussed above Ethanol generates free radicals which decrease the resistance of mucosal barrier and there by destroy the integrity of membranes. This also results in the leakage of proteins into the gastric juice. This disruption of cell membranes might probably be due to lipid peroxidation of the produced free radicals.

Ethanol induced gastric lesion formation may be due to stasis in gastric blood flow which contributes to the development of the haemorrhage and necrotic aspects of tissue injury (Soll 1990). Alcohol rapidly penetrates the gastric mucosa apparently causing cell and plasma membrane damage leading to increased intra cellular membrane permeability to sodium and water. The massive intracellular accumulation of calcium represents a major step in the pathogenesis of gastric mucosal injury. Finally, this suggests the cytoprotective activity of the extract, which was higher than the standard drug that does not actually contain any antioxidant activity. This was similar to that of the activity produced by quercetin.

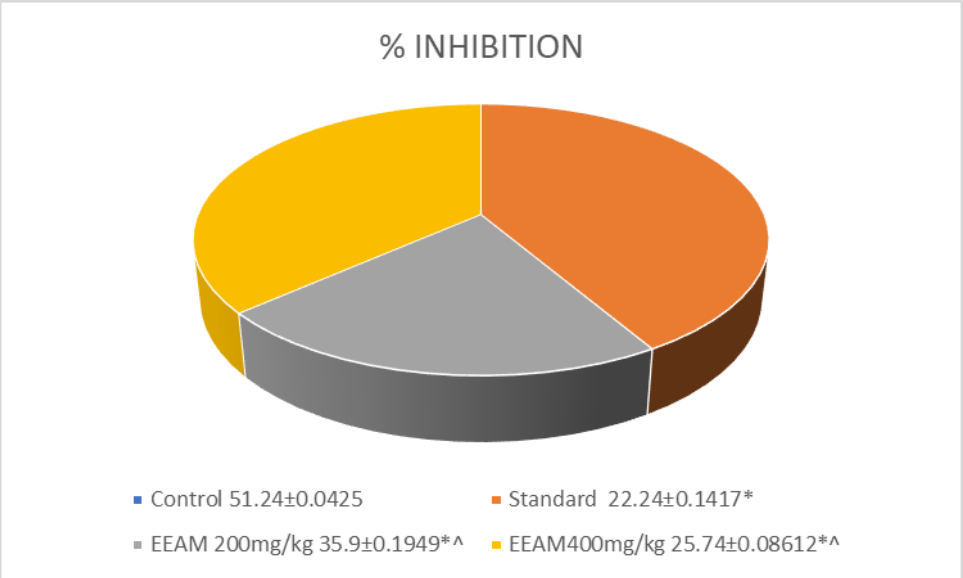

Fig: Antiulcer activity of aegle marmelos(L) extract in Ethanol model.

CONCLUSION

In this work the pharmacognostical, phytochemical and pharmacological activity on the Leaves of Aegle Marmelos (Rutaceae) were studied. The material was collected from Dr.KV. Subba Reddy Institute of pharmacy, Kurnool, Andhra Pradesh, identified and authenticated by K.Vanitha Kumari ,HOD, Dept of botany, ST.Joseph Degree college . Macro-microscopical characters, powder studies were carried out.Proximate analysis values include percentage of total ash, percentage of acid insoluble ash, percentage of water soluble ash, percentage of moisture content and percentage of extractive values in different solvents like water and alcohol were analysed.

Methanolic extract of Aegle Marmelos was found to be nontoxic in Wistar albino rats up to 200 mg, 400 mg/kg body weight. Methanol extract of Aegle Marmelos was subjected to Antiulcer activity on albino Wistar rats. Thus the present work substantiates the use of Aegle Marmelos as antiulcer actvity.

It is concluded that, scientific parameters based on taxonomical, pharmacognostical and phytochemical studies are essential in identifying and distinguishing the plant from other species. These parameters along with physiochemical constants not only help in standardization of these drugs but also aid in formulating pharmacopoeial standards of drugs. The exomorphic characters have been found to be useful tools to identify the species taxonomically.

The pharmacognostical study comprises of taxonomical characters of taxon, macro and microscopical characters of part used, and physic chemical parameteres. The qualitative phytochemical investigation gave valuable information about different phyto constituents present in various extracts, which help future investigators regarding the selection of particular extract for further investigation.

The ethanol extract were screened for antiulcer activity. Ethanol extract showed significant antiulcer activity effect when compared to control and reduces the liver toxicity when compared to normal. From this study, it is concluded that leaves of Aegle Marmelos showed

antiulcer activity.

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