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A Comprehensive Review on Ulcer and Their Treatment

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Abstract A peptic ulcer is a lesion (sore) on the stomach lining, or duodenum. Peptic ulcers are probably a twentieth-century condition. The ulcer disease continues to be a significant source of worldwide morbidity and mortality. The Gastrointestinal ulcers and duodenal ulcers are considered the two most extreme types of peptic ulcers. Peptic ulcers are found to be caused by an excess of violent factors including Hydrochloric acid (HCL) pepsin, refluxed bile leukotrienes (LT), reactive oxygen species (ROS) and protective factors, these include mucus-bicarbonate barrier functions, prostaglandins (PGs), mucosal blood flow, cell regeneration and migration, non-enzymatic and enzymatic and certain growth factors. The primary cause of peptic ulcer disease is pylori infection and the use of NSAIDs. This review article underscores the importance of a multidisciplinary approach in the management of ulcers to improve patient outcomes and quality of life.

Keywords Peptic ulcer; Stomach; Sore; *H.pylori*; Infection

1. Introduction

Gastric ulcer disorder is when painful lesion occurs in the lining of the stomach, duodenum (beginning of the small bowel). Ulcers may cause discomfort in the belly, and quite often, a hemorrhaging or an abdomen hole. Sores are dense lesions that infiltrate the whole digestive tract thickness and mucosal muscle. Unquestionably, gastric ulcer a twentieth century epidemic. The most common type of ulcer is peptic sore, that seemed to be caused by harm to the membrane of the abdomen and also duodenal ulcer

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(Bandyopadhyay et al., 2001). There are two primary causes of peptic ulcer. Firstly, the most severe is an acute peptic ulcer that absorbs the lamina muscularis of the mucosa but it will not enter submucosa any further. It is associated mainly with discomfort in the form of serious burns (ulcer curling) and brain injury (ulcer Cushing). Second, the recurrent gastric ulcer that absorbs the muscles maximum thickness is propria and has its origin in or out of the organs serosa layer (Kumar et al., 2012).

2. Types of stomach ulcer

There are two distinct kinds of peptic sore which are as follows:

- Gastric ulcers, which form in the stomach lining.
- Duodenal ulcers that develop in the small bowel at the upper part.

All forms of peptic sores are most often either caused by infections with Both types of peptic ulcers are most commonly caused either by infection with bacteria from Helicobacter pylori or by continuous use of anti-inflammatory nonsteroidal drug (NSAID).

Gastric ulcer

A gastric sore is a disintegration of the stomach lining that interferes with the mucous output that coats the lining, causing stomach acid to come into contact with the stomach. This causes pain to the patient after eating which stimulates stomach acid development. The acid will eat right through the lining over time, exposing the capillaries below, leading to bleeding.

Most patients with a gastric ulcer do not feel symptoms when their stomach is empty, as eating produces stomach acid. This can lead to food avoidance when undiagnosed, which becomes easier since the bacteria also affects appetite. Despite never feeling hungry the patient begins to lose weight.

Gastric ulcers can be hard to diagnose. The symptoms may be confused for other common digestive system ailments from acid reflux to gallstones, depending on the location of the ulcer. There are just three ways to confirm there is an ulcer:

- Treat the patient, and hope to improve the symptoms. This is not recommended for patients who are sensitive to potent antibiotics, however, and treatment takes at least one week.
- Do an endoscopy there. This is, however, considered an invasive procedure and can normally only be done on an empty stomach.
- Carry out a test on carbon-14. That is to take a patient's breath sample and then give them a cap.(3)

Common symptoms possibly include:

- Blogging
- Belching
- Feeling sick in your gut
- Deprived hunger
- Sputtering
- Energy loss

