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A METHODICAL REVIEW ON ANTIULCER POTENTIAL OF HERBAL MEDICINES FROM NATURAL ORIGIN

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ABSTRACT

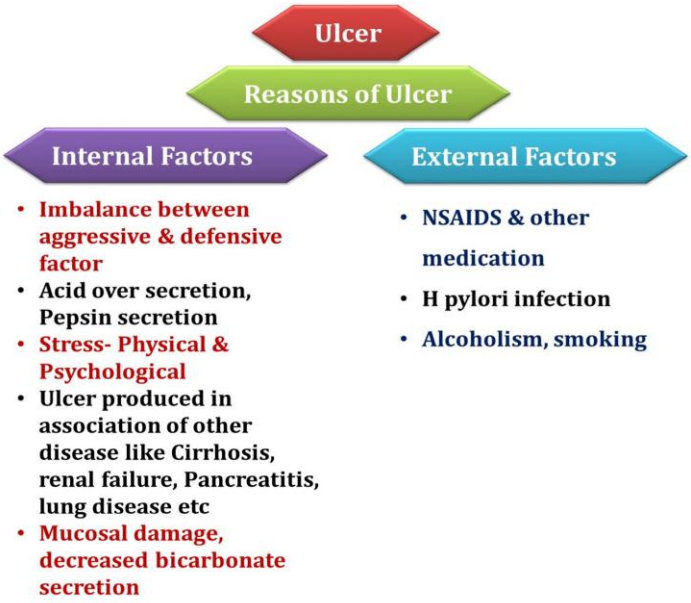
Ulcers are most common disease with human body. Worldwide it is studied that, amongstall ulcers associated with gastrointestinal tract are majorly occurred. These ulcers are sore lining in different areas of GIT like stomach, duodenum and intestine. Peptic ulcers can be acute, if left untreated it can be chronic ulcers. These ulcers caused due to imbalance between aggressive factors and defensive factors, *H.pylori* infections, stress, alcoholism and smoking due to certain medications like nonsteroidal anti-inflammatory drugs (NSAIDs). Idea to treat these ulcers is by use of acid neutralizing agents (antacids), agents that lowers gastric acid production (PP blocker, H_2 blockers), antibiotics and ulcer protecting agents. But the repeated use of this therapy causes side effect to body. Thus, now a days treatment of peptic ulcer moves keen interest towards useof medicines from natural sources which are safe and cost efficient. Hence main objective of this review article is to summarize and configure the plants having potential for the treatment of peptic ulcers.

KEYWORDS: Peptic ulcer**,** H_2 blockers, NSAIDs, aggressive factors and defensive factors.

INTRODUCTION

Gastric ulcers are most common gastric disorder in human with different pathogenesis. The occurrences of open sores or deep lesions in various region of gastrointestinal tract

(stomach, intestine and duodenum) are impression of ulcer which severely turn out in to bleeding, epigastric pain and reflux. In ulcer formation of lesion on gastricepithelial cells due to oversecretion of acid, *H.pylori* infection, alcohol intake, certain medication like NSAIDs and sometimes due to stress and other illness. Almost 75% patients are treated with antisecreatory and protective therapy while 5% patient suggest for antibiotic therapy.



Sign and symptoms of ulcer

- Most common symptoms of ulcer are abdominal discomfort, nausea with epigastric pain.
- Sometime intolerance to fatty foods, sudden weight loss, loss of appetite.
- Anaemia and hoematemesis also seen.
- Sometimes ulcers are asymptomatic.
- Most common symptoms of ulcer are abdominal discomfort, nausea with epigastric pain.
- If pain is radiated towards back is indication of ulcer has penetrated posteriorly. Other manifestation of ulcer includes chest pain, heartburn, bleaching and bloating.

Diagnosis of ulcer

Ulcer diagnosis is depending on earlier symptoms observed and history of patients like alcoholism, smoking, NSAIDs therapy or any stress. Most reliable technique to diagnose the ulcer is endoscopy (Gastroscopy) so that it can observe region of ulcer and size of ulcer H.pylori is another reason for ulcer which can be tested with different methods like urea breath test, test for H.pylori presence: stool antigen test. Other supportive test like completeblood count test to check if there is blood loss or not in cases of bleeding ulcer,

tissue culture test to observe any bacterial/ fungal infections and gastric biopsy studies. After proper diagnosis, specific drug therapy (antacids, antisecreatory or antibiotics) is given to patients.[1]

Pathophysiology of ulcers[2,3]

Gastric ulcers are ulcer, which associated with gastric and duodenal region of gastric area. The presence of ulcers for certain period of time are acute ulcers which can be managed with antisecreatory and ulcer protective agent but chronic ulcer need to treat for long period with antiulcer agents and antibiotic therapy sometime need surgical treatment.

