Market Feasibility Study of Dexlansoprazole

A Research paper submitted to the Department of Pharmacy,
East West University in conformity with the requirements for
the degree of Bachelor of Pharmacy

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Abstract

Dexlansoprazole, an enantiomer of Lansoprazole, is a proton pump inhibitor, which irreversibly blocks the hydrogen/potassium adenosine triphosphatase enzyme system (the H+/K+ ATPase, or more commonly just gastric proton pump) of the gastric parietal cell. The purpose of this study is to analyze the market feasibility study of Dexlansoprazole and to launch Dexlansoprazole in Bangladesh pharma market. Many books, journals, articles were also used to know efficacy and safety profile of drugs. International Market Strategy (IMS) data was used to determine the market size. Dexlansoprazole gives prolonged action which is almost double than Lansoprazole. It shows better efficacy in erosive oesophagitis, GERD, NERD than the other proton pump inhibitor. Therefore, the total market size of Dexlansoprazole will be increased and it will capture the Rabeprazole, Esomeprazole and Pantoprazole. The estimated market size for Dexlansoprazole is 11.0 crore taka and the estimated growth rate for Dexlansoprazole is 10-12% in the next year. So it is better to launch Dexlansoprazole in the next year.

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1. Introduction

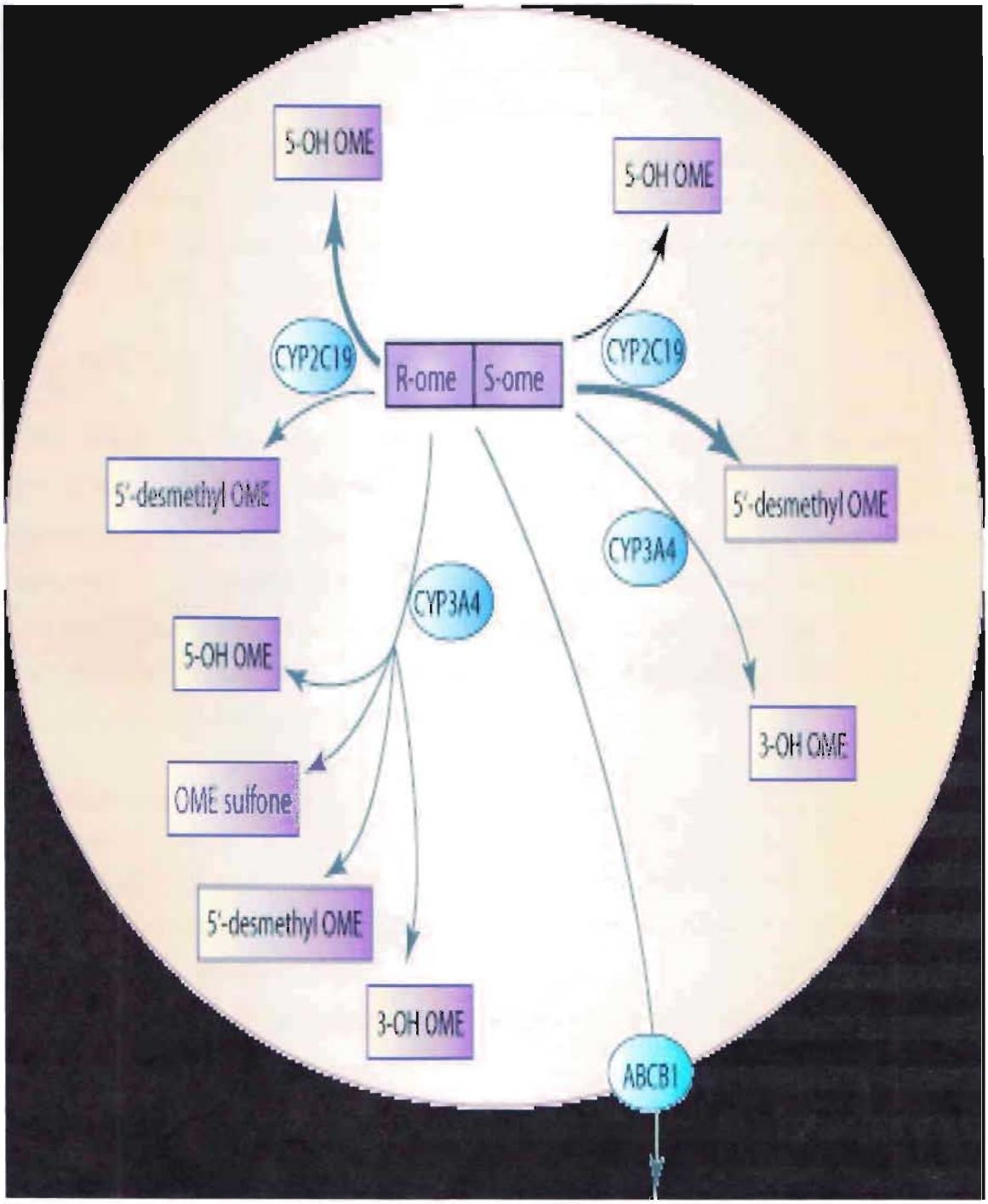
1.1. Proton Pump Inhibitor

Proton-pump inhibitors reduce the production of acid by blocking the enzyme which is present in the stomach wall. This enzyme produces acid. The reduction of acid prevents ulcers. PPIs are used for the prevention and treatment of acid-related conditions such as ulcers, gastro esophageal reflux disease (GERD), and Zollinger-Ellison syndrome. They also are used in combination with antibiotics for eradicating Helicobacter pylori. H. pylori are a bacterium that causes ulcers of the stomach and duodenum together with acid (Omudhome O, 2008).

1.1.1. Mechanism of Action

Proton pump inhibitors irreversibly block the hydrogen/potassium adenosine triphosphatase enzyme system (the H^+/K^+-ATPase, or more commonly just gastric proton pump) of the gastric parietal cell. The terminal stage in gastric acid secretion is the proton pump and it is directly responsible for secreting H^+ ions into the gastric lumen (Philip OK, 2005). Proton pump inhibitors are significantly more effective than H_2 antagonists. It reduces gastric acid secretion 99% by targeting the terminal-step in acid production. The lack of the acid in the stomach usually helps in the treatment of duodenal ulcers, and causes reduction the pain due to indigestion and heartburn. But lack of stomach acid may also cause hypochlorhydria. It means lack of sufficient hydrochloric acid, or HCl. Hydrochloric acid is essential for absorption of nutrients, particularly calcium. The proton pump inhibitors are usually given in an inactive form. This inactive form is neutrally charged (lipophilic). It is easily capable of crossing cell membranes into intracellular compartments. In an acid environment, the inactive drug is protonated and converted into its active form (Philip OK, 2005). They are activated by a proton catalyzed process. This occurs through the formation of a thiophilic sulfonamide or sulfenic acid. This activated from reacts with the sulfhhydryl group of cysteines by covalent binding. These cysteines come from the extra cellular domain of the H^+/K^+-ATPase.binding to cysteine 813 (North R, 2004; Baulkham H, 2005). That means, the active form covalently and irreversibly bind to the gastric proton pump and deactivate it (Philip OK, 2005).

