WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.084
Volume 9, Issue 7, 807-820. Review Article ISSN 2277– 7105

REVIEW ON MEDICINAL PLANTS USED IN TREATMENT OF ANTIULCER

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Article Received on
03 May 2020,

Revised on 23 May 2020,
Accepted on 13 June 2020,

DOI: 10.20959/wjpr20207-17869

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ABSTRACT

An ulcer is a common gastrointestinal disorder which is seen in many people it is the disease of mucous membrane lining the alimentary track the formation of ulcer depend on the presence of acid and peptic activity in gastric juice and also break down in mucosal membrane. number of synthetic drug are available to treat ulcer but these drugs are expensive and also produce more side effect as compare to herbal medicine. Medicinal plant that contain a active ingredient and chemical constituent that are useful in the treatment of antiulcer so herbal medicine are better alternative for the treatment of ulcer. As herbal medicine are considered as safe for the treatment of ulcer with less economical effect, side effect and relatively less toxic. The present review focuses on history of ulcer, its types, pathophysiology, material and methods, chemical constituents, Anti-ulcer drugs, Anti-ulcer medicinal plants, diagnostic tests for ulcers and current status of global clinical trials conducted on ulcers and the plant features provide antiulcer activity.

KEYWORDS: Medicinal plants, Ulcer, Antiulcer.

1] INTRODUCTION

Ulcer is a gastrointestinal disorder and can be characterized by inflammation of the mucosa and tissue that protect the gastrointestinal tract. Damage of mucus membrane which normally protects the duodenum, stomach and esophagus from gastric acid. The pathological process of gastric ulcers remains widespread, it is various factors disease where diverse factors such as a stressful lifestyle, alcohol consumption, irregular food habits, severe illness, shock, burns, severe emotional disturbance, use of steroidal and nonsteroidal anti-inflammatory drugs (NSAIDs) and drugs which stimulate gastric acid and pepsin secretion , smoking, lower

socio-economic status. The most common cause of peptic ulcers is infection by a bacterium called Helicobacter pylori (H. pylori). H. pylori infection breaks down the protective mucous barrier, exposing the stomach and duodenum to digestive juices.

The prevention or cure of peptic ulcers is one of the most important challenges confronting medicine nowadays, as it is certainly a major human illness affecting nearly 8 to 10 % of the global population and of these 5% suffer from gastric ulcers. The prevalence of this disease is higher in men than in women. The two most common types of peptic ulcer are called “gastric ulcers” and “duodenal ulcers. A number of synthetic drugs are available for the treatment of peptic ulcers mainly based on antacids, anticholinergics, proton pump inhibitors and H2-receptor antagonists. But these drugs are expensive and are likely to produce more side effects. The major drawbacks of these treatments are intolerance excessive development of breasts in males, erectile dysfunction, cardiac arrhythmia and haematological disorders. Thus, there is an emergent need to develop the alternative therapies for the treatment of gastric ulcers. Plants are a rich resource used for centuries to cure various illness. The literature revealed that many medicinal plants and polyherbal formulations are used for the treatment of ulcer. Several medicinal plants have been reported with potent anti-ulcer activity.[1]

1.1] Peptic ulcer

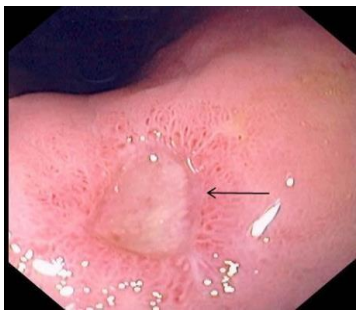


Fig no. 1.