Peptic ulcer formation in epithelial lining of GIT involves imbalance between defensive factors (mucosal blood flow, prostaglandin cellular regeneration, mucus gel and mucosal bicarbonate layer) and Aggravating factors (H.pylori, Acid hyper secretion, ischemia, NSAIDS, psychological and physical stress, tobacco and alcohol, bile salts, pepsin) The size of peptic ulcer ranges from several millimeters to several centimeters. H.pylori has plays central role in aggravation of peptic ulcer, chronic gastritis and gastric cancers. It produces gastric epithelium infiltration and underlying lamina propria by immune cells such as neutrophills, macrophages, lymphocytes and mast cells.

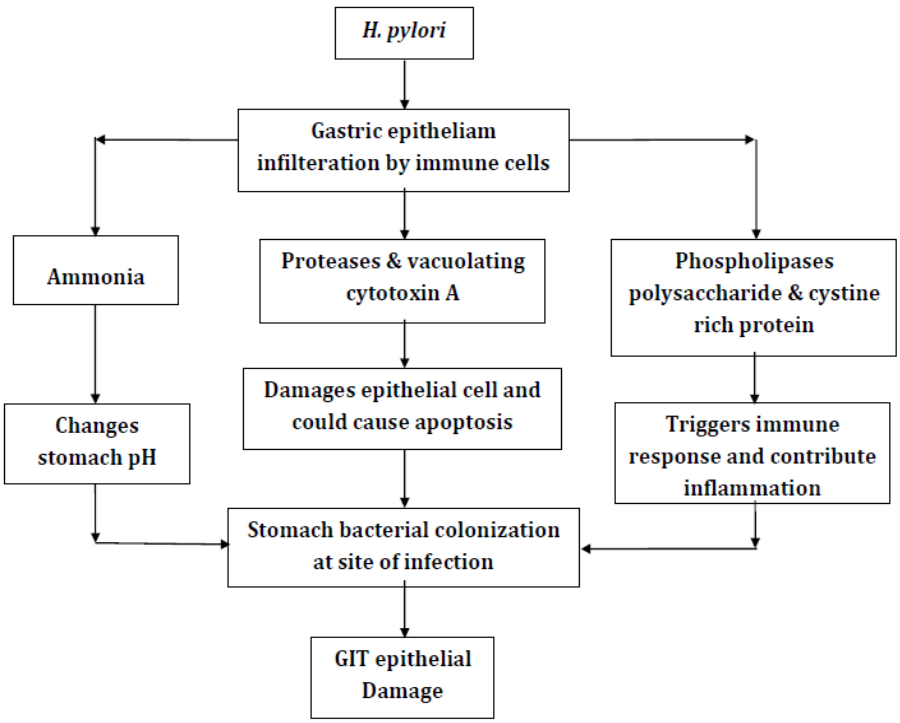


Fig. 1: Pathophysiology of Ulcer by *H.pylori* infection.

H.pylori also responsible to produce some toxic biomolecules such as ammonia, proteases, cytotoxin A, phospholipases that causes irreversible harm to epithelial cells that lead to produce apoptosis.

It is reported to produce lipopolysaccharides and cystine rich protein that stimulates immune response which releases immune products which induces inflammation of gastric lining.

The prolonged administration of nonsteroidal anti-inflammatory drugs is reported to produce gastric ulcers. NSAID use could damage gastric and duodenal mucosal lining with episodes of several mechanism like impairment of mucosal membrane, reduction in gastric blood flow and irritation of gastric epithelium. Also presence of acid in stomach lumen is one of the reason for NSAID induced ulcers.

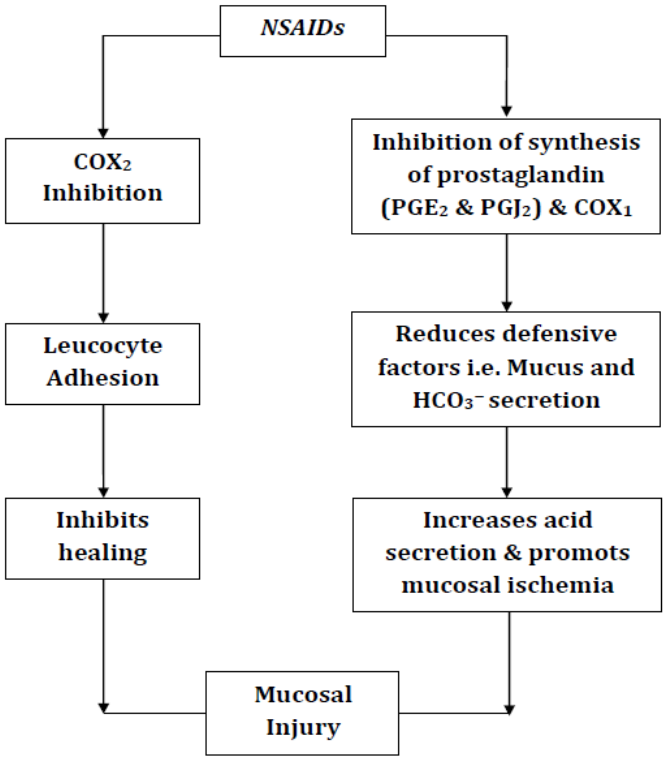


Fig. 2: Pathophysiology of Ulcer by *NSAIDs* infection.