1.1.2. Proton Pump Inhibitor Pathway (Ryan O, 2007)



1.1.3. Pharmacokinetics

The absorption of proton pump inhibitors is not affected by co-administration with food. The rate of Omeprazole absorption is decreased by concomitant food intake. The absorption of Lansoprazole and Esomeprazole is decreased and delayed by food. These pharmacokinetic effects have no significant impact on efficacy.

The elimination half-life of proton pump inhibitors is usually 0.5–2 hours. The effect of a single dose on acid secretion usually persists up to 2–3 days. Because the drug is accumulated in parietal cell canaliculi and the irreversible nature of proton pump inhibition (Philip OK, 2005).

1.1.4. Drug Interaction

PPIs interact with few drugs. The absorption of some drugs is affected by the presence of acid in the stomach. Because PPIs reduce acid in the stomach, so they may affect the absorption of these drugs. Specifically, PPIs reduce the absorption and concentration of ketoconazole in the blood. But it increases the absorption and concentration of digoxin. This may reduce effectiveness of ketoconazole and an increase in digoxin toxicity. PPIs can reduce the break-down of some drugs by the liver cause an increase in their concentration in the blood (Omudhome O, 2008).

1.1.5. Adverse effects

Generally proton pump inhibitors are well tolerated and their adverse effects are relatively uncommon. The range and occurrence of adverse effects are similar for all of the proton pump inhibitors.

Common adverse effects include: Headache, nausea, diarrhea, abdominal pain, fatigue, dizziness.

Infrequent adverse effects include: Rash, itch, flatulence, constipation.

Long-term use of PPIs may reduce the absorption of cyanocobalamin (vitamin B_{12}). Sometimes PPI cause 'idiosyncratic' reactions such as erythema multiform, pancreatitis, Stevens Johnson syndrome and acute interstitial nephritis.

It has been observed that using H_2-receptor antagonists and proton pump inhibitors may increase risk of community-acquired pneumonia.

It is suspected that acid suppression results in insufficient elimination of pathogenic organisms. It has therefore been suggested that patients at higher risk of pneumonia should only be prescribed proton pump inhibitors at lower doses and only when necessary.

PPIs may also increase risk of Clostridium difficile infection (Sachs G, Shin JM, Howden CW, 2006).

1.1.6. Examples of Proton Pump Inhibitor

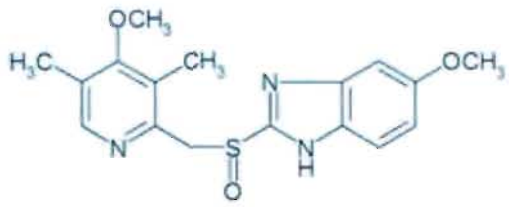
Clinically used proton pump inhibitors:

- Omeprazole
- Lansoprazole
- Esomeprazole
- Pantoprazole
- Rabeprazole (Philip OK, 2005; Tripathhi KD, 5th edition).

1.1.6.1. Omeprazole

Omeprazole is a substituted benzimidazole, 5-methoxy-2-[[(4-methoxy-3, 5-dimethyl-2 pyridinyl) methyl] sulfinyl]-1Hbenzimidazole. Its empirical formula is $C_{17}H_{19}N_3O_3S$, with a molecular weight of 345.42.

The Structure



Omeprazole is a white to off-white crystalline powder. It melts with decomposition at about 155°C. It is a weak base. It is freely soluble in ethanol and methanol, and slightly soluble in acetone and isopropanol and very slightly soluble in water. The stability of Omeprazole is dependent on pH. It is rapidly degraded in acid media, but has acceptable stability under alkaline conditions.

Mechanism of Action

Omeprazole belongs to a new class of antisecretory compounds, the substituted benzimidazoles, that do not exhibit anticholinergic or H_2 histamine antagonistic properties, but that suppress gastric acid secretion by specific inhibition of the H^+/K^+-ATPase enzyme system at the secretory surface of the gastric parietal cell. Because this enzyme system is regarded as the acid (proton) pump within the gastric mucosa, Omeprazole has been characterized as a gastric acid-pump inhibitor, in that it blocks the final step of acid production. This effect is dose-related and leads to inhibition of both basal and stimulated acid secretion irrespective of the stimulus. Animal studies indicate that after rapid disappearance from plasma, Omeprazole can be found within the gastric mucosa for a day or more.

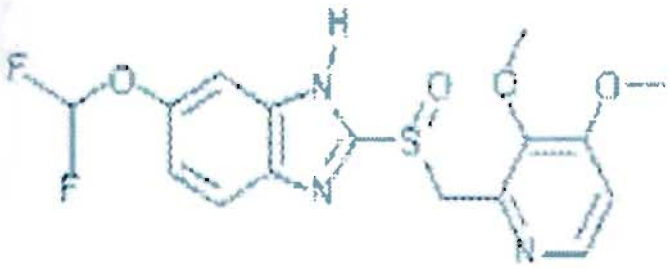
Indications

- Treatment of gastric ulcer (GU), erosive esophagitis (EE), gastro esophageal reflux disease (GERD) with or without esophageal lesion.
- Maintenance therapy of EE.
- Eradication of Helicobacter pylori in triple therapy with clarithromycin and amoxicillin or in double therapy with clarithromycin only (Sreedhar D, Kumar D, Pise A, Manthan DJ, Subramanian G, Udupa N, 2006).

1.1.6.2. Pantoprazole

Pantoprazole sodium is a substituted benzimidazole, sodium 5-(difluoromethoxy)-2-[[(3, 4-dimethoxy-2-pyridinyl) methyl] sulfinyl]-1H-benzimidazole sesquihydrate. Its empirical formula is $C_{16}H_{14}F_2N_3NaO_4S$ x 1.5 H_2O, the molecular weight is 432.4.

The Structure



Pantoprazole sodium sesquihydrate is a white to off-white crystalline powder. It is racemic. It is weakly basic and acidic in nature. It is freely soluble in water and very slightly soluble in phosphate buffer at pH 7.4. It is insoluble in n-hexane. The stability of the compound is pH-dependent in aqueous solution. The rate of degradation is increased when pH is decreased. At ambient temperature, the degradation half-life is approximately 2.8 hours at pH 5.0 and approximately 220 hours at pH 7.8.