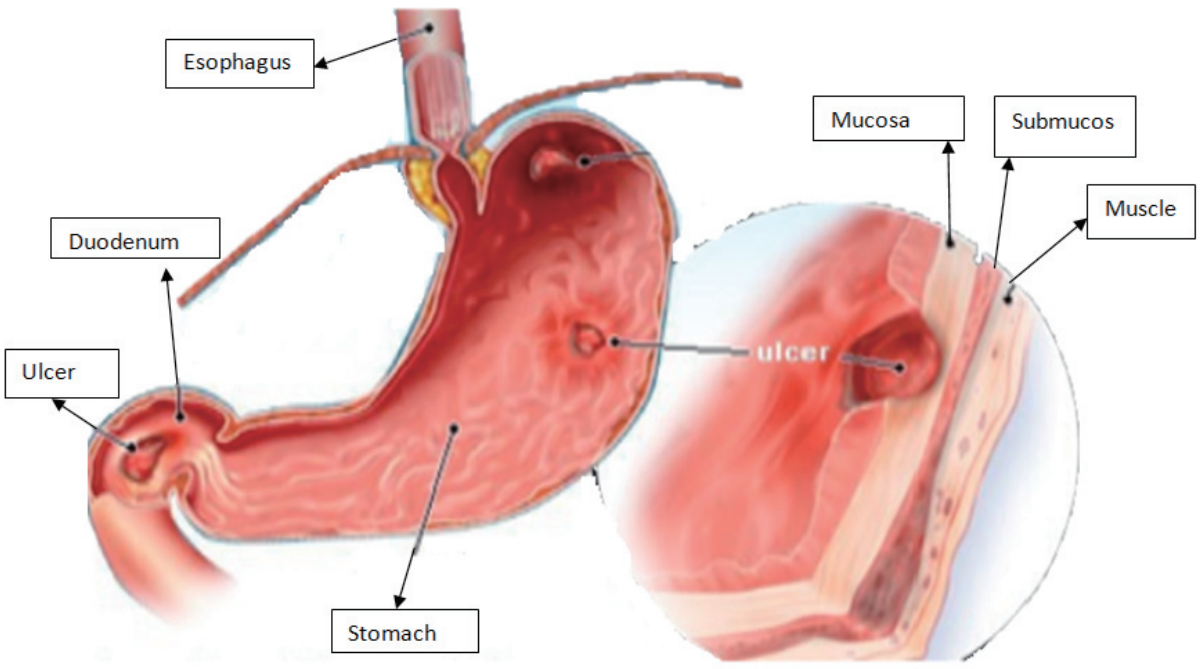

Figure 1: Areas indicated for peptic ulcer

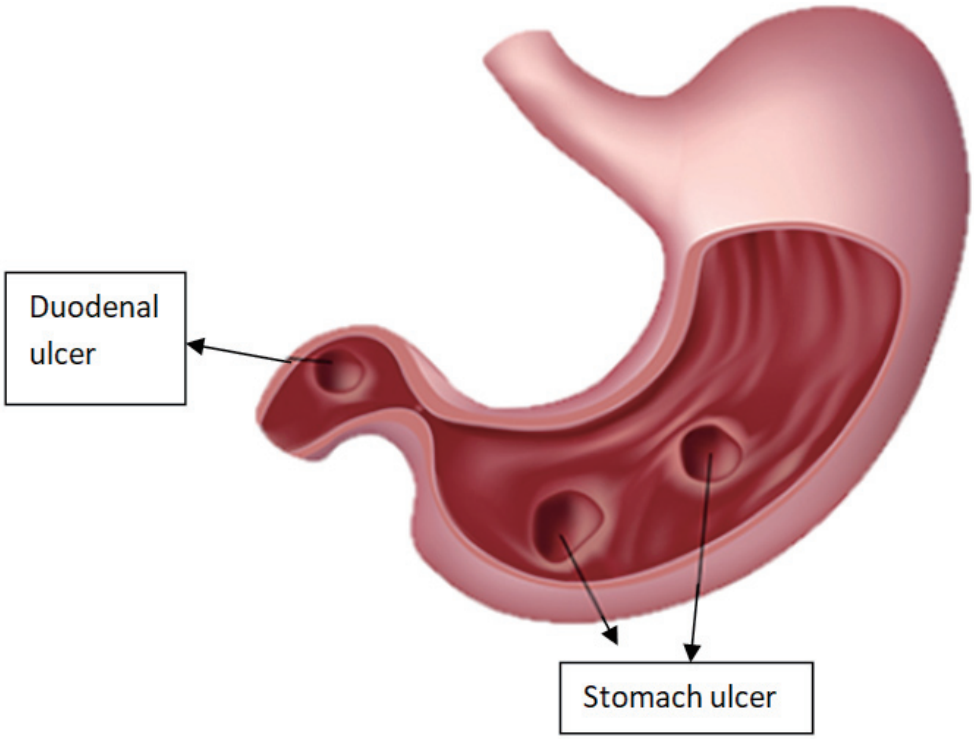

Figure 2: Duodenal ulcer image

Peptic ulcer factors are included:

- Continuous use of non-steroidal anti-inflammatory drugs (NSAIDs), such as aspirin and ibuprofen.
- Outbreak of Helicobacter pylori virus (H. pylori).
- Rare cancerous and non-cancerous tumors in the stomach, duodenum, or pancreas — known as Zollinger-Ellison syndrome.
- Peptic sores are occasionally because of the use of NSAID and H. Pylori. (4)

Duodenum sores

A duodenal ulcer is a sore in the membrane of the duodenum. The duodenum is our small intestine' s starting part, the part of our intestinal system that leaves our stomach straight after food passes through. The duodenum bulb is the site for duodenal ulcers. Duodenal ulcers are more common than gastric ulcers, and are caused by increased gastric acid secretion as opposed to gastric ulcers. Duodenal ulcers are commonly found anteriorly, and rarely thereafter.(5)

Perforation can make anterior ulcers difficult, while the posterior ones bleed. Anterior to duodenum is the peritoneal or abdominal cavity. Therefore, if the ulcer grows deep enough, it will perforate, while if a subsequent ulcer grows deep enough, it will penetrate and bleed the gastroduodenal artery.(6)

Causes of duodenal ulcers

- Bacterial infection named *Helicobacter pylori* is the main cause of this damage. The bacteria can cause inflammation of duodenum lining and can form an ulcer.
- Many medicines, particularly anti-inflammatory drugs such as ibuprofen and aspirin, can also cause duodenal ulcer. Many drugs or medical conditions have less chance of causing ulcer.

Symptoms of a duodenal ulcer

- Have gastric or abdominal pain.
- Possess nausea.
- Feel completely bloated and full after eating.
- Lose weight.
- Just feel ill.

Diagnosis of ulcer in duodenum

- A Gastroscopy in which a professional usage a long, pliant tube with a camera at the end to focus through the belly and duodenum.
- A blood test, a stool sample or a breath test to determine if we have an *H.pylori*.

Treatment for a duodenal ulcer

If our sore is caused by *H.pylori*, the normal treatment is 'triple therapy'. We need to take 2 antibiotics to kill the bacteria, and a drug to lower the amount of acid the stomach produces.

If we don't have an infection with pylori and we are using anti-inflammatory drugs, we will have to stop taking them (if possible) and start taking a medication to eliminate our production of stomach acid.