A stress ulcer occurs in almost 75% of chronic disease and hospitalized patients. These ulcers develops at the specific area where blood vessels are damaged thus it interferes with the proper nourishment of mucosal cells which will leads to formation of ulcers.

Alcoholism is another reason behind occurrence of peptic ulcer, this rate is equals in

both male and females due to change in lifestyle. Presence of alcohol in stomach produces reactive oxygen species (ROS) and cyclooxygenase2 which are inflammatory mediators, increases acidity and oxidative damage of gastric cells. Further it damages gastric mucosa that forms ulcers in various regions of GIT.

TREATMENT FOR PEPTIC ULCER[4]

The ulcer can be treated with appropriate drug therapy. Some of drugs with theirmechanism of action are described in table no.1

Table No.1.

Class of drug	Name of Drug	Description
H_2 Antihistiminics	Cimentidine, Ranitidine, Famotidine, Roxatidine, Loxatidine	H_2 blockers suppress all basal, psychic, neurogenic and gastric secretionIt acts by Inhibition of gastric acid secretion. Blocking of H_2 receptor onparietal cell reduces histamine induced gastricacid secretion.
Proton pump inhibitors	Omeprazole, Lansoprazole, Pantoprazole, Rabeprazole, Esmoprazole.	Acid secretion in stomach takes place when H^+-K^+Atpase molecules aresynthesized. Suppression of gastric acid secretion with SH group of H^+-K^+Atpaseenzyme,that inactivates H^+-K^+ pump irreversibly.
Anticholinergic agents	Pirenzine	Decrease in gastric juice volume without raising its pH and dilute secretedgastric acid. It has weak action on gastric acid secretion and also delays gastricemptying.
Prostaglandine analogue	Misoprostol, Enaprostil, Rioprostil.	These act by enhancing action • Promotes mucosal bicarbonate (HCo_3^-) secretionby underlyingepithelial cell in gastric and duodenal region. • Increases mucosal blood flow that reduces mucosal hypoxia and actas cytoprotective agent.
Antacids	Systemic: sodium bicarbonate Nonsystemic: magnesium hydroxides, magnesium trisilicate, aluminium hydroxide gel, magaldrate, Calcium carbonate.	These are acid neutralizing agent. They do not interfere with acid secretion but neutralize gastric acid, raisesthe pH of acid to the normal.
Ulcer protective	Sucralfate Colloidal bismuth subcitrate(CBS)	Sucralfate is aluminium salt of sulfated sucrose. It polymerises at pH< 4 and crosslinking in the molecule assumes a gel likeconsistency that adheres to ulcer base. It precipitates surface proteins present at ulcer and forms protective layerthat prevents direct contact between gastric content and ulcer. CBS mode of action is not clear but reported to increase mucus and bicarbonate secretion that coats to ulcer surface which acts as barrierbetween ulcer

		and gastic acid. Also detaches *H.pylori* from surface and kills other organism involved information of ulcers.
Ulcer healing drugs	Carbenoxolone sodium	It is steroidal derivative of glycerrhetinic acid. It is reported to produce healing effect by preventing bile reflux, slowing of prostaglandine degradation, prolongation of lifespan of epithelial cells, increase of mucus production. It do not alters volume or acidity of gastric juice.
Anti *H.pylori*	Amoxicillin, Clathromycin, Metronidazole, tinidazole, Tetracyclines	*H.pylori* isgram negative bacillus. Antibiotic therapy is recommended totreat ulcer that involves *H.pylori* related infection. In hostile environmentof stomach *H.pylori* attaches to surface epithelium has high urease activity and produces ammonia. Infection of *H.pylori* also responsible to produce immune response, it releases cytokines, lipoxigenasand other inflammatory product. *H.pylori* infection starts with neutrophillic gastritis. These antibacterial agents are effective against *H.pylori* .some drugs workseffective in combination in two or three.

There are number of drugs studied to detect its antiulcer effect. Majorly many plants extracts are responsible to cure ulcer by exerting its different mechanism of action. While studying some invitro models are used to evaluate plant's desired antiulcer activity. All this information is listed in table no.2-

Table No 2.