Mechanism of Action

Pantoprazole is a proton pump inhibitor (PPI) that suppresses the final step in gastric acid production. It forms a covalent bond to two sites of the H^+/K^+-ATPase enzyme system. This effect is dose-related. It leads to inhibition of both basal and stimulated gastric acid secretion. The binding to the H^+/K^+-ATPase results in a longer duration of antisecretory effect that is more than 24 hours.

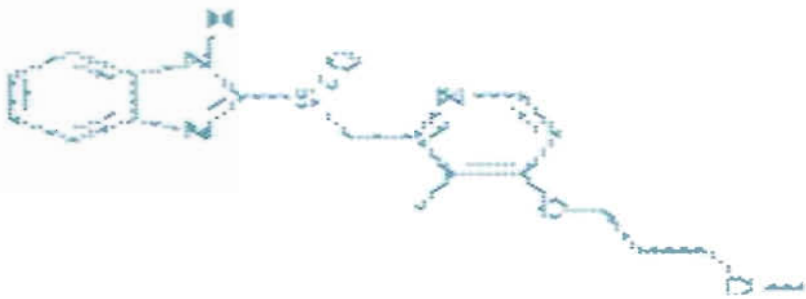
Indication:

- Treatment of EE associated with GERD.
- The manufacturer of Pantoprazole IV is also pursuing the GERD indication for this formulation (Sreedhar D, Kumar D, Pise A, Manthan DJ, Subramanian G, Udupa N, 2006).

1.1.6.3. Rabeprazole

Rabeprazole sodium is a substituted benzimidazole. Rabeprazole sodium is known chemically as 2-[[[4-(3-methoxypropoxy) 3-methyl-2- pyridinyl]-methyl] sulfinyl]-1H–benzimidazole sodium salt. It has an empirical formula of $C_{18}H_20N_3NaO_3S$ and a molecular weight of 381.43.

The Structure



Rabeprazole sodium is a white or slightly yellowish-white solid. It is very soluble in water and methanol, freely soluble in ethanol, chloroform and ethyl acetate and insoluble in ether and n-hexane. The stability of Rabeprazole sodium is dependent on its pH. It is rapidly degraded in acid media, and is more stable under alkaline conditions.

Mechanism of Action

Rabeprazole is an antisecretory compounds (substituted benzimidazole proton-pump inhibitors). It has no anticholinergic or histamine H_2-receptor antagonist properties. But it suppresses gastric acid secretion by inhibiting the gastric H^+/K^+-ATPase. Rabeprazole has been characterized as a gastric proton-pump inhibitor. Rabeprazole blocks the final step of gastric acid secretion.

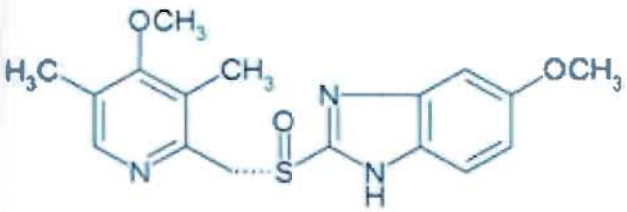
Indications:

- Treatment of erosive or ulcerative GERD, DU and hypersecretory syndromes including ZES.
- Maintenance of erosive or ulcerative GERD (Sreedhar D, Kumar D, Pise A, Manthan DJ, Subramanian G, Udupa N, 2006).

1.1.6.4. Esomeprazole

Esomeprazole sodium is (S)-5-methoxy-2[[(4-methoxy-3, 5 dimethyl-2-pyridinyl)-methyl] sulfinyl] - 1 H-benzimidazole sodium. Esomeprazole is the S-isomer of Omeprazole. It is a mixture of the Sand R- isomers. Its empirical formula is $C_{17}H_{18}N_3O_3SNa$ with molecular weight of 367.4 g/mol (sodium salt) and 345.4 g/mol (parent compound). Esomeprazole sodium is very soluble in water and freely soluble in ethanol (95%).

The Structure



Mechanism of Action

Esomeprazole is a proton pump inhibitor that suppresses gastric acid secretion. It causes by specific inhibition of the H^+/K^+-ATPase enzyme. The S- and R-isomers of Omeprazole are protonated. Then it converted into the active inhibitor in the acidic compartment of the parietal cell. The active inhibitor is called achiral sulphenamide. Esomeprazole blocks the final step in acid production and reduces gastric acidity. This effect is dose-related up and leads to inhibition of gastric acid secretion.

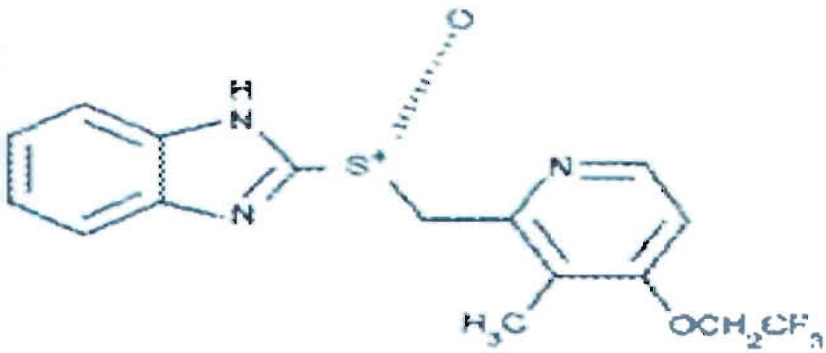
Indications

- GERD
- Healing of EE
- Maintenance of healing of EE
- H. pylori Eradication to reduce the risk of duodenal ulcer recurrence in triple therapy with clarithromycin and amoxicillin (Sreedhar D, Kumar D, Pise A, Manthan DJ, Subramanian G, Udupa N, 2006).

1.1.6.5. Lansoprazole

Lansoprazole is a substituted benzimidazole, 2-[[[3-methyl-4-(2, 2, 2-trifluoroethoxy)-2-pyridyl] methyl] sulfinyl] benzimidazole. Its empirical formula is $C_{16}H_{14}F_3N_3OS$ with a molecular weight of 369.37 (Sreedhar D, Kumar D, Pise A, Manthan DJ, Subramanian G, Udupa N, 2006).

The Structure



Lansoprazole is a white to brownish-white odorless crystalline powder. It melts with decomposition at approximately 166°C. It is freely soluble in dimethylformamide; soluble in methanol; sparingly soluble in ethanol; slightly soluble in ethyl acetate, dichloromethane and acetonitrile; very slightly soluble in ether; and practically insoluble in hexane and water. Lansoprazole is stable in presence of light for up to two months. The compound degrades in aqueous solution and the rate of degradation increasing with decreasing pH. At 25°C the t½ is approximately 0.5 hour at pH 5.0 and approximately 18 hours at pH 7.0 (Sreedhar D, Kumar D, Pise A, Manthan DJ, Subramanian G, Udupa N, 2006).