Peptic ulcer disease is a break in the inner lining of the stomach, the first part of the small intestine, or sometimes the lower esophagus. An ulcer in the stomach is called a gastric ulcer, while one in the first part of the intestines is a duodenal ulcer. The most common symptoms of a duodenal ulcer are waking at night with upper abdominal pain and upper abdominal pain that improves with eating. With a gastric ulcer, the pain may worsen with eating. The pain is often described as a burning or dull ache. Other symptoms include belching, vomiting, weight loss, or poor appetite. About a third of older people have no symptoms. Complications may include bleeding, perforation, and blockage of the stomach. Bleeding occurs in as many as

15% of cases. The diagnosis is typically suspected due to the presenting symptoms with confirmation by either endoscopy or barium swallow. H. pylori can be diagnosed by testing the blood for antibodies, a urea breath test, testing the stool for signs of the bacteria, or a biopsy of the stomach. Other conditions that produce similar symptoms include stomach cancer, coronary heart disease, and inflammation of the stomach lining or gallbladder inflammation.

The medication used to decrease acid is usually either a proton pump inhibitor (PPI) or an H2 blocker, with four weeks of treatment initially recommended. Ulcers due to H. pylori are treated with a combination of medications, such as amoxicillin, and a PPI. Antibiotic resistance is increasing and thus treatment may not always be effective. Bleeding ulcers may be treated by endoscopy, with open surgery typically only used in cases in which it is not successful. Peptic ulcers are present in around 4% of the population. New ulcers were found in around 87.4 million people worldwide during 2015. About 10% of people develop a peptic ulcer at some point in their life. Peptic ulcers resulted in 267,500 deaths in 2015, down from 327,000 in 1990. The first description of a perforated peptic ulcer was in 1670, in Princess Henrietta of England. H. pylori was first identified as causing peptic ulcers by Barry Marshall and Robin Warren in the late 20th century, a discovery for which they received the Nobel Prize in 2005.

2] Some synthetic drug used in anti-ulcer treatment with their adverse effects

Class	Drugs	Mechanism of action	Adverse effects
Antacids	Magnesium hydroxide, Aluminum hydroxide.	Increases gastric pH to greater than four, and inhibits the proteolytic activity of pepsin, Causes osmotic retention of fluid	Nausea, Vomiting, Hypophosphatemia Chalky taste, Constipation, Abdominal cramping, Diarrhea, Electrolyte imbalance.
H2 Receptor Blockers	Famotidine, Nizatidine, Ranitidin, Cimetidine.	Blocking the action of histamine at the histamine H2 receptors of parietal cells	Headache, Anxiety, Depression, Dizziness, Cardiovascular events, Thrombocytopenia.
Proton Pump Inhibitors (PPIs)	Lansoprazole, Rabeprazole, Esomeprazole, Pantoprazol, Omeprazole.	Inhibition of the gastric H+/K+ - ATPase (proton pump) enzyme system	Headache, Abdominal pain, Diarrhea, Nausea, Vomiting, Constipation, Flatulence, Vitamin B12 deficiency, Osteoporosis.

3] Why natural drugs are more safe than synthetic drug used in anti ulcer activity ?

Since ancient times, plants and plant derived-products have been used in folklores around the world for the treatment of several illness and diseases. Nowadays, herbal medicine is becoming a viable alternative treatment over the commercially available synthetic drugs on PU management/treatment. This is premised on its lower cost, perceived effectiveness, availability as well as little or no adverse effects. A number of these herbal remedies have demonstrated gastroprotective properties and have been used in the treatment of PU, digestive disorders and other related ailments for several centuries.[2] As shown in table no. 1 below.[3]