Getting antacids, drinking less alcohol, and quiting smoking.(7)

Ulcer Causative agents and pathogenesis

Peptic ulcer is generally caused by bacterial mucous coating of the stomach and duodenum and allow the acid in the lining of stomach. These bacteria and acid cause sore or ulcer. *H.Pylori* induced ulcer: *H.pylori* bacteria fragile the defence mucous coating of the stomach and duodenum and allow the acid in the lining of stomach. These bacteria and acid cause sore or ulcer.(Majumdar et al., 2011) *H.pylori* infection can result in either hypochlorhydria or hyperchlorhydrea. The main moderator of *H.pylori* infection are cytokines, that inhibit parietal cell secretion but *H.pylori* without moderator can affect the H^+/K^+ ATPase α-subunit, or inhibit the production of gastrin.(Ludovico et al., 2011) With complete resolution of mucosal inflammation and a minimal chance of recurrence of ulcers, the appropriate antibiotic regimens can successfully eradicate the infection.(Martin., 1997)

Drug induced ulcer: NSAIDs , that inhibit the COX1 and COX2 in the human body. COX1 and COX2 are responsible for the prostaglandin synthesis. Because the cyclooxygenase pathway produces prostaglandin D,E & F. Prostaglandins controls the gastric juice secretions , because of that mucosal lining damages and cause ulcer. These drugs damage the mucus phospholipids , which leads to mucosal damage. Further NSAID also results in marked reduction of mucosal blood flow, mucus-bicarbonate secretions, impaired platelet aggregation, decreased epithelial cell renewal and increased leukocyte adherence responsible for ulceration pathogenesis.(Fan et al., 1996)

Steroids induced ulcer: Steroids are the synthetic substance , which is mainly used to treat the inflammatory conditions like- inflammatory of blood vessels and myositis(inflammation of muscle). If we take this in a low doses form then they not cause any side effects like- cortisteroids in low doses do not cause ulceration. They mainly act on cell membrane(phospholoipid) , which inhibit the phospholipase because of this inhibit arachidonic acid(fatty acid) , then no prostaglandin which is used to treat the ulcer and damages of lining of the mucosal.(Ludovico et al., 2011)

Ulcer due to genetic defect: In some cases of O '+ve' blood group the size of the parietal cell increase , which induce cell demand as HCL secretions increase , cause damages of lining of the mucosal which leads to ulcer. (Ludovico et al., 2011)

Gastric acid secretions: Gastric acid is founded as one of the main ulcerative inducing variable of gastric ulcer disease. About 50% of stomach ulcer patients have been reported to be pepsin and acid hypersecretors.(Szabo et al., 1998) Three principal secretagogues histamine, acetylcholine, and gastrin are suggested to stimulate acid secretion. The receptors on the parietal cell surface include H2 receptors that react to histamine released from specific mast cells, receptors that are sensitive to the muscarinic effects of acetylcholine released from the vagus nerve, and receptors that are possibly responsive to endogenous circulating gastrin.(Aihara et al., 2003) The only source of the acetylcholine (Ach) which can act directly on the parietal cell is from the enteric nervous system's postganglionic fibres. The muscarinic-1 agonist McN-A-343 stimulates acid secretion without affecting histamine release, suggesting the parietal cell's muscarinic receptor.(Sandvik et al., 1988)

Reserpine: Reserpine is one of the medications; extracted from the rawolfia serpentine roots that have been reported to play a pivotal role in ulcer progression. Various reports suggest that reserpine induces degranulation of mast cells through sympathetic activation with an increase in gastric acid secretion.(Cho et al., 1985)

Ethanol: There are a number of reasons for ethanol-induced stomach lesions, including loss of stomach mucus content, reduced blood flow to the mucosal cells and damage to them. Ethanol has been reported to cause severe damage to the gastrointestinal mucosa beginning with microvascular injury resulting in increased vascular permeability, oedema production and epithelial elevation. Ethanol has also induced apoptosis that results in cell death. Ethanol.(Mahmood et al., 2011) releases superoxide anion and hydroperoxy-free radicals that contribute to increased lipid peroxidation after metabolism. Increasing the amount of lipid peroxide and free radicals extracted from oxygen leads to significant changes in cellular levels, causing membrane damage, cell proliferation, exfoliation, and epithelial degradation.(Umamaheswari et al., 2007)

Gross morbid Anatomy

The peptic sore is generally a single, round or oval elliptic ulcer, often strongly elongated located near the lower curvature in the posterior wall of the pyloric portion of the stomach. The edge closer to the pyloric orifice is flattened or less straight in many of the terraced or conical ulcers than the other sections of the surface, possibly due to the rubbing of the food as it reaches and passes through the small pyloric portion of the gastric. Opposite to early ulcers the peritoneal surface also shows a local fibrinous.

The base of lifelong broad lesions can be fairly clean, with many of the lesions covered and partially loaded with the granular or slimy, rusty, muddy or brown tinged exudate adherent. Below this is a film of gelatinous, grayish brown, or often brown infused, relatively solid, necrotic and granulated tissue material. The next layer is of strong scar tissue, which can cause serious permanent deformation of the stomach due to its retractability, if sufficiently extensive.

Hyperemia is indeed common around ulcer but sometimes throughout much of the stomach that has been surgically removed. Haemorrhage is common in earlier excudate ulcers, and may occur elsewhere in the mucosa and submucosa. Chronic gastritis hypertrophy is an accompaniment which is normal, but not constant.(Majumdar et al., 2011)

Pathophysiology

Acid peptic disease occurs when the mucosal membrane is overcome by the injurious effects of acid and pepsin. Visualizing acid peptic illness in the form of a pseudoequation is beneficial.

Acid peptic disease $\propto$ ***acid+pepsin/mucosal barrier***

Where the likelihood of contracting acid peptic disease is equivalent to the amount of acid and gastric juice (pepsin) created and is inversely proportional to the integrity of the mucosal barrier.

Acid secretion

The parietal cell present in the oxyntic glands of the fundus and of the stomach is the source of the production of gastric acids. The parietal cell is the clear winner among all epithelial cells in its ability to produce a gradient in the concentration of hydrogen ions. The pH of the gastric lumen is often as low as 1 to 2, as opposed to a blood pH of 7.4. For example, this difference in concentration of 6 logs is much greater than the average difference in concentration of hydrogen ions between the urine and the blood. The extraordinary parietal cell's ability to create a steep pH gradient has attracted the attention of both fundamental sciences and clinical researchers.