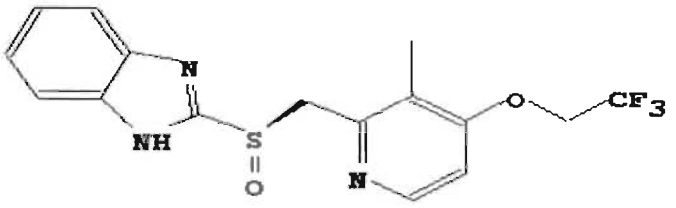
Indications:

- Treatment of duodenal ulcer (DU), both H. pylori positive and negative, active benign GU, GERD, EE and pathological hypersecretory conditions, including Zollinger-Ellison syndrome (ZES).
- Maintenance therapy of DU and EE.
- Eradication of H. pylori in triple therapy with clarithromycin and amoxicillin, or in double therapy with amoxicillin only (Sreedhar D, Kumar D, Pise A, Manthan DJ, Subramanian G, Udupa N, 2006).

1.1.6.6. Dexlansoprazole

Dexlansoprazole is an enantiomer of Lansoprazole. It is 2-Pyridinylmethylsulfinylbenzimidazoles, Pyridines, Small-molecules, and Sulfoxides. So it is a proton pump inhibitor. It has molecular formula C_{16} H_{14} F_3 N_3 O_2 S.

Chemical Structure



(Zhang W, Wu J, 2008)

Mechanism of action

Lansoprazole come from a class of antisecretory compounds. It has no anticholinergic or histamine H_2-receptor antagonist properties. It can suppress gastric acid secretion by specific inhibition of the H^+/K^+-ATPase enzyme system. Lansoprazole has been characterized as a gastric acid-pump inhibitor, because it can block the final step of acid production. This effect is dose-related. It leads to inhibition of both basal and stimulated gastric acid secretion (Sreedhar D, Kumar D, Pise A, Manthan DJ, Subramanian G, Udupa N, 2006).

Pharmacokinetics

Dexlansoprazole leading to prolonged plasma concentrations than the Lansoprazole. It is almost double of Lansoprazole. Dexlansoprazole resulted in extended drug exposure compared to Lansoprazole. It also provides a prolonged pH profile across all dose levels compared to Lansoprazole (Zhang W, Wu J, 2008).

Indication

Dexlansoprazole is mainly used in the treatment of the following diseases. These are given below:

- Acid-related disorders
- The treatment and maintenance of patients with erosive oesophagitis
- Non-erosive reflux disease, i.e. gastro-esophageal reflux disease (GERD or GORD).
- Treatment of peptic ulcer.
- Zollinger-Ellison syndrome (ZES) (Zhang W, Wu J, 2008; Sreedhar D, Kumar D, Pise A, Manthan D J, Subramanian G, Udupa N, 2006; Sharon G, 2008).

1.2. Stomach

The stomach is an expanded section of the digestive tube. It is present between the esophagus and small intestine. The right side of the stomach is called the greater curvature and the left side of the stomach is called the lesser curvature. The most distal and narrow section of the stomach is called the pylorus. When food is liquefied in the stomach it goes into the small intestine through the pyloric canal. The wall of the stomach has an extra, oblique layer which conducts complex grinding motions. This layer is composed of smooth muscle inside the circular layer (Tripathhi KD, 5th edition; Bertram GK, 8th edition; Rang HP, Dale MM, Ritter JM, Moore PK, 2003; Guyton, 8th edition).

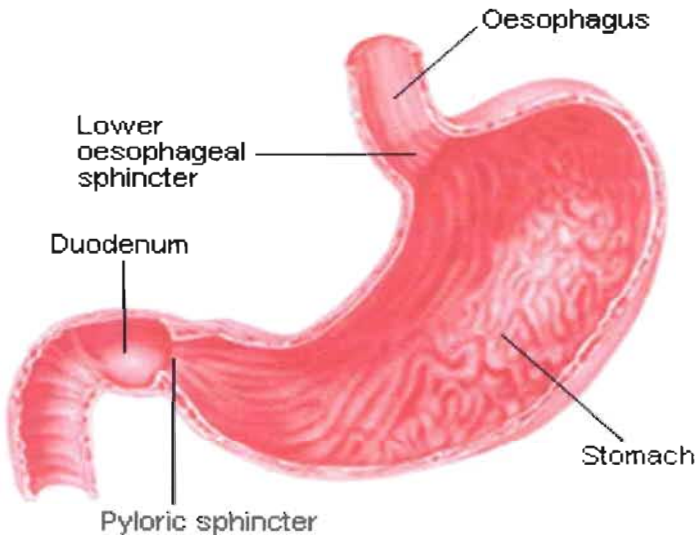


Fig: Stomach (MyDr, 2002)

1.2.1. Four major types of secretory epithelial cells

Mucous cells

It secretes alkaline mucus. It protects the epithelium against shear stress and acid. The mucosa is present in longitudinal folds (gastric folds or rugae). It disappears when the stomach is fully distended (Rang HP, Dale MM, Ritter JM, Moore PK, 2003, Guyton, 8th edition). A network of shallow grooves divides the mucosa into gastric areas (1-5 mm). The mucosal surface contains funnel-shaped depressions (gastric pits). The entire mucosa is engaged by simple, tubular gastric glands. It is open into the bottom of the gastric pits (Slomianka L, Gieson V, 2006).

Parietal cells

They are situated deeper, below chief cells and in lower parts of the gland. Parietal cells secrete the hydrochloric acid (Slomianka L, Gieson V, 2006).

Chief cells

It secretes pepsin. Pepsin is proteolytic enzymes. They are the most numerous of the four types. They occur primarily in the body of the glands. They produce pepsinogen, which is a precursor of the proteolytic enzyme pepsin. The optimum pH of pepsin is about 2. This enzyme is able to break down collagen (Slomianka L, Gieson V, 2006).

G cells

It secretes the hormone gastrin (Guyton, 8th edition). During parasympathetic stimulation gastrin-releasing peptide is released by the post-ganglionic fibers of the vagus nerve onto G cells. Gastrin-releasing peptide stimulates the release of gastrin from the G cells. Gastrin stimulates enterochromaffin-like cells to release histamine (John EH, 2006). Gastrin also targets parietal cells by increasing the amount of histamine and the direct stimulation by gastrin. It causes the parietal cells to increase HCl secretion in the stomach (Bowen R, 2002).

1.2.2 Physiology of Gut Fluid and Electrolyte Transport

Usually secretion and absorption of fluid and electrolytes occur in the gastrointestinal tract. Normally 7 to 8 L of fluid is secreted in each day and all of these fluids are absorbed by the end of the colon.