Sr.No	Name of plant	Part of plant	Extract	Dose	Model Used	Ref.
1	*Solanum tuburosum* **(Solanaceae)**	Tubers	Aqueous	100, 200, 400mg/kg	1. Pylorus ligationmodel, 2. Stress induced ulcer	[5]
2	*Anvillea garcinii* **(Asteraceae)**	Shrub	ethanolic, chloroform andn-butanol	200, 400 mg/kg	Pylorus‐ligated rats Gastric lesions inducedby various ulcerogens (80% EtOH, 25% NaCl or 0.2 mol/L NaOH) Gastric lesions inducedby indomethacin Ulcers induced by hypothermic restraint stress	[6]
3	*Madhuka indica* **(Sapotaceae)**	Leaves	Aqueous	100, 200, 400mg/kg	Naproxen induced ulcer	[7]
4	*Citrullus lanatus* **(Cucurbitaceae)**	Seeds	Methanolic	200, 400 mg/kg	Ethanol induced ulcer	[8]
5	*Markhamia tomentosa* **(Bignoniaceae)**	Leaves	Ethanolic and ethyl acetate	50, 100,150 mg/kg	1. Ethanol induced ulcer 2. Indomethacin induced ulcer	[9]
6	*zea mays* **(Poaceae)**	Corns	Methanolic	10,20,40,60,80,100 µg/Kg	Ethanol induced ulcer	[10]
7	*Oscimum sanctum*	Leaves	Ethanolic and	AE: 100,200 mg/Kg	Pylorus ligated ulcer	[11]
	(Lamiaceae)		aqueous	EE: 50, 100 mg/Kg		

8	*Terminalia loxiflora* **(Combretacae)**	Laeves	Methanolic	50, 100 mg/Kg	Aspirin induced ulcer	[12]
9	*Carica papaya* **(Caricaceae)**	Unripe fruits	Hydroalcoholic	250 mg/kg	1. Pylorus Ligationmethod 2. Swimming pool induced ulcer	[13]
10	*Garuga pinnata* **(Burseraceae)**	Stem bark	Hydroalcoholic	200,400 mg/Kg	pylorus ligation-induced gastric ulcer	[14]
11	Listed medicinal plants	Different parts	_	-	-	[15]
12	*Hibiscus rosa Sinensis* **(Malvaceae)**	Leaves	Methanolic	200 and 400 mg/kg	pylorus ligation-induced gastric ulcer	[16]
13	*Kalanche pinnata* **(Crassulaceae)**	Leaves	Hydroethanolic	1. hydroethanolic extract (100, 200 and 400 mg/kg) 2. ethyl acetate fraction (50, 100 and 200 mg/Kg)	Ethanol/HCl-inducedulcer model	[17]
14	*Jatropa gossypifolia* **(Euphorbiaceae)**	Entire plant	Methanolic	10 µl	1. α- Chymotrypsin assay 2. α-Glucosidase assay	[18]
15	*Azadirecta indica* **(Meliaceae)**	Leaves	Aqueous	150,300,600 mg/Kg	1. Pylorus Ligation induced ulcer 2. Aspirin Induced ulcer 3. Cold restraint stress induced	[19]
					ulcer model	

16	*Calotropis procera* **(Apocynaceae)**	Leaves, flowers, fruits	Ethanolic	200, 400 mg/Kg	1. pylorus-ligated Shay rats 2. indomethacin induced gastric mucosal lesions 3. stress-induced intraluminal bleeding and gastric lesions	[20]
17	*Passiflora alata* **(Passifloraceae)**	Aerial parts	Ethanolic	100, 200, 400 mg/kg	ethanol-induced ulcers	[21]
18	*Grewia flavescens* Juss (**Tiliaceae)**	Entire plant	Ethanolic	100, 200, 400 mg/kg	pylorus ligation and aspirin induced ligation models	[22]
19	*Beta vulgaris* **(Amaranthaceae)***Ficus religiosa* **(Moraceae)**	RootBark	Ethanolic	250, 500 mg/Kg	Pylorus Ligation-Induced Ulcer Model	[23]
20	*Wedelia trilobata* **(Asteraceae)**	Leaves	Aqueous	200, 400 mg/ kg	1. Aspirin Induced Gastric Ulcer 2. pyloric ligation Induced Gastric Ulcer	[24]
21	*Ageratum conyzoides* **(Asteraceace)** *Vermonia amygdalina*(**Asteraceae)** *Citrus aurantifolia* **(Rutaceae)**	Whole plant Roots Roots	Aqueous, alcoholic, acetone, chloroform	100, 200, 400 and 800 mg/kg	Ethanol Induced Gastric Mucosa Injury	[25]
22	*Leea Indica* **(Vitaceae)**	Seeds	Methanolic	200, 400 mg/ kg	1. Pylorus LigationMethod 2. Aspirin induced	[26]