Morphology of parietal cell

The parietal cell undergoes a rather surprising morphological change with stimulus. In the resting state, an extensive intracellular membranous tubulovesicular network characterizes the parietal cell.The interior of this tubovesicular network is acidic and some agents such as omeprazole, useful for the treatment of ulcer disease, accumulate in these highly acidic compartments.With stimulation, this membrane tubulovesicular network disappears and is replaced by a broad intracellular cananicular network that interacts directly with the lumen of the oxyntic gland and, in turn, greatly amplifies the surface area of the cell's apical membrane.

This morphological transition is apparent within 3 minutes of parietal cell stimulation and is complete in 30 minutes. Current evidence indicates that this morphological transition represents a fusion of these tubulovesicular structures with the apical cell membrane.This fusion process delivers the "acid" pump, which is hydrogen and potassium ion triphosphate (H^+,K^+ ATPase), to the apical membrane.(Wallmark et al., 1985)

Regulation of acid secretion

Various compounds are known to induce the parietal cell to secrete acid Which include acetylcholine, histamine and gastrine and current evidence indicates that the parietal cell has different receptors for each of these secretagogues. Histamine is released in the gastric mucosa from advanced mast cells and possibly diffuses to the parietal cell where it interacts with a particular receptor, the H_2 receptor. Histamine's interaction with the H_2 receptor is inhibited by antagonists of the H_2 receptors such as cimetidine, ranitidine or famotidine. Stimulation of this receptor results in activation of adenylate cyclase and increased intracellular adenosine levels, which likely cause the chemical reaction and the calcium concentration in the cytoplasm of the parietal cell appears to increase. Gastrin binds to the third receptor and its linking is not inhibited by either an atropine or H_2 receptor antagonists.(Olson et al., 1984)

3. Medicine for peptic ulcer (Tripathi., 2003)

Medication to suppress acid secretion

Proton pump inhibitor- lansoprozole, Omeprazole, pantoprozole, dexlansoprazole, rabeprozole, esomeprozole.

Anticholinergics- Pirenzipine, propantheline, oxyphenonium.

H_2 receptors antagonist- Ranitidine, famotidine, cimetidine, roxatidine, loxatidine, nizatidine.

Prostaglandine analogue- Misoprostol, enprostil, rioprostil.

Drugs design to neutralize gastric acid (antacid)

Nonsystemic- Aluminium-hydroxide, magnesium-hydroxide, Magaldrate, magnesium trisilicate, calcium carbonate.

Systemic- sodium citrate ,Sodium bicarbonate.

Ulcer protective

Sucralfate, colloidal bismuth Subcitrate and bismuth subsalicylate, ranitidine bismuth citrate.

Newer cytoprotectives- Rebamipide, ecabet."

Antimicrobial drugs for H.pylori eradication

Amoxycillin, Clarithromycin, metronidazole, tinidazole, tetracycline.

Proton pump inhibitor

These are a group of drugs whose main action is marked, long-reduction in the production of stomach acids. They are the most effective acid secretion inhibitors available. A group of drugs preceded and eventually superseded another group of drugs with similar effects, but a separate mode of action, called antagonists to the H_2 receptors.(Qadeer et al.,2006)

H2 receptor antagonist: In the comparison of PPI therapy, H2 receptor antagonist has a limited role against peptic ulcer. They bind to the H2 receptor on the basolateral membrane of parietal cells. The first compound, burimamide was left shortly, because of toxic response. The second compound, metiamide, was orally active, but have a toxic effect on bone marrow. The third compound, was cimetidine, is still widely used as an anticancer.(Fedorowicz et al., 2012)

Anticholinergic: They also suppress the acid secretion in the stomach and decrease the gastrointestinal movement , irritation , cramps.

Prostaglandin: The analogs of prostaglandin are a class of drugs that bind to a prostaglandin receptor. Prostaglandin analogs including Misoprostol are used in the therapy of duodenal and gastric ulcers. Misoprostol and other prostaglandin analogs secure the gastrointestinal tract's lining from harmful stomach acid and are particularly indicated for the elderly on prolonged doses of NSAIDs.(Winkler et al., 2014)

Antacids: They neutralize the gastric acid which reduces the irritation. For people with acid reflux, when enormous amount of acid being formed in the stomach, the normal mucous membrane that protects the stomach lining may harm the esophagus. Antacids contains alkaline ions that chemically neutralize gastric acid in the stomach, reduce damage, and relieve pain.(Weberg et al., 1990)

Ulcer protectives: It works mainly in the stomach lining by adhere to the site of the ulcer and protect them from the acid, enzyme, bile salts. They heal the ulcer.

Diagnosis

For patients with epigastric discomfort and pain, peptic ulcer disease is suspect; however, these signs are not clear. Failure to respond to traditional peptic ulcer disease treatment may indicate causes other than normal peptic ulcers and should require endoscopy or gastrointestinal imaging.

Barium swallow: This is achieved as part of series of x-rays that appears like the entire upper GI tract. A continuous x-ray beam, or fluoroscopy, is often used to record movement across GI tract during a barium swallow. It is widely available and accepted method for diagnosing stomach or duodenal peptic ulcer.