Mouth and Throat

Salivary fluid is secreted through the parotid and salivary glands. It produces a hypotonic alkaline solution. It is stimulated by activation of muscarinic receptors. Acinar cells secrete a fluid that is similar composition to serum and the secreted fluid is modified by Na^+ and Cl^- absorption and HCO_3^- secretion. The apical membrane transport proteins

alter the composition of secreted protein. This occurs when stimulation remain to be defined. But HCO_3^- secretion may occur via an anion channel, possibly the CFTR Cl^- channel. When stimulated, up to 1 L/d fluid is produced .This alkaline secretion serves to protect the mucosa of the mouth, throat, and esophagus and it has little impact on serum [HCO_3^-] (Melvin JE, Yule D, Shuttle worth T, Begenisich T, 2005).

Duodenum

Though gut contents have the pH and tonicity that enter the duodenum. Duodenum restores isotonicity through water and solute absorption, and the pH rises to 7.0. Acid is neutralized by HCO_3^-. It is secreted by pancreatic and biliary secretions. It is also secreted by direct secretion in Brunner's glands along the duodenum. The specific ion transporters involved in duodenal HCO_3^- secretion (Charney AN, Donowitz M, 2005).

Pancreas

Gastric acid enter into the duodenum and it give signals the pancreas to secrete its highly alkaline solution ([HCO_3^-] approximately 70 to 120 mmol/L) into the gut. The anion transporter is primarily responsible for apical membrane Cl^-/HCO_3^- exchanger process. The activity of this ion exchanger is regulated by the CFTR Cl^- channel, which recycles Cl^- across the apical membrane (Lee MG, Choi JY, Luo X, Strickland E, and Thomas PJ, Muallem S, 1999).

Under maximal stimulation, some secreted HCO_3^- may enter into the lumen directly via the CFTR channel as well as by Cl^-/HCO_3^- exchange (Melvin JE, Yule D, Shuttle WT, Begenisich T, 2005). Pancreatic HCO_3^- secretion is stimulated by the hormone secretin. It is secreted when acidic fluid (pH <4.0) enters the duodenum. Thus, HCO_3^- secretion occurs to counterbalance the acid secretion in the stomach and only when this acidic fluid is passed into the duodenum. At other times, the secretion is primarily isotonic NaCl. Pancreatic secretion amounts to 1 to 2 L/d (Guyton, 8th edition; Spirli C, Granato A, Zsembery K, Anglani F, Okolicsanyi L, LaRusso NF, Crepaldi G, Strazzabosco M, 1998).

Biliary Secretion

The pancreas is the far major source of the HCO_3^- which is added to the duodenal contents. Biliary secretion is stimulated by the hormones secretin and cholecystokinin. They also produce an alkaline solution that contains HCO_3^- in a concentration higher than in plasma (approximately 40 to 60mol/L) (Melvin JE, Yule D, Shuttle worth T, Begenisich T, 2005). This secretion is typically approximately 1 L/d (Turnberg LA, Fordtran JS, and Carter NW, Rector FC, 1970).

Jejunum and Ileum

Jejunum and Ileum is the segment of the bowel. They are responsible for both absorption and secretion of fluid. The absorption normally predominates. They reduce the total gut fluid content to approximately 1 L/d by the time when it enters the colon. Absorption is driven by sodium and chloride uptake (driving water uptake). It occurs via two linked transporters, the Na^+/H^+ exchanger and the Cl^-/HCO_3^- exchanger (Lee MG, Choi JY, Luo X, Strickland E, and Thomas PJ, Muallem S Charney AN, Donowitz M, 1999). These two transporters take up Na^+ and Cl^- from the gut lumen and secrete H^+ and HCO_3^- into it. The latter two ions combine to form H_2CO_3 which dehydrates to form CO_2 in the intestinal lumen (Turnberg LA, Fordtran JS, Carter NW, Rector FC, 1970). The Cl^-/HCO_3^- exchanger present in the small intestine. It is the "down regulated in adenoma" (DRA) gene product, also named CLD (for chloride diarrhea) (Spirli C, Granato A, Zsembery K, Anglani F, Okolicsanyi L, LaRusso NF, Crepaldi G, Strazzabosco M, 1998). At the end of the ileum, Cl^-/HCO_3^- exchange is predominate. It results in an alkaline solution Chloride secretion. It occurs in specialized cells in the intestinal crypts via a series of apical Cl^- ion channels, one of which is the CFTR channel, recycling Cl^- into the lumen. Like the colon, the small intestinal secretory cells do not have an apical K^+ channel. Potassium movement across the membrane is required for passive diffusion and solvent drag (Turnberg LA, Fordtran JS, and Carter NW, Rector FC, 1970). These absorptive and secretory processes leave the fluid that enters the colon slightly hypotonic

with a [HCO_3^-] of approximately 30 mol/L and with a [K^+] of 5 to 10 mol/L (Wesson DE, Laski M, 2005).

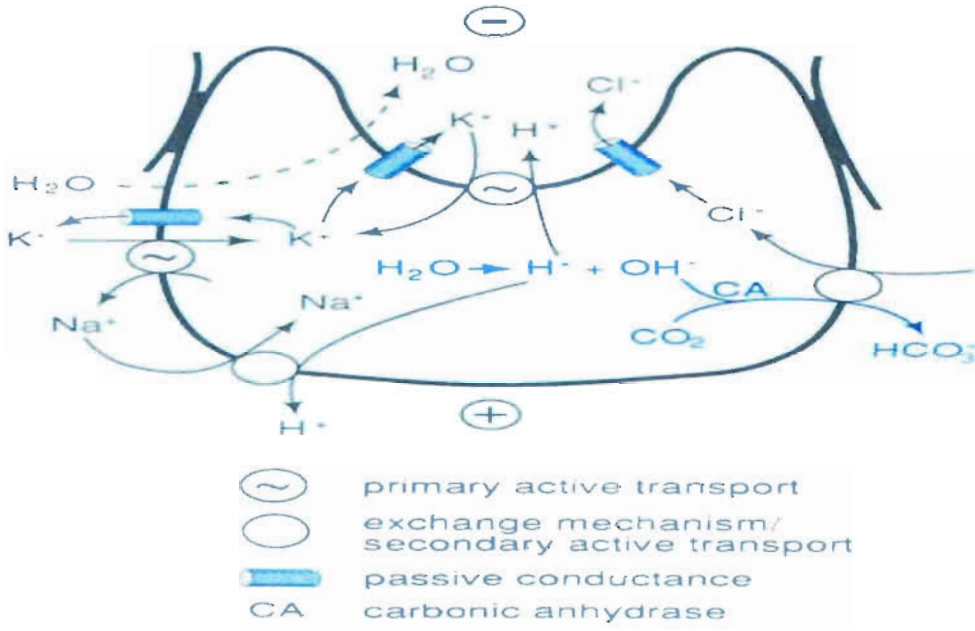
Colon

In the colon, the fluid volume of the stool is normally reduced to <50 ml/d. The concentrations of Na^+ and Cl^- are reduced to <30 mmol/L. Na^+ is absorbed via an apical membrane Na^+ channel. It is regulated by aldosterone. The HCO_3^- secreted by the Cl^- /HCO_3^- exchanger is consumed in the colon (along with much of the HCO_3^- delivered from the ileum). This HCO_3^- used in buffering organic acids produced by colonic bacteria (Guyton, 8th edition). Some of the organic anions are produced by this reaction. These organic anions are absorbed via a linked HCO_3^- exchange transporter (Wesson DE, Laski M, 2005). But the rest of them are excreted and make up the volume 30 to 40 mol/d of potential alkali lost in the stool despite the absence of measurable HCO_3^- in the stool. The colonic absorptive epithelial cells also have a unique apical membrane H^+/K^+-ATPase. It absorbs K^+ and secretes H^+ into the gut lumen (Guyton, 8th edition).