Table no. 1

Plant	Family	Part used	Chemical constituent
Acacia Arabica	Mimosaceae	Gum	Phenolic compounds, tannins, and flavonoids
Adansonia digitata	Malvaceae	Leaves, bark	Phobaphenes, mucilage, gum, albuminoids, tannin, acid gum, albuminous carbonate, glucoside adansonin
Aegle marmelos	Rutaceae	Leaves, fruit	Marmelosin, luvangetin, psoralen, tannins, marmin
Alchornea castaneaefolia	Euphorbiaceae	Leaves, bark, root	Alchorneine, Alchorneinone, Alkaloids, Anthranilic acid, Gentisinic acid Yohimbine, flavonoids, glycosides
Balospermum montanum	Euphorbiaceae	Root	Montanin, baliospermin, 12-deoxyphorbol-13palmitate, 12-deoxy-16-hydroxyphorbol- 13palmitate, glycosides, terpenoids
Balsamodendron mukul	Burseraceae	Gum	Volatile oil, gum-resin
Bauhinia variegata	Fabaceae	Root, bark, leaves	Carbohydrates, glycosides, furanoids, flavonoids, tannins, phenolic compounds, proteins, gums and mucilages, flavonol glycoside, 5, 7, 3′, 4′-tetrahydroxy-3-methoxy- 7-O-alpha-L rhamno pyranosyl(1→3)-O-betagalactopyranoside
Berberis aristata	Berberidaceae	Root, bark	Alkaloid (berberine)
Butea frondosa	Fabaceae	Leaves, seeds, fruits	Alkaloids, Cynogenic glycosides, Phenolic compounds, Flavonoids, Terpenoids, Tannins, Saponins, protein and sterols
Careya arborea	Myrtaceae	Leaves, bark	Tannins and saponins
Carica papaya	Caricaceae	Seed	Papain, chymopapain, pectin, carposide, carpaine, carotenoids, and antheraxanthin
Citrullus colocynthis	Curcubitaceae	Fruit, root	Flavanoids, saponins, alkaloids and tannins
Coleus vettiveroides	Lamiaceae	Whole plant	Flavonoids, terpenoids and tannins (β-sitosterol, Gluanol acetate)
Eclipta alba	Asteraceae	Root	Coumestans, alkaloids, flavonoids, glycosides, polyacetylenes, triterpenoids, polyacetylene substituted thiophenes.
Euphorbia	Eurphorbiaceae	Plant	Euphorbon, resin, gum, caoutchouc, malate of calcium

neriifolia			
Ficus microcarpa	Moraceae	Bark, leaf	Flavonoid, tannins, terpenoids
Ficus religiosa	Moraceae	Stem, bark, Leaves, Tender Shoots, Latex, Seeds, Fruits	Triterpenoids, Flavonoids, Saponins, Steroids, Tannins and Phenolic compounds, Carbohydrate, Protein
Galega purpurea	Papilionaceae	Root	Gum, a trace of albumen, quercetin or querritrin, glucoside rutin
Gloriosa superb	Liliaceae	Roots, rhizome	Annins, flavonoids, steroids, alkaloids, and carbohydrates, glycosides and Mucilages
Hydrocotyle asiatica	Umbelliferae	Grain	Vellarin, fatty aromatic body, gum, sugar, tannin, albuminous matter, and salts, mostly alkaline sulphates
Indigofera tinctoria	Papillonaceae	Leaf, fruit	Flavonoids, tannins, saponin, and terpenoids
Jasminum	Oleaceae	Leaves, flower	Alkaloids, Terpenoids, Steroids, Fatty acids, Flavonoids
Lagenaria siceraria	Cucurbitaceae	Fruit	Flavonoid, steroids, polyphenol, saponins, carbohydrate proteins
Mangifera indica	Anacardiaceae	Leaves, flower	Mangiferin alkaloids, sterols, saponins, tannins, and flavonoids
Murraya koenigii	Rutaceae	Leaf	Mahanimbine and koenimbine
Musa paradisiacal	Musaceae	Root, leaves, trunk	Carbohydrates, Catechol-amines such as norepinephrine, serotonin, dopamine tryptophan, indole compounds. Leucocyanidin, quercetin and its 3-Ogalactoside, 3-O-glucoside, and 3-O- rhamnosyl glucoside Serotonin, nor-epinephrine, tryptophan, indole compounds, tannin
Nerium indicum	Apocynaceae	Root, leaves, whole plant	Alkaloids, glycosides, carbohydrates, tannins, phenolic compounds and flavonoids
Ocimum sanctum	Lamiaceae	Whole plant	alkaloids, flavonoids, phenolics, essential oils, tannins and saponins
Oryza sativa	Gramineae	grains oil	Starch, proteins and a trace of mineral matter
Oxystelma esculentum	Asclepiadaceae	Leaves, petiole, stem, root and rhizome	Tannins, flavonoids, terpenoids, cardiac glycosides and alkaloids
Phyllanthus emblica	Euphorbiaceae	Root, bark	Terpenoids, alkaloids, flavonoids, and tannins
Phyllanthus niruri	Euphorbiaceae	Aerial part	Alkaloids-4-methoxy-securinine, ellagic acid, beta sitosterol, gallic acid, and hypophyllanthin
Polyalthia longifolia	Annonaceae	Whole plant	Steroids, alkaloids, biterpenoids, carbohydrates, amino acids, essential oil, phenolics and flavonoids
Pongamia pinnata	Papillonaceae	Whole plant	Flavonoids (pongamones A-E), Karangin, pongamol, pongagalabrone and pongapin, pinnatin and kanjone