Endoscopy (EGD): An endoscopy is passed through the mouth and pharynx (a thin, flexible, lighted tube) and into the esophagus. It also offers a chance to detect hidden mucosal lesions and to create histopathological bases for biopsy lesions. Endoscopic biopsies are indicated at the time of diagnosis for all gastric ulcers, whereas duodenal ulcers are almost always benign, and do not require biopsy under normal circumstances. Also, endoscopic biopsy appears to be the best and most effective tool of diagnosing H.pylori. Histological research with normal hematoxyl and eosin staining offers an excellence diagnostic method. In an attempt to accelerate treatment of H.pylori following a gastric mucosal biopsy used urease operation. Biopsy specimens are placed in a red solution or gel of urea and phenol.(Ryan., 1978)

Treatment

Nanoscale particle therapy for ulcer and wounds: In addition, bacterial infections in the mucosal environment cause unhealing wounds resulting in gastrointestinal sores. Helicobactor pylori is the most significant cause of gastrointestinal infection.(Furuta, Delchier., 2009) The bacteria live under the stomach mucous lining adhering to the stomach epithelium, thereby restricting access to the site

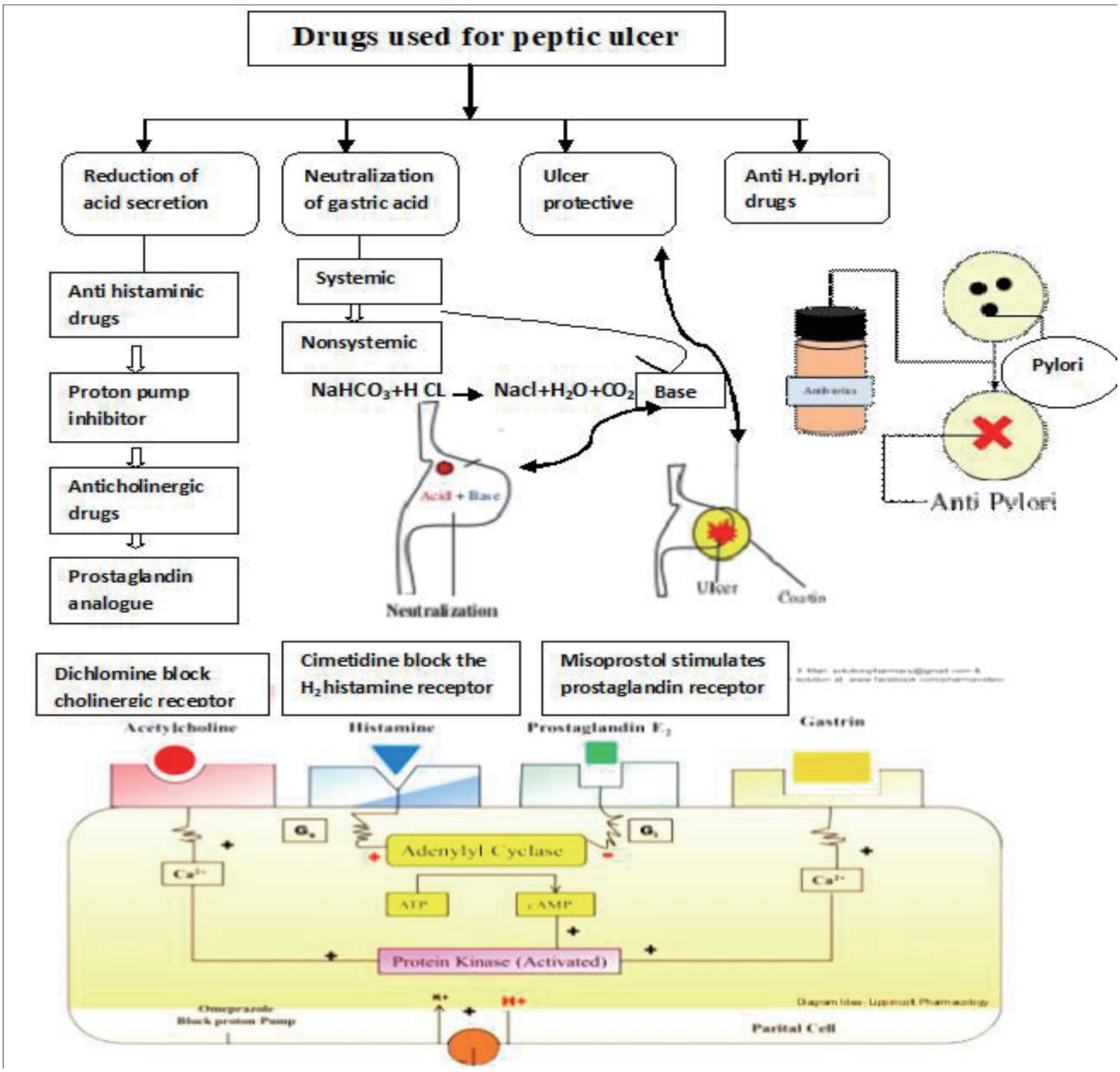

Figure 3: Mechanism of drug to treat ulcer

of infection by antimicrobial drugs. Antibiotics in appropriate amounts and in fully active formulations are not administered to the site of the contamination.(Bornschein., Rokkas., 2009) In clinical applications for gastrointestinal infection the nanoparticles embedded with antibiotics have been shown to be successful in formulating these. Indeed, the biggest benefit of tiny particles is their tendency to be more adhesive and to act better in the gastrointestinal mucosa against bacteria.(Graham., Shiotani., 2008) Nanotechnology offers great opportunities to improve therapies for the healing of wounds. The nanometer scale open the way for new materials to be developed for use in advanced medical research.(McColl., 2009), (Lai et al., 2009)

Proliferation

Growth factor: It ambitions at bringing cells into the wound and facilitating the movements of cells into the wound region, stimulating the increase of epithelial cells and fibroblasts, including the formation of latest blood vessels and having a profound influence at the formation of matrix and scar remodeling.(Johnstone., Farley et al., 2005), (Hantash et al., 2008), (Murphy., Nagase., 2008) One way to improve the in vivo effectiveness of the growth factors is to promote the continued release of bioactive molecules through inclusion polymer nanocarriers.(Williams., 2009), (Maham et al.2009)

Opioids: opioids have recently been shown to

Table 1: Medicinal plants used in ulcer treatment.