1.3. Hydrochloric acid (HCl)

Parietal cells contain an H^+ ATPase. This transmembrane protein secretes H^+ ions (protons) by active transport and using the energy of ATP. The concentration of H^+ in the gastric juice can be as high as 0.15 M. It has a pH less than 1. With a concentration of H^+ within these cells of only about 4×10^{-8} M, causes active transport produces more than a million-fold increase in concentration. These cells are stuffed with mitochondria and are extravagant consumers of energy (Kimball WJ, 2007).

1.3.1. Mechanism of Acid Secretion



The secretion of hydrogen ion concentration in parietal cell is roughly 3 million fold higher than in blood. Chloride is secreted against both a concentration and electric gradient. The ability of the parietal cell to secrete acid is dependent on active transport.

The key player in acid secretion is an H^+/K^+- ATPase or "proton pump". It is located in the cannalicular membrane. This ATPase is magnesium-dependent. The current model for explaining acid secretion is as follows:

- Hydrogen ions are generated from dissociation of water. It occurs within the parietal cell. The hydroxyl ions also form in this process. Then it is rapidly combine with carbon dioxide to form bicarbonate ion. This reaction is catalyzed by carbonic anhydrase (Tripathhi KD, 5th Edition). Bicarbonate is transported out of the basolateral membrane in exchange for chloride. The outflow of bicarbonate into blood results in a slight elevation of blood pH. This process is known as the "alkaline tide". This process serves to maintain intracellular pH in the parietal cell.
- Chloride and potassium ions are transported by conductance channels into the lumen of the cannaliculus. It is necessary for acid secretion.
- Hydrogen ion is pumped out from the cell in exchange for potassium into the lumen. Potassium is thus effectively recycled. This whole process occurs through the action of proton pump inhibitor.
- Osmotically-active hydrogen ions are accumulated in the cannaliculus. This hydrogen ion generates an osmotic gradient across the membrane. It results in outward diffusion of water and the resulting gastric juice is 155 mM HCl and 15 mM KCl with a small amount of NaCl.

1.3.2. Control of gastric acid secretion

Gastric multiple central acid secretion is a complex, continuous process. It is controlled by multiple central (neural) and peripheral (endocrine and paracrine) factor. The secretion of H^+ is caused by parietal cells. Parietal cells are located in the body and fundus of the stomach. Neural (acetylcholine ACh), paracrine (histamine) and endocrine (gastrin) factor all play important roles in the regulation of acid secretion. Two major pathways are present within the parietal cells: the cyclic AMP-depended pathway and the ca2+-dependent pathway. Histamine use first pathways, while gastrin and Ach use second pathways. The cyclic AMP-dependent pathways results in phosphorylation of proteins which affect parietal cells. The Ca^{2+} dependent pathway leads to an increase in cytosolic Ca2+. Both of the pathways activate the H^+/K^+ -ATPase. The H^+/K^+ -ATPase consists of a large Alpha-subunit and smaller Beta-subunit. This pump generates the largest ion gradient known in vertebrates, with an intercellular PH of about 7.3 and an intracellular PH of about 0.8. Histamine is released from ECL cells through multifactorial pathways. It is a critical regulator of acid production through the H_2 subtype of receptor. Histamine activates the parietal cell in a paracrine fashion. Histamine diffuses from its release site to

the parietal cell. The ECL cell is the sole source of gastrin histamine involved (Wesson DE, Laski M, 2005). Somastatin present in the antral D cells. It may inhibit gastrin secretion in a paracrine matter. Its exact role in the inhibition of gastric acid secretion is unknown (North R, 2005).