In an attempt to find an effective treatment for various diseases, the modern medicine turns to traditional medicine. There are few animal models developed in ulcers research, usually including rats. All ethical principles for using of animals in experiments should be followed and protocols approved by the Institutional Ethics Committee. On the other hand, the

evaluation of the chronic gastroprotective activity is usually performed on animals with gastric ulcer induced by acetic acid. The growing interest in herbal medicines is partly derived from the results of many animal studies, indicating that plant extracts have lower toxicity than synthetic drugs. However, for using specific plants extracts as antiulcer agents, the data of acute and chronic toxicity should be obtained. Rats and mice are usually used to the in vivo assessment of drugs safety.[2]

3.1] Some natural drugs used in ulcer are described below

Table no. 2

	Synonym	Biological source	Marketed formulation
Allium sativum	Garlic	This consist of bulb of the plant known as allium sativum linn. Belonging to family liliceae. It consist not less than 0.20per cent of alline on dried basis.[4]	Alsarex
Carica papaya	Pawpaw	It is the fruit of plant carica papaya, belonging to the family caricaceae.[5]	Aurohealth papaya leaf herbal extract
Magnifera indica	Mangot, Mangue, Ambrah	It is the tropical fruit of plant magnifera indica belonging to family Anacardiaceae.[6]	Acipres-MS
Terminalia chebula	Black myroblans, harad	It is a dried ripe fruit of plant terminalia chebula belongs to the family Combretaceae.[7]	Srisri tattya harithaki
Punica garantum	pomegranate	It is the ripen fruit of plant punica garantum belonging to family Punicaceae.[8]	Muktacid tab, room punica granatum capsule

3.2] Chemical constituents of above medicinal plants

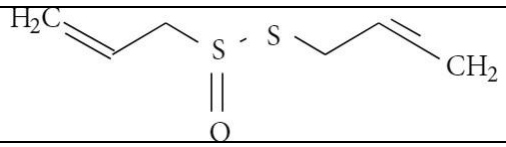
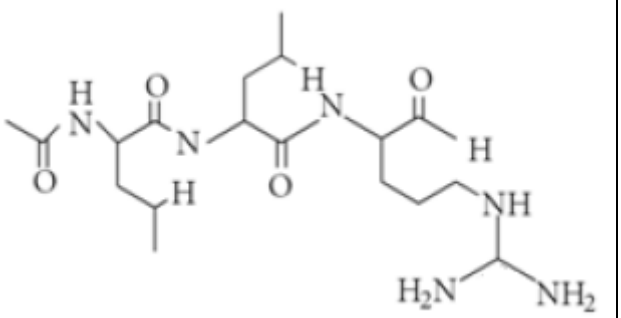
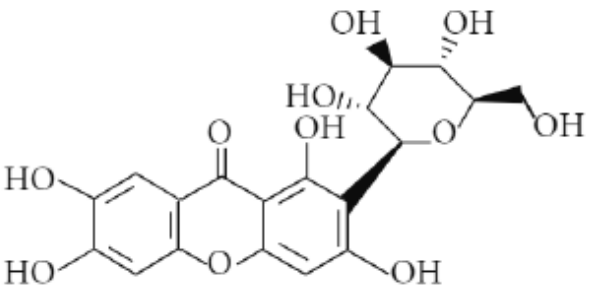
Table no. 3