s.no	Medicinal plants	Antiulcer activity	Active constituents	references
1.	Aegle marmelos	Extract of leaves administered orally for 21 days, daily dose of 1g/kg.	Luvangetin	50,51
2.	Allium sativum	Garlic juice combined with 3 or 4 parts of ordinary or purified water is used as a cleaning lotion for wounds and foul ulcers.	Volatile oil, alliin, and allicin	52,53
3.	Shorea robusta	Extract from S. Robusta was given orally in rats at doses of 150 and 300 mg / kg against ethanol and pylorus induced gastric u lcer.	Ursolic acid and amyrin	54,55
4.	Psidium guyava	P. guyava methanol leaf extract was orally administered in rats for 10 days at doses of 500 and 1000 mg / kg.	Quercetin, guaijaverin, flavonoids, and galactose-specific lecithins	56,57
5.	Euphorbia neriifolia	Plant juice is used mostly with clarified or fresh butter to treat unhealthy ulcers.	Euphorbon, resin, gum, caoutchouc, malate of calcium	58
6.	Galega purpurea	Root powdered and mixed with honey is applied to ulcers.	querritrin, and glucoside rutin	59
7.	Myrtus communis	Powder of leaves is a useful application in wounds and ulcers.	Myrtle (Volatile oil)	60,61

improve the process of wound healing by enhancing keratinocyte migration.(Wolf et al., 2009).

Remodeling

Gene therapy: non-viral polymer gene delivery systems provide enhanced nuclease degradation safety, enhanced plasmid DNA uptake and regulated dosing to maintain plasmid DNA administration period. It is possible to devise these gene delivery systems from biocompatible and biodegradable polymers such as PLGA, polysaccharides and chitosan.(Mayo et al., 2009)

Medicinal plant for ulcer

In this modern age, 75-80% of the population of the world still uses herbal remedies mostly in underdeveloped countries due to greater cultural acceptability, better human body enforcement and fewer side effects. Histological tests showed no acute toxicity to these medicinal plants. Preliminary photochemical screening of this medicinal plant detected the presence of essential secondary metabolites such as flavanoids and tannins.

Indian Ayurvedic book Meteria Medica and online databases like science direct, pubmed, scopus and google scholar were explored for each of the peptic ulcer medicinal plants and all articles collected were analyzed to obtain any in vitro, in vivo or clinical proof of their efficacy and potential mechanisms.(Kumar., 2011) The studies obtained either obviously demonstrates the efficacy of these herbs or unintentionally demonstrate their effectiveness on the underlying mechanisms in the therapy of gastric sores. Meteria Medica offers a lot of information on ethno-medicinal herbs that are useful as antiulcerants and that many researchers have scientifically tested and demonstrated for their antiulcerative activity.(Patel., jain., et al., 2010), (Nadkarni. Et al., 1976)

Acasia Arabica: The fresh plant part are considered as an antimicrobial with good nutritional value in the traditional indian medicinal system. The moistened leaves are poulticated and used to treat ulcers.(Omayma et al., 2011) As a gargle it is useful for washing in haemorrhagic ulcer and wounds. Acasia Senegal gum is covered in rates against cold stress-induced gastric ulcer. Aqueous extract from this gum provided protection against intestinal damage caused by meloxicam and attenuated bowel enzyme activity.(

Abd El-Mawla., Osman. Et al., 2011)

Active constituents: Phenolic compounds, tannins and flavanoids are treated.

Tamarindus indica: It is a long-lived and beautiful fruiting tree with a dense, spreading crown growing upto 30 meters tall. The bark can be used to relief sores, ulcers. Leaf decoction is used as a cleaner for indolent sores, which promotes positive response. Seed coat methanolic extract of this indica greatly reduces the total amount of gastric juice at doses of 100 and 200mg/kg.(Nandkarni. Et al., 1976), (kumar et al., 2011)

Active constituents. Tannins are treated

Adansonia digitata: The fresh juice of the leaves in combination with powdered ginger and the expressed juice of the fresh root of salvadora indica is applied with considerable benefit for indolent syphilitic ulcer.(Nandkarni. Et al., 1976)

Active constituents. Phenol compounds.

Ocimum sanctum: For many years millions of Indians take the fresh leaves as Prasad. O"s set gasoline. In rats in which ulceration is caused by aspirin, indomethacin, alcohol and stress-induced ulceration, sanctum was administered intraperitoneally at doses of 1,2, and 3 ml/kg.(Nandikarni. Et al., 1976) This reduces the index of ulcer in a dose-dependent way.(Singh., Majumdar. Et al., 1999)

Active constituents. Fixed oil eugenol are taken.(Singh. Et al., 1999)

4. Conclusion

Peptic ulcer therapy has evolved significantly in recent times. This disease remains a growing health issue in our society affecting mainly people of all ages. The combination of herbal products and traditional anti-gastric ulcer medications could have a synergistic effect against H.pylori and stomach ulcer disease and enhance the outcome of patients with stomach ulcer.

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Author contribution

All authors contributed to idea and design of the review, with drafting of the article, and have equal contribution.

Conflicts of interest

The authors declare that there is no conflict of interest.