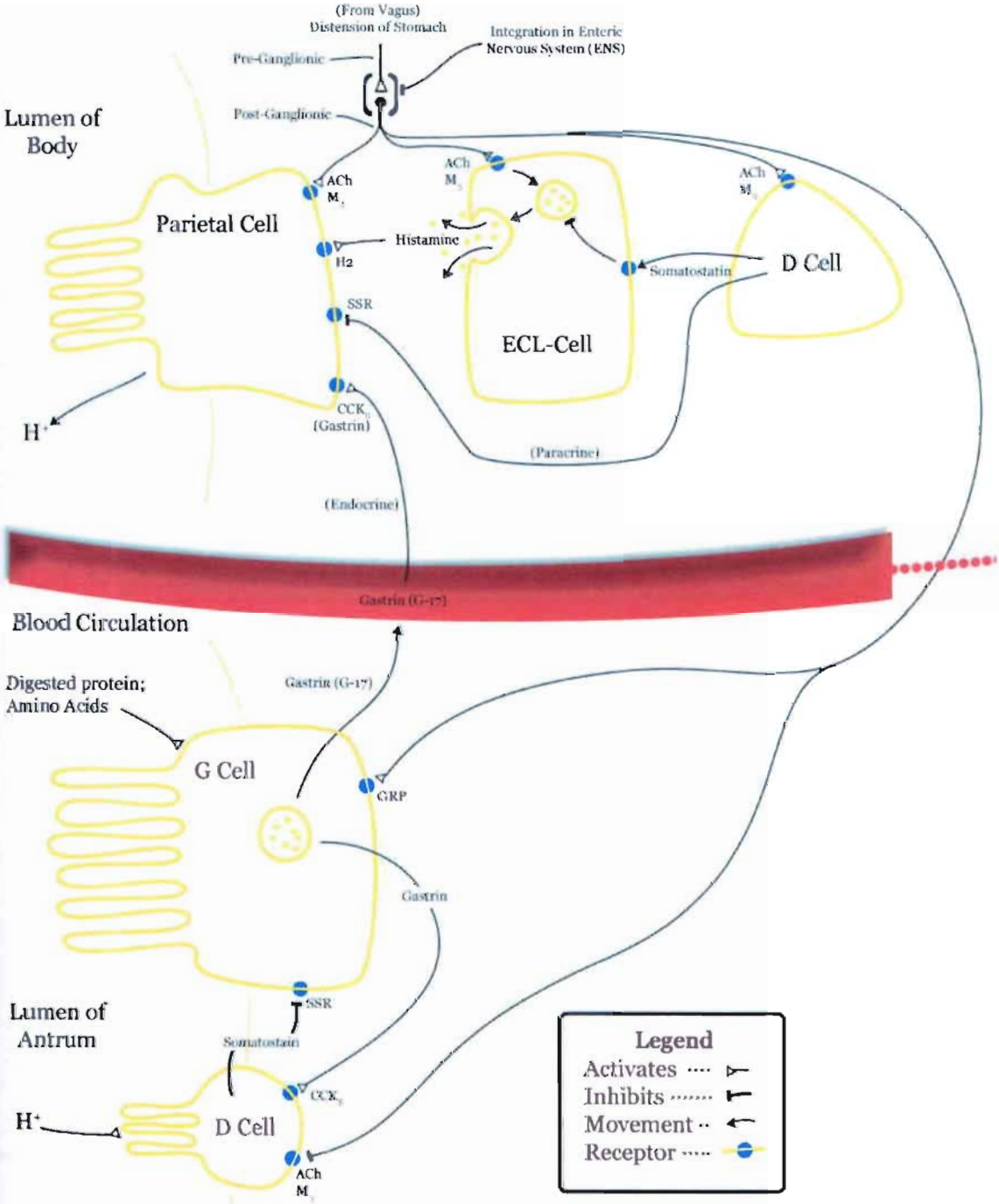


Diagram: Control of stomach acid secretion (John EH, 2006).

1.4. Drugs affecting GI secretions

1. Histamine (H_2) receptor antagonist/blockers
2. Antacids
3. Proton pump inhibitors
4. Mucosal protect ants
5. Prostaglandin analogs

1.4.1. Histamine (H_2) receptor blockers

These drugs block the release of hydrochloric acid in the stomach in response to gastrin (Rang HP, Dale MM, Ritter JM, Moore PK, 2003; Bertram GK, 2003; Tripathi KD, 5th edition).

1.4.2. Antacids

These drugs interact with the gastric acids in the stomach and help to neutralize them. These drugs are the inorganic chemicals that have been used for years to neutralize acid in the stomach. These agents are used to neutralize the acidic pH in the stomach. But they do not affect the rate of gastric acid secretion. The administration of antacid may cause an acid rebound (Bertram GK, 8th edition). Antacids neutralize the stomach content to an alkaline level. It stimulates gastrin production to cause which increase in acid production and return the stomach to its normal acidic state. These agents are taken orally and act locally in the stomach (Rang HP, Dale MM, Ritter JM, Moore PK, 2003).

1.4.3. Proton pump inhibitors

These drugs inhibit the secretion of hydrochloric acid into the lumen of the stomach. These are the newer agents used for ulcer treatment, Omeprazole, Lansoprazole, Esomeprazole, Pantoprazole (Bertram GK, 8th Edition; Rang HP, Dale MM, Ritter JM, Moore PK, 2003; Tripathhi KD, 5th edition). They inhibit specific secretory surface receptors. It is used to prevent the final step of acid production and thus decrease the level of acid in the stomach. The "pump" in the parietal cell is conducted by H^+/K^+-ATPase enzyme system. It is present on the secretory surface of the gastric parietal cells (Rang HP, Dale MM, Ritter JM, Moore PK, 2003).

1.4.4. Mucosal protectants

These are agents that coat any injured area in the stomach. Thus they prevent further injury from acid. This is given to protect the eroded ulcer sites in the GIT. So that, further damage by acid and digestive enzymes cannot be occurred (Rang HP, Dale MM, Ritter JM, Moore PK, 2003; Bertram GK, 5th edition; Tripathhi KD, 5th edition).

1.4.5. Prostaglandin analogs

These are agents that inhibit the secretion of gastrin. They also increase the secretion of mucus lining of the stomach which is providing a buffer (Rang HP, Dale MM, Ritter JM, Moore PK, 2003; Bertram GK, 5th edition; Tripathhi KD, 5th edition).

1.5. Problem arises with Hyperacidity

There are many diseases that are arising with hyperacidity these are given below:

1. Gas Esophageal Reflux Disease (GERD)
2. Zollinger- Ellison Syndrome
3. Peptic ulcer
4. Cushing's ulcer

1.5.1. Gas Esophageal Reflux Disease (GERD)

Gastro esophageal reflux occurs in almost everybody (Bennett PN, Brown MJ, 9th Edition). Gastro esophageal reflux occurs when the stomach contents reflux or back up into the esophagus and/or mouth. People with gastro esophageal reflux disease (GERD) experience with some symptoms as a result of the reflux. These symptoms are heartburn, vomiting, or pain with swallowing. The reflux of stomach acid can adversely affect the vocal cords. It can also be inhaled into the lungs is called aspiration (Peter JK, 2008; Omudhome O, 2008).

Factors contributing to pathological reflux include:

- Incompetence of the gastro esophageal sphincter.
- Delayed esophageal clearance of acid.
- Delayed gastric emptying (Bennett PN, Brown MJ, 9th Edition).

When we eat, food is carried from the mouth to the stomach through the esophagus. It is a tube-like structure. It is approximately 10 inches long and 1 inch wide in adults. The esophagus is made of tissue and muscle layers. The esophagus expand and contract to propel food to the stomach through a series of wave-like movements called peristalsis. At the lower end of the esophagus, there is a circular ring of muscle called the lower esophageal sphincter (LES). In this part it joins to the stomach. After swallowing, the LES relaxes to allow food to enter the stomach. After that it contracts to prevent the back-up of food and acid into the esophagus. But sometimes the LES is weak or becomes relaxed because the stomach is distended. As a result it allows liquids in the stomach to wash back into the esophagus occasionally in all individuals. This is most commonly occurred after meals, are brief, and do not cause symptoms. Normally, reflux should occur only rarely during sleep (Peter JK, 2008).

Reflux

Reflux considered gastro esophageal reflux disease (GERD) when it shows bothersome symptoms or injury to the esophagus. The amount of reflux required to cause GERD varies. In general, damage to the esophagus occurs when acid refluxes frequently, the reflux is very acidic, or the esophagus is unable to clear away the acid quickly. (Peter JK, 2008).