					model	
23	*Citharexylum quadrangular* **(Verbenaceae)**	Leaves	Ethanolic	500 mg/Kg	1. Ethanol Induced ulcer	[27]
24	*Musa paradisiacal* **(Musaceae)**	Ripe fruit	Aqueous	100, 200, and 300 mg/kg	1. pylorus ligation model 2. Ethanol induced ulcer Model	[28]
25	*Swietenia mahagoni* **(Meliaceae)**	Leaves	Ethanolic	250 and 500 mg/kg	Ethanol induced gastric ulcer	[29]
26	*Deglycyrrhizinated liquorice* **(Fabaceae)**	Roots	Ethanolic	250 mg/kg	1. Ethanol induced, 2. Aspirin induced 3. Stress induced gastric ulcers.	[30]
27	Antiulcer activity of medicinal herbs	-	-	-	-	[31]
28	*Canavalia gladiate* **(Fabaceae)**	Pods	Ethanolic	250 mg/kg	Aspirin induced ulcer model	[32]
29	*Polygonum hydropiper* **(Solanaceae)**	Whole plant	Crude extract from saponinand essential oil	100, 200, and 400 mg/kg	Aspirin induced ulcer model pyloric ligation ulcerogenesis model	[33]
30	*Tiliacora acuminate* **(Menispermaceae)**	Bark	Aqueous	200, 400 mg/kg	1. Pyloric Ligation Induced Gastric Ulceration 2. Aspirin induced ulcer	[34]
31	*Punica grantum* **(Punicaceae)**	Peels	Methanolic	25, 50 and 100 mg/kg	Indomethacin induced ulcer	[35]

32	*Virola oleifera* **(Myristicaceae)**	Whole plant	Resin	10, 100 mg/kg	1. HCl/ethanol-induced ulcer Indomethacin-induced ulcer	[36]
33	*Glycyrrhiza glabra* **(Fabaceae)**	Roots	Hydroalcoholic	1. 50–200 mg/kg 2. 50-150 mg/kg	1. HCl/ethanol-induced ulcer 2. Indomethacin-induced ulcer	[37]
34	*Solenostemon monostychus* **(Lamiaceae)**	Aerial parts	Aqueous and chloroform	75 - 225 mg/kg	Ethanol, indomethacin, reserpine and histamine induced ulcer models.	[38]
35	*Peltophorum pterocarpum* **(Leguminosae)**	Leaves	Methanol	100,200 mg/kg	Gastric Lesions Induced by Indomethacin and Pylorus Ligation Model	[39]
36	*Osyris quadripartite* **(santalaceae)**	Leaves	Methanolic	100, 200, 400 mg/kg	1. pylorus ligation- induced and 2. Ethanol-induced models	[40]
37	*Magnifera indica* **(Anacardiaceae)**	Seed kernel	Ethanolic	400mg/kg	Acid alcohol induced gastric ulcer.	[41]
38	*Salvodra indica* **(Salvadoraceae)**	Leaves	Ethanolic	150, 300 and 600 mg/kg	Pylorus ligation, ethanol and cysteamine induced ulcer models	[42]
39	*Morinda Citrifolia*	Root Bark	Methanolic	200 and 400 mg/kg orally	Ethanol, aspirin	[43]

	(Rubiaceae)				pyloric ligation cysteamine hydrochloride induced ulcer	
40	*Delosperma ressei* **(Aizoaceae)**	Whole plant	Aqueous	Tannin extract 10%	Phenylbutazone induced ulcer	[44]
41	*Citoria ternatea* **(Fabaceae)**	Leaves	Different Extract	200 mg/kg and 400 mg/kg body wt	Indomethacin induced ulcer	[45]
42	*Musa paradisiacal* **(Zingiberales)**	Tepal and skin	Methanolic	100 mg/kg	Indomethacin plus pylorus ligation inducedUlceration	[46]
43	*Vinga mungo* and *mung* **(Fabaceae)**	Entire plant	Ethanolic	100mg/kg	Pylorus ligation ulcer	[47]
44	*Plantago rugelii* **(Plantaginaceae)**	Entire plant	Methanolic	200 and 400 mg/kg	aspirin and HCl in 60% (v/v) ethanol induced ulcer	[48]
45	*Moringa Oleifera* **(Moringaceae)**	Roots, seeds, leaves, pods	Ethanolic, hydroalcoholic extract of pods	100, 200, 400 mg/kg	Pylorus Ligation model, Ethanol induced ulcer, Aspirin induced ulcer.	[49,50,51, 52,53 49-53]
46	*Centellaasciatica* **(Apiaceae)**	Leaf Extract	Ethanolic	50 , 250 mg/kg	Indomethacin inducedUlcer	[54]
47	*Pithecellobium jiringa* **(Fabaceae)**	plant extract	Ethanolic	Orally 250 and 500 mg/kg,	ethanol-induced gastric mucosal ulcers in rats	[55]
48	*Parkia speciosa* **(Fabaceae)**	leaf extract	Ethanolic	50, 100, 200 and 400 mg/kg	ethanol-induced gastric mucosa injury in rats.	[56]
49	*Mucuna pruriens* **(Fabaceae)**	*leaves*	Ethanolic	62.5, 125, 250, and 500 mg/kg, extract control group (500 mg/kg)	ethanol-induced gastricmucosal injuries in rats	[57]