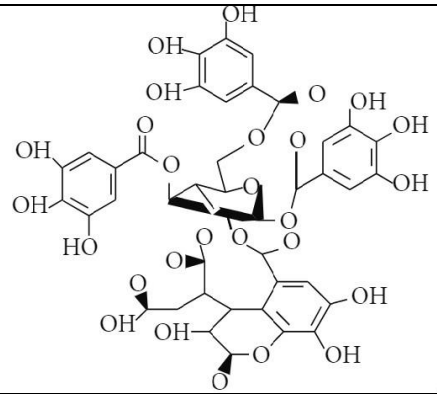
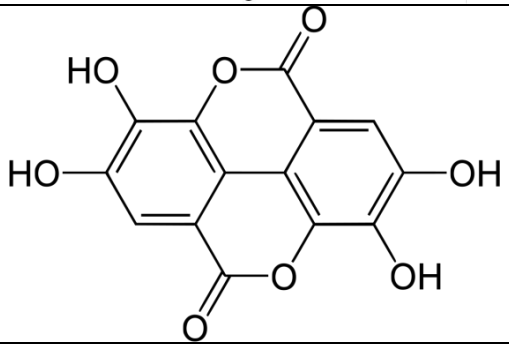
	Chemical constituents	Active constituent
Allium sativum	(29%)carbohydrates, (56%) of protein (albumin), 0.1% of	Alline
	volatile oil, 0.1 % of fat and mucilage. It also contain phosphrous, iron and copper. Alline by action of enzyme alliinlyase is converted into allicin.[4]	
Carica papaya	Carotenoids, vitamin C, thiamin, riboflavin, niacin, vitamin B-6 and vitamin K. The red-fleshed pawpaw contains five beta carotene: beta-crytoxanthin, while the yellow fleshed contains only beta carotene, beta-cryptoxantain and zeta-Carotene.[9]	Papain
Magnifera indica	Polyphenolics, flavonoids, triterpenoids. Mangiferin a xanthone glycoside major bio-	Mangiferin

	active constituent, isomangiferin, tannins & gallic acid derivatives.	
	32% of tannin. they contain 14 components of hydrolysable, 1,2,3,4,6- penta-Ogalloyl-ß-D-glucose, 1,6,-di-O-galloyl-D- Flavonol glycosides, triterpenoids, coumarin conjugated with gallic acid called chebulin, as well as	Tannins
	phenolic compounds were also isolated. Ethyl gallate and luteolin were isolated from the fruit of T. chebula. It also consists of nutrients such as vitamin C, protein, amino acids and minerals.[11]	
Punica garantum	phenolics, flavonoids, ellagitannins, and proanthocyanidin compounds, minerals, mainly potassium, nitrogen, calcium, phosphorus, magnesium, and sodium, and complex polysaccharides. The edible part of the pomegranate fruit (50%) consists of 40% arils and 10% seeds. Arils contain 85% water, 10% total sugars, mainly fructose and glucose, and 1.5% pectin, organic acid	Ellagic acid

3.3] Structure of active constituent of above medicinal plants

Table no.4

Active constituent	Structure
Allium sativum (alline)	
Carica papaya (papain)	
Magnifera indica (magniferin)	

Terminalia chebula (tannins)	
Punica garantum (ellagic acid)	

3.4] Some medicinal plants are described in briefly

3.4.1] Allium sativum

Fig. 2: Allium sativum.