References

1. Bandyopadhyay, D., Biswas, K., Bhattacharyya, M., Reiter, R. J., Banerjee, R. K. 2001. Gastric toxicity and mucosal ulceration induced by oxygen- derived reactive species, protection by melatonin. Curr Mol Med, 1:501-513.
2. Kumar, s., Kaur A., Singh, R., Sharma, R. 2012. Peptic ulcer: A review of etiology and pathogenesis. IRJP, 3(6).
3. https://www.medicalnewstoday.com/articles/322849.php
4. https://www.health24.com/Medical/Heartburn/Peptic-ulcers/risk-factors-for-peptic-ulcers-20160309-2
5. https://www.healthdirect.gov.au/duodenal-ulcer
6. https://doi.org/10.1016/B978-0-12-811837-5.00013-7
7. https://patient.info/digestive-health/dyspepsia-indigestion/duodenal-ulcer
8. Majumdar, D., Bebb, J., Atherton J. 2011. Helicobacter pylori infection and peptic ulcers. Med:39;154-161.
9. Ludovico, B., Eric, S., Annemarthe, G., Van, D,V., Rino, R., Antonello, C. et al. 2011.Helicobacter Pylori cytotoxin-associated gene A subverts the apoptosis-stimating protein of p53 ASPP2 tumor suppressor pathway of the host.; 1-6.
10. Martin, J,B., 1997.Not all Helicobacter pylori strains are created equal; should all be eliminated. Lancet;349:1020-22.
11. Fan, X,G., Kelleher, D., Fan, X,J., Xia, H,X., Keeling, P,W., 1996. Helicobacter pylori increases proliferation of gastric epithelial cells. Gut ,38:19-22.
12. Szabo, S., Vincze, A., Sandor, Z., Jadus, M., Gombos, Z., Pedram, A., 1998. Vascular approach to gastroduodenal ulceration. New studies with endothelins and VEGF. Dig Dis Sci , 43:40-45.
13. Aihara, T., Nakamura, E., Amagase, K., Tomita, K., Fujishita, T., Furutani, K. 2003. Pharmacological control of gastric acid secretion for the treatment of acid-related peptic disease: past, present, and future. Pharmacol Ther ,98:109-127.
14. Sandvik, A,K., Kleveland, P,M., Waldum, H,L. 1988. Muscarinic M2 stimulation releases histamine in the totally isolated, vascularly perfused rat stomach. Scand J Gastroenterol ,23: 1049-56.
15. Cho, C,H., Ogle, CW., Dai, S. 1985.A study on the etiology of reserpine ulceration and the antiulcer action of solcoseryl in rat stomach. J Pharm Pharmacol ,37:823-82.
16. Mahmood, A,A., Al-Bayaty, F,H., Salmah, I., Nor, Syuhada, AB., Harita, H., Mughrabi, FF. 2011. Enhacement of gastric ulcer of gastric ulcer by areca catechu nut in ethanol induced gastric mucosal injuries in rats. Journal of medicinal plant Research , 5:2562-2569.
17. Umamaheswari, M., Asokkumar, K., Rathidevi, R., Sivashanmugam, AT., Subhadradevi V, Ravi TK. 2007. Antiulcer and in vitro antioxidant activities of