50	*Utleria salicifolia* **(Apocynaceae)**	Rhizome	50% Ethanolic extract	50-200 mg/kg	pylorus ligation Ulcer model	[58]
51	*Alstonia scholaris* **(Apocynaceae)**	Leaves	Ethanolic extract	50, 100, and 200 mg/kg	ethanol-induced ulcer model	[59]
52	*Phyllanthus niruri L.* **(Euphorbiaceae)**	Leaves	Methanolicextract	100, 200 and 400 mg/kg	ethanol-acid induced gastric mucosal injury	[60]
53	Allium sativum **(Amaryllidaceae)**	Bulb juice	Ethanol	250 mg/kg and 500 mg/kg	ethanol-induced and indomethacin-induced gastric ulcer	[61]
54	*Euphorbia umbellate* **(Euphorbiaceae)**	Bark	polyphenols	400mg/kg	Acid alcohol induced gastric ulcer	[62]
55	*Myrica esculenta* **(Myricaceae)**	Bark	Ethanolic	100mg/kg and 200mg/kg	Pyloric ligation ulcer	[63
56	*Baccharis trimera* **(Asteraceae)**	Aerial parts	aqueousextract .	1.0 , 2.0 mg /kg	Cold restraint ulcer model in plylorus ligated ulcer model	[64]
57	*Tanacetum larvatum* **(Compositae)**	Aerial parts	chloroform extract	200mg/kg	NSAIDs induced ulcer	[65]
58	*Hieracium gymnocephalum* **(Compositae)**	Aerial blooming part	Dichloromethane	200mg/kg	Ethanol induced ulcer	[66]
59	*Vernonia condensate* **(Asteraceae)**	leaves	crude ethanolic extract	30 and 300mg/kg	Ethanol and indomethacin induced ulcer	[67]
60	*Solidago chilensis* **(Asteraceae)**	Leaves	methanolic extract	100 mg/kg	Indomethacin induced ulcer	[68]
61	*Cordia dichotoma Forst.* **(Boraginaceae)**	Bark	methanol extract	500 mg/kg	Acid alcohol induced gastric ulcer	[69]

62	Capparis zeylanicaLinn **(Capparaceae)**	Leaves	methanolicextract	200 mg/kg	ulcer inhibition in HCl-ethanol induced ulcer and inhibition in indomethacin induced ulcer.	[70]
63	Salvadora indica **(Salvadoraceae)**	Leaves	ethanolicextract	150, 300 and 600 mg/kg	ethanol and cysteamineinduced ulcer models in albino rats	[71]
64	Maytenus robusta Reissek **(Celastraceae)**	aerial parts	Hydroalcoholic	1-10mg/kg	acetic acid-induced ulcer	[72]
65	Momordica cymbalaria (**Cucurbitaceae)**	Fruits	Aqueous	500 mg/kg	Ethanol induced ulcer	[73]
66	Mukia maderaspatana (**Cucurbitaceae**)	Root	Ethanolic extract	30 mg/kg b.wt.	Indomethacin-induced gastric ulcer in rats	[74]
67	*Cibotium barometz* (**Dicksoniaceae)**	Leaves	ethanolicextract	500 mg/kg	Ethanol-induced gastric hemorrhagic abrasions in Sprague Dawley rats	[75]
68	Cyperus rotundus L **(Cyperaceae)**	Rhizome	methanolic extract	250 mg/kg and 500 mg/kg	Aspirin-induced gastric ulceration in animals	[76]
69	*Caesalpinia sappan* Linn. **(*Caesalpiniaceae*)**	Heartwood	hydroalcoholic extract	250 and 500 mg/kg	Indomethacin-inducedulcer in Wistar albinorats	77
70	Pithecellobium Jiringa **(Legumnasea)**	Beans	EthanolExtract	250 and 500 mg/kg	Ethanol-Induced Gastric Mucosal Injuries in *Sprague-Dawley* Rats	[78]

71	*Alhagi maurorum* **(Fabaceae)**	Aerial parts	Ethanol Extract	100 mg/kg	against administration of aspirin ASP	[79]
72	*Kigelia africana* **(Bignoniaceae)**	Leaf	aqueous extract	1.75, 3.5, 7 and 14 mg/kg	ethanol-induced ulcer in rats	[80]
73	*Parkia speciosa* **(Fabaceae)**	Leaves	ethanolic extract	50, 100, 200 and 400 mg/kg	ethanol-induced gastric ulcer in rats.	[81]
74	*Calamintha officinal* **(Lamiaceae)**	leaves	methanol extract	50, 100, 200 mg/kg	ethanol-induced ulcer in rats	82]
75	*Hyptis suaveolens* ***(*Lamiaceae*)***	Aerial	Ethanolicextract &hexanic fraction	62,5, 125, 250 and 500 mg/kg	HCl/ethanol, ethanol, NSAIDs and hypothermic restraint-stress	83]

The antiulcer activity exhibited by above listed plant is due to presence of phytoactive principles. The different extracts of plants when analyzed for phytochemical screening showed presence of alkaloids, flavonoids, tannins, saponins etc. All these constituents have Pharmacological mechanism of action that possess reducing rate of ulceration, decreasing acid secretion, enhancing action of defensive factors, ulcer protection etc. It is summarized in table no.3.