The native land of garlic is Asia. There are also found in a West China, around Tien Shan Mountains to Kazakhstan and Kyrgyzstan. In ancient China, garlic was one of the most used remedies since 2700 BC. In ancient Indian medicine, garlic was a valuable remedy used as a tonic, roborans, to cure a lack of appetite, common weakness, cough, skin disease, rheumatism, hemorrhoids. Garlic was used for reducing the body temperature. They prepared tea from garlic and solid resin, which was used against constipation. Garlic emulsion was also used against muscle inflammation.[12]

Sample of garlic clove was purchased by mansor and majeed which was originated from China. During the project, all the samples were maintained in lab at appropriate conditions.[13]

Reagent like Methanol was used as a HPLC grade from and deionised water used was purified by Milli-Q purification system.[13]

In 100 ml of deionised water 10 gm of garlic cloves were blended for 1min with the help of blender.[13] Ultrasonic-Assisted Extraction was performed in an ultrasound cleaning bath., at the fixed- frequency of 35 kHz. Parameters optimised were extraction time (30 min, 60 min, 90 min, 120 min and 150 min), extraction temperature (25 °C, 30 °C, 35 °C) and particle size (Blended and sliced garlic bulb). After sonication the solution was then separated from impurities by centrifugation at 3,000 g for 2 min. Then the solution is filtered to remove the undissolved garlic and stored at 4 °C.[13]

Quantification of allicin is done by HPLC method at the temperature of 25 °C with 10 uL injection. The total running time was 20 min. The absorbance of allicin or garlic extract was monitored at 254 nm.[13]

Animal study was performed by taking 24 albino Wistar rats of both sexes weighing between 120 g and 150 g. This rat were divided into groups and were kept under standard conditions of temperature 23°C and humidity. They were maintained on unrestricted supplies of food and water. The rats were randomly shared into six study groups, two control groups and four treated groups (four rats of each).

3.4.2] Carica papaya

Fig. 3: Carica papaya.

Papaya is native to tropical America, from Southern Mexico through the Andes of South America. It was spread to the south by Indians, and throughout the Caribbean with Spanish exploration. Papaya was introduced to Hawaii in the 1800s, and Hawaii remains the only state in the USA to produce papaya commercially.

Potassium meta-bi-sulphite, Casein, Cysteine, latex of papaya were collected. Latex was collected by cutting the skin of unripe and matured papaya. Cuts should be longitudinal or vertical and was more than 1-2mm deep since it causes the risk of juices and starch from the fruit). Foreign matters like dirt and insects should be avoided.[14]

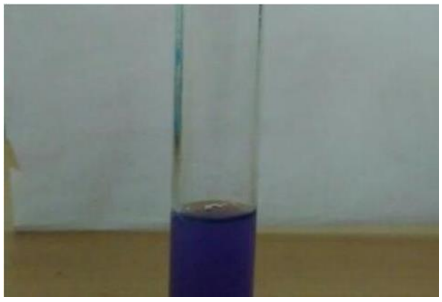


Fig. 4: Protein estimation.

Formation of blue color during the Ninhydrin reagent test and Purple color during Folin Ciocaltau's reagent test as shown in Fig 4 indicates that the extracted material (Papain) is a protein.[14] Isolation of Papain was done by blending papaya latex with meta bi sulphate. the tar is isolated from the latex and kept for 40 degrees Celsius for 1 hour. The result of the response is known as tyrosine.[14] Papain is activated by the activators.by blending Papain with cysteine. Equal amount of Papain and cysteine is taken in a beaker. Mixing the reaction mixture by using magnetic stirrer. Citrate phosphate buffer is added to maintain the pH of the solution. After adding the buffer, solution will maintain pH 6.0[14] animal study was performed by taking albino rats of both sexes and size of 150 to 200 g. They were maintained in well conditioned room temperature of 24℃.the animal were fed with standard diet and water.