Jasminum grandiflorum L. J. Ethnopharmacol ,110: 464- 470
18. Majumdar, D., Bebb, J., Atherton, J. 2011. Helicobacter pylori infection and peptic ulcers. Med ,39;154-161.
19. Wallmark, B., Larsson, H., Humble, L. 1985. The relationship between gastric acid secretion and gastric H+, K+-ATPase activity. J biol chem , 260:13681-13684.
20. Olson, C., Soll, AH. 1984. The parietal cell and regulation of gastric acid secretion. Viewpoints Dig Dis, 16: 1-4.
21. Tripathi, KD.,2003. Sulfonamides, Cotrimoxazole and Quinolones. In: Essentials of Medical Pharmacology. 5th edition. Section 12, chapter 48, Jaypee Brothers Medical Publishers (P) Ltd. New Delhi, India;p. 646-52.
22. Qadeer, MA., Phillips, CO., Lopez, AR., Steward, DL., Noordzij, JP., Wo, JM. 2006. "Proton pumps inhibitor therapy for suspected GERD-related chronic laryngitis: a meta-analysis of randomized controlled trials". The American Journal of Gastroenterology.,101(11): 2646–54. doi:10.1111/j.1572-0241.2006.00844.x
23. Fedorowicz, Z., van, Zuuren, EJ., Hu, N. Histamine H2-receptor antagonists for urticaria. Cochrane Database Syst Rev,2012(3).
24. Winkler, NS., Fautsch, MP. 2014. "Effects of prostaglandin analogues on aqueous humor outflow pathways". Journal of Ocular Pharmacology and Therapeutics. 30 (2–3): 102–9. doi:10.1089/jop.2013.0179. PMC 3991965. PMID 24359106
25. Weberg, R., Berstad, K., Berstad, A. 1990. Acute effects of antacids on gastric juice components in duodenal ulcer patients.Eur. J. Clin. Invest, 20(5):511-5
26. Ryan, AJ. 1978. Peptic ulcer disease: introduction. Postgrad Med. 63(4):81.
27. Furuta, T., Delchier, JC. 2009. Helicobacter pylori and non-malignant diseases. Helicobacter 14(Suppl. 1), 29–35.
28. Bornschein, J., Rokkas, T., Selgrad, M., Malfertheiner, P. 2009. Helicobacter pylori and clinical aspects of gastric cancer. Helicobacter 14(Suppl. 1), 41–45.
29. Graham, DY., Shiotani, A. 2008. New concepts of resistance in the treatment of Helicobacter pylori infections. Nat. Clin. Pract. Gastroenterol. Hepatol. 5(6), 321–331.
30. McColl, KE. 2009 Effect of proton pump inhibitors on vitamins and iron. Am. J. Gastroenterol. 104(Suppl. 2) S5–S9.
31. Lai, SK., Wang, YY., Hanes, J. 2009. Mucuspenetrating nanoparticles for drug and gene delivery to mucosal tissues. Adv. Drug Deliv. Rev. 61(2), 158–171.
32. Johnstone, CC., Farley, A.2005 The physiological basics of wound healing. Nurs. Stand. 19(43), 59–65.
33. Hantash, BM., Zhao, L., Knowles, JA., Lorenz, HP.2008. Adult and fetal wound healing. Front. Bio sci. 1(13), 51–61.
34. Murphy, G., Nagase, H. 2008. Progress in matrix metalloproteinase research. Mol. Aspects Med. 29(5), 290–308.
35. Williams, DF. 2009 On the nature of biomaterials. Biomaterials 30(30), 5897–5909 (2009).
36. Maham, A., Tang, Z., Wu, H., Wang, J., Lin, Y.2009. Protein-based nanomedicine platforms for drug delivery. Small 5(15), 1706–1721.
37. Wolf, NB., Küchler, S., Radowski, MR. 2009. Influences of opioids and nanoparticles on in vitro wound healing models. Eur. J. Pharm. Biopharm. 73(1), 34–42.
38. Mayo, AS., Ambati BK., Kompella UB. 2009. Gene delivery nanoparticles fabricated by supercritical fluid extraction of emulsions. Int. J. Pharm. 387(1–2), 278–285.
39. Kumar, R. 2011. "A review on medicinal plants for peptic ulcer. Scholar Research Library," Der Pharmacia Lettre, vol. 3, no. 3, pp. 414–420.
40. Patel, G., Jain, S., "Antiulcer activity of Neriutn indicum in rats," Research Journal of Pharmacology, vol. 4, no. 3, pp. 66–68, 2010.
41. Nadkarni's, KM. 1976. Indian Materia Medica, Volume 1, pp. 9-10, Popular Prakashan, Mumbai, India.
42. Omayma, KH., Mohamed, MY., Elnaa, M. 2011. "Possible protective effect of Gum Arabic on experimentally induced gastric ulcer in adult male albino rats: a histopathological and immunohistochemical study," Egyptian Journal of Histology, vol. 34, pp. 546–553.
43. Abd El-Mawla, AMA., Osman, HEH. 2011. "Effects of Gum acacia aqueous extract on the histology of the intestine and enzymes of both the intestine and the pancreas of albino rats treated with Meloxicam," Pharmacognosy Research, vol. 3, no. 2, pp. 114–121.
44. Nadkarni's, KM. 1976. Indian Materia Medica, Volume 1, pp. 1191– 1193, Popular Prakashan, Mumbai, India, 1976.
45. Kumar, s., Suman, s., Sharma, S., Kalra, P.2011. "Antiulcer effect of the methanolic extract of Tamarindus indica seeds in different experimental models," Journal of Pharmacy and Bioallied Sciences, vol. 3, no. 2, pp. 236–241.
46. Nadkarni's, KM. 1976. Indian Materia Medica, Volume 1, pp. 38-39, Popular Prakashan, Mumbai, India.
47. Nadkarni's, KM. 1976. Indian Materia Medica, Volume 1, pp. 865–867, Popular Prakashan, Mumbai, India.
48. Singh, s., Majumdar, DK. 1999. "Evaluation of the gastric antiulcer activity of fixed oil of Ocimum sanctum (Holy Basil)," Journal of Ethnopharmacology, vol. 65, no. 1, pp. 13–19.
49. Singh, s. 1999."Evaluation of gastric anti-ulcer activity of fixed oil of Ocimum basilicum Linn. and its possible mechanism of action," Indian Journal of Experimental Biology, vol. 36, no. 3, pp. 253– 257, 1999.
50. Ilavarasan, JR., Monideen, S., Vijayalakshmi, M. 2002. "Antiulcer activity of Aegle marmelos," Ancient Science of Life, vol. 21, no. 4, pp. 23–26.
51. Goel, RK., Maiti, RN., Manickam, M., Ray, AB. 1997. "Antiulcer activity of naturally occurring pyrano-coumarin and iso-coumarins and their effect on prostanoid synthesis using human colonic mucosa," Indian Journal of Experimental Biology, vol. 35, no. 10, pp. 1080–1083.
52. Nadkarni's, KM. 1976. Indian Materia Medica, Volume 1,

pp. 65–71, Popular Prakashan, Mumbai, India.
53. Azamthulla, M., Asad, M., Prasad, VS.2009. "Antiulcer activity of Allium sativumbulb juice in rats," Saudi Pharmaceutical Journal, vol. 17, no. 1, pp. 70–77.
54. Nadkarni's, KM. 1976. Indian Materia Medica, Volume 1, pp. 1132- 1133, Popular Prakashan, Mumbai, India.
55. Santhishkumar, M., Anusuya, N., Bhuvaneswari, P. 2013. "Antiulcerogenic effet of resin from Shorea robusta on experimentally induced ulcer models," International Journal of Pharmacy and Pharmaceutical Sciences, vol. 5, no. 1, pp. 269–272.
56. Nadkarni's, KM. 1976. Indian Materia Medica, Volume 1, pp. 1017– 1019, Popular Prakashan, Mumbai, India.
57. Umana, Uduak., Timbuak, JA., Musa, SA.,Ikyembe, DT., Abdurrashid, S., Hamman, WO. 2012."Ulceroprotective effect of methanol extract of Psidium guajava leaves on ethanol induced gastric ulcer in adult wistar rats," Asian Journal of Medical Sciences, vol. 4, no. 2, pp. 75–78.
58. Nadkarni's, KM. 1976. Indian Materia Medica, Volume 1, pp. 524– 526, Popular Prakashan, Mumbai, India.
59. Nadkarni's, KM. 1976. Indian Materia Medica, Volume 1, pp. 561–563, Popular Prakashan, Mumbai, India.
60. Nadkarni's, KM. 1976. Indian Materia Medica, Volume 1, pp. 838, Popular Prakashan, Mumbai, India.
61. Rezaie, A., Mohajeri, D., Khamene, B., Nazeri, M.,Zakhireh, S., 2013. "Effect of Myrtus communis on healing of the experimental skin wounds on rats and its comparison with zinc oxide," Current Research Journal of Biological Sciences, vol. 4, pp. 176– 185.