Table No. 3: Mechanism of antiulcer action by phytoconstituents.[2]

Sr. No.	Active Principle	Mechanism of Action
1	Alkaloids	Alkaloids represent a group of natural products that display aconsiderable antiulcer activity. Following are listed mechanism:- 1. An alkaloid protects against ulcers by reducing pro-inflammatory cytokines and oxidative stress and increasing gastric mucosal blood flow.[84] 2. Also alkaloid compound reduced gastric injuries treatment resulted in increased mucosa GSH, SOD and PGE2 levels, while decreased IL-6 and TNF-levels.[85] 3. Acts against ulcer by increasing GSH levels and an antioxidant response and adecrease in H+/K+-ATPase activity.[86] 4. Alkaloids have shown highly selective antibacterial activity against H. pylori.[87]
2	Terpenes and Terpenoids	Monoterpene decreased gastric and duodenal lesions, increased gastric mucus production and mucosal in experimental ulcers models induced by ethanol, NSAIDs, stress, H. pylori.[88]
3	Flavonoids	Flavonoids are natural antioxidants present in different kinds of fruits and vegetables-Recent studies indicated that flavonoids (Quercetin, Hesperidin, rutin and kaempferol) are capable to shows a wide spectra of pharmacological activities,including as anti-inflammatory, antimicrobial, antiallergic, anti-cancer, antidiarrheal and antiulcer. Flavonoids inhibit the mucosal content of platelet-activating factor in rats with gastric damage produced by acidified ethanol.[89] Also exhibits antiulcer activity though opioid and adrenergic receptors and primary afferent neurons in gastric ulcers induced by ethanol, acidified ethanol, acetic acidor indomethacin.[90] Flavoniods suppress superoxide anion, hydroxyl radical and methyl radical with acute ulceration stress induced by indomethacin and water immersion in rats.[91]
4	Saponins	show evidence of invivo antiulcer activity possibly due to the presence of antioxidant saponins, e.g. the aqueous extract from Bauhinia purpurealeaf.[92]
5.	Phenolic Acids	A synergistic antiulcer activity using gallic acid and famotidine combination was observed against aspirin and pyloric ligation induced ulcer in rats.[93]
6.	Tannins	Tannins exhibit antiulcer effect bydecreasing COX-2 levels, enhanced angiogenesis and increased mucus secretion.[94] Ellagitannin-richfraction reduces ulceration in rats with ethanol-induced gastric ulceration model through empoweringgastric protective factors.[95]

DISCUSSION

Peptic ulcer is common disorder of GIT but tend to severe if kept untreated. The

pharmacotherapy applied to treat ulcer can cure it but in between therapy or after the therapy the produces side effect that are harmful. So the interest of therapy is focused towards herbal medicine that shows no or least side effects as compared with clinical pharmacotherapy.

In this review paper all the listed natural plant extracts are analyzed for antiulcer activity by using different rat/mice models. All these extract proved their desired activity against ulcer lesions.

In literature survey pylorus ligation rat model, NSAID (aspirin, paramacetamol, indomethacine, naproxane, phenylbutazone,) induced ulcer, alcohol induced ulcer, stress (physical, Psychological) induced ulcer, acid induced ulcer models, cysteamine induced ulcer models are used to evaluate the antiulcer activity with different doses of plant extract with suitable solven. The aqueous extract of tubers of *Solanum tuburosum*[5] ethanolic, chloroform and n-butanol extract of *Anvillea garcinii* shrub[6], aqueous extract of leaves of *Madhuka indica*[7], methanolic extract of seeds of *Citrullus lanatus*[8], ethanolic and ethyl acetate extract of *Markhamia tomentosa* leaves[9], methanolic extract of corns of *zea mays*[10], aqueous and ethanolic extract of leaves of *Oscimum sanctum*[11], methanolic extract of *Terminalia loxiflora* leaves[12], hydroalcoholic extract of unripe fruits of *Carica papaya*[13], hydroalcoholic extract of stem bark of *Garuga pinnata*[14], Potential gastroprotective activity of medicinal plants[15], methanolic extract of leaves of *Hibiscus rosa Sinensis*[16], hydroethanolic extract of leaves of *Kalanche pinnata*[17], methanolic extract entire plant of *Jatropa gossypifolia*[18], aqueous extract of *Azadirecta indica* leaves[19], ethanolic extract of leaves, flowers, fruits of *Calotropis procera*[20], ethanolic extract of aerial parts of *Passiflora alata*[21], ethanolic extract of *Grewia flavescens* Juss entire plant[22], ethanolic extract of tap root of *Beta vulgaris* and bark of *Ficus religiosa*[23], aqueous ectract of leaves of *Wedelia trilobata*[24], aqueous, alcoholic, acetone, chloroform extract of herbal mixture of whole plant of *Ageratum conyzoides*, roots of *Vermonia amygdalina* and roots of *Citrus aurantifolia*[25], methanolic extract of seeds of *Leeaindica*[26],ethanolic extract of *Citharexylum quadrangular* leaves[27], aqueous extract of *Musaparadisiacal* ripe fruits[28], ethanolic extract of leaves of *Swietenia mahagoni*[29], ethanolic extract of roots of *Deglycyrrhizinated* liquorice[30], different medicinal herbs[31], ethanolic extract of *Canavalia gladiata* pods[32], crude extract of isolated saponin and essential oil from *Polygonum hydropiper*[33], aqueous extract of *Tiliacora*