3.4.3] Magnifera indica

Fig. 5: Magnifera indica.

The cultivation of mango in India is as old as 4,000 years. Hsüan-tsang was the first person to bring the mango to the people outside India. Mughal emperor Babar recognized the mango as the choicest fruit of India. His descendants cultivated mango by evolving grafting techniques and growing technologies and making huge collection of varieties.[15]

Extraction of magniferin is done by taking Mangifera indica L. leaves in flasks. (100 g in each) and 800 ml of a mixture of propan-2-ol and water was added and boiled with a reflux condenser in a water bath with mixing for 1 h. Extracts were cooled, filtered, and evaporated to a volume of about 200 ml. Each resulting solution was washed with n-hexane (3200 ml). The residue was then supplemented with 1 M H2 SO4 to pH 2 and heated in a reflux condenser for 1 h. Solution was evaporated to a volume of about 40 ml, after which 40 ml of dioxane and 0.5 g of activated charcoal were added. The mixture was boiled for 5 min, after which it was filtered and held for 24 h at 4°C. The resulting precipitate was collected by filtration, washed with cold ethanol (3 30 ml), and dried for 3 h at 100°C. This yielded technical mangiferin. Technical mangiferin (2 g) was then recrystallized from 75 ml of a mixture of propan-2-ol and water (50:50 v/v) in a 250-ml beaker. The mixture was boiled with mixing for 5 min. the hot solution was filtered, cooled, and held for 24 h at 4°C. The resulting precipitate was collected by filtration, washed with cold ethanol (3 30 ml), and dried for 3 h at 100°C, which yielded purified product.[16]

Animal study was performed by taking Albino rats of both sexes weighing 100- 120 g. They were maintained in well equipped polypropylene cages at room temperature of 24°C. All the animals were allowed to adapt for two weeks in animal house. The animals were fed with standard pelleted diet and water was allowed ad libitum. The container for the food and water was washed daily.[6]

3.4.4] Terminalia chebula

Fig. 6: Terminalia chebula.

Extraction of Tannins was done by taking immature fruit powder of Terminalia chebula Fructus Retz was extracted with water (100 ml) at 50°C. Thereafter, the extracts were weighted. Content of tannin extracts was measured and optimal extraction and purification technology (OEPT) was determined. The extracts were added to ethanol of 95% concentration, and the concentration of extract solutions were diluted to 80%. The extract solution was deposited for 12 hours and centrifuged at 4000 rpm for 10 min. After filtration, the content of tannin extracts was analyze by the casein method.[7]

Animals study was performed by taking Wistar albino rats wt. of 150-250 g and albino mice wt of 25–30g of either sex. were used in this study. The animals were kept for 10 days under standard husbandry conditions as: room temperature 26°C and relative humidity. They were allowed free access to standard diet and water ad libitum, one week before and during experimental period.[11]

3.4.5] Punica garantum

Fig. 7: Punica garantum.

Wild punica garantum seeds were collected and seeds were cleaned washed and dried and grinded as a pores powder under several condition with temp not more than 20℃ and were kept in white protected container.

The powdered seeds were extracted with ethanol by simple maceration process for 24 hrs. The solvent was completely removed using rotary evaporator at 40-45°C under reduced pressure. The crude extract was defatted with hexane. Extract obtained was stored in the refrigerator at 0-4°C to prevent any degradation. This extract was used for various investigations such as antioxidant and antiulcer activity.[8]

The wild punica garantum ethanolic seed extract was subjected to different phytochemical screening for the presence of various constituent such as alkaloid, proteins, flavonoids,

saffonin, sterols, tannin and carbohydrates.

The animal study was performed by taking whister albino rats which was divided into six groups with the size of 150 to 250 g of both sexes. The animal where kept in animal house at the condition of temperature at 24℃ and relative humidity.[8]

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