acuminate bark[34], methanolic extract of *Punica grantum* peels[35], resin from *Virola oleifera*[36], hydroalcoholic extract of *Glycyrrhiza glabra* roots[37], aqueous and chloroform extract of *Solenostemon monostychus*aerial parts[38], methanolic extract of *Peltophorum pterocarpum* leaves[39], methonolic extract of *Osyris quadripartite* leaves[40], ethanolic extract of *Magnifera indica* seed kernel[41], ethanolic extract of *salvodra indica* leaves[42], methanolic extract of *Morinda Citrifolia* Linn root bark[43], aqueous extract of *Delosperma ressei* whole plant[44], different extract of *Citoria ternatea* leaves[45], methanolic extract of *Musa paradisiacal* tepal and skin[46],ethanolic extract of *Vinga mungo* and *mung* entire plant[47], methanolic extract of *Plantago rugelii* entire plant[48] with different doses shows potent antiulcer effect. The doses range from100, 200, 400mg/kg shows satisfactory antiulcer effect against any ulcer rat model. The interesting part of showing this activity by these plants is due to presence of principle constituents which are capable to fight against ulcer lesions. The abundance presence of alkaloids, terpenoids, flavonoids, saponins and tannins are responsible to exert effective antiulcerogenic effect through different mechanism of actions. The different parts of *Moringa olefira* was studied for antiulcer activity ethanolic extract of roots[49,50], ethanolic extract of seeds[51,52], ethanolic extract of leaves[53], this is interesting part of this plant, it is rich in tannins and flavonoids thus any part of plant proves potential antiulcer activity.

Based on this data, the study of the main constituents of plant extracts could also shows an approach in evaluation of possible antiulcer activity of plant products and performing toxicitystudies with specific substances. When study performed using the methanolic extract of bark of fraction of *Euphorbia umbellata* (Euphorbiaceae) bark, it was reported that the antiulcerogenic activity proved by the plant was due to occurrence of active phytochemicals like polyphenols, primarily ellagic and gallic acids derivatives and flavonols,though there are no toxicity studies.[63]

The overall research studies shared in this review report clearly proves that plant products represent a rich source of bioactive molecules with antiulcer potential. The efficacy of certain herbal remedies has been substantially investigated by in vitro and even in vivo studies from traditional uses to preclinical studies. The antiulcer effect of these plants has been focused towards specific group of phytoactive constitute, such as alkaloids, tannins, flavonoids, saponins and turpenes.

Literature study for antiulcer effect of medicinal plants indicated that phytochemicals are

safe, natural and effective resources that can be incorporated in the prevention and also in treatment of ulcers.

It seems like pharmacological and toxicological screening of medicinal plants for the treatment of gastric ulcer using different in-vivo, in-vitro models is rather notable however only some of these have succeeded clinical trials and still few have been prescribed for therapy. This reveals that limited benefits of research towards society due to insufficient utilization of time, money, manpower, resources, etc. Thus, there is wide scope for pharmacologists concerning clinically effective and globally competitive active research approach towards potential antiulcer activity and standardization of herbal drugs.

CONCLUSIONS

Current review provides insights on list of various medicinal plants that evaluated for antiulcer activity using different ulcer models. For research and treatment of peptic ulcer the proper knowledge of the control of gastric acid secretion and its mechanism, aggressive anddefensive factor balancing and other factors that responsible to cause ulcer is important to evaluate medicinal plants. This elaborative study reveals that many claims in traditional system of medicines across the world should be adequately reviewed and practiced again. Hence, scientific validation of these claims may come up with novel polyherbal formulationas substitute in the field of modern medicine.

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