Symptoms

People having heartburn at least two to three times a week may have gastro esophageal reflux disease, or GERD. It is estimated that 10 million adults are affected by heartburn in the United States on a daily basis. Heartburn is experienced as a burning sensation in the center of the chest. But sometimes it spreads to the throat. There also may be an acid taste in the throat. Less common symptoms include:

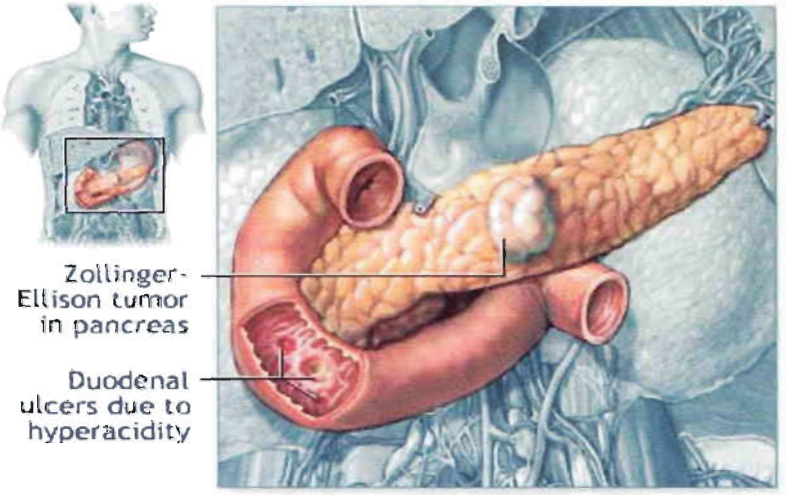
- Stomach pain (pain in the upper abdomen)
- Non-burning chest pain
- Difficulty swallowing (called dysphagia), or food getting stuck
- Painful swallowing (called odynophagia)
- Persistent laryngitis/hoarseness
- Persistent sore throat
- Chronic cough, new onset asthma, or asthma only at night
- Regurgitation of foods/fluids; taste of acid in the throat
- Sense of a lump in the throat
- Worsening dental disease
- Recurrent pneumonia
- Chronic sinusitis
- Waking up with a choking sensation

The following signs and symptoms may indicate a more serious problem, and should be reported to a healthcare provider immediately:

- Difficulty or pain with swallowing (feeling that food gets "stuck")
- Unexplained weight loss
- Chest pain
- Choking
- Bleeding (vomiting blood or dark-colored stools) (Peter JK, 2008).

1.5.2. Zollinger- Ellison Syndrome

Zollinger-Ellison syndrome (ZES) is a rare disorder that causes tumors in the pancreas and duodenum. This gastrin-secreting tumor of the non-beta endocrine cells of the pancreas leads to increase acid secretion (David EG, 2005). It also causes ulcers in the stomach and duodenum. The pancreas is a gland located behind the stomach. It produces enzymes and hormones. These enzymes cause break down fat, protein, and carbohydrates from food and hormones like insulin that break down sugar. The duodenum is the first part of the small intestine. The tumors secrete the gastrin hormone that increases the production of acid in the stomach. Then that will turn to cause stomach and duodenal ulcers (peptic ulcers). The development of ZES is unknown. Approximately 25 percent of ZES cases are caused by a genetic disorder called multiple endocrine neoplasia type 1, which is associated with additional disorders. Usually Zollinger-Ellison syndrome is rare. It may occur at any age but people between the ages of 30 and 60 are more likely to develop it. The tumors are cancerous in 50 percent of the cases (Sharon G, 2008). There is a chance of developing ECL hyperplasia in case of Zollinger-Ellison syndrome patients and also some development of carcinoid tumors. But there is no increase in carcinoid tumors. Hypergastrinemia can result in rebound hypersecretory of acid. In those case the proton pump inhibitor is discontinued (David EG, 2004).



(Chey WD, Wong BC, 2007)

Causes of Zollinger-Ellison Syndrome

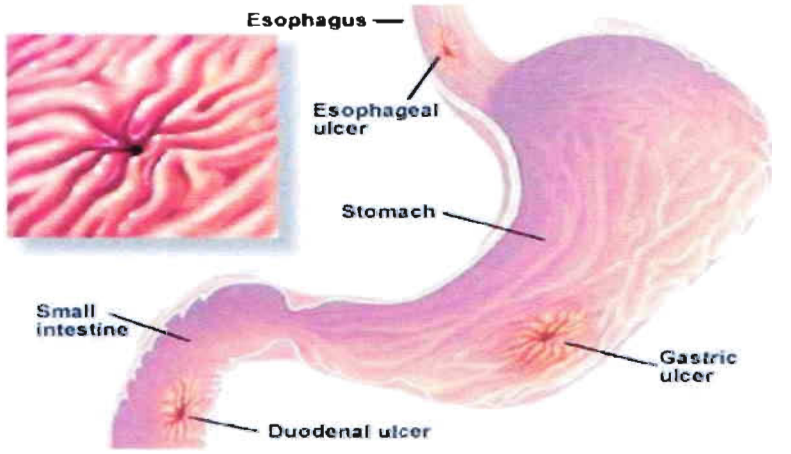
ZES is caused by a tumor is called gastrinoma. The tumor is usually present in the pancreas and the upper small bowel (duodenum). These tumors produce the hormone gastrin and are called gastrinomas. High levels of gastrin cause overproduction of stomach acid. That causes increase in acidity which leads to the development of peptic ulcers in the stomach and duodenum (Sharon G, 2008; Omudhome O, 2008).

Symptoms of Zollinger-Ellison Syndrome

1. **Gnawing, burning pain in the abdomen:** This pain is usually located in the area between the breastbone and the navel.
2. **Sensation of pressure, bloating, or fullness:** This pain usually develops 30 to 90 minutes after a meal, and is often relieved by antacids.
3. **Pain or burning sensation in the abdomen that travels up toward the throat:** This is caused by heartburn, or gastro esophageal reflux, and occurs when stomach contents back up into the esophagus.
4. **Vomiting:** The vomit may contain blood or resemble coffee grounds.
5. **Diarrhea:** Stools may be foul smelling.
6. **Black, tarry stools**: Blood in the stools will turn them dark red or black, and make them tarry or sticky.
7. Nausea
8. Weakness
9. Weight loss (Sharon G, 2008).

1.5.3. Peptic ulcer

A peptic ulcer is a hole in the gut lining of the stomach, duodenum, or esophagus. It is also called a gastric ulcer; of the duodenum, a duodenal ulcer; and of the esophagus, an esophageal ulcer (Bertram GK, 8th edition; Chey WD, Wong BC, 2007). Acid peptic diseases include peptic ulcer, gastro esophageal reflux, and Zollinger-Ellison syndrome (Bertram G. K, 8th edition). Peptic ulcer is a very common disease (David EG, 2005; Chey WD, Wong BC, 2007; Bortoli M, Leonardi G, Ciancia E, 2007; Gancz H, Jones KR, Merrell DS, 2008).



For more than a century, peptic ulcer disease was most often managed surgically. It results high morbidity and mortality rates. The introduction of histamine H_2-receptor antagonists (H_2RAs) lead to effective pharmacologic suppression of gastric acid secretion in the 1970s which greatly improved clinical outcomes (Tripathi KD, 5th edition; Yuhong Y, Ireneusz TP, Richard HH, 2006). Ulcer is a break in the mucosa of the stomach or duodenum (David EG, 2005). Peptic ulcers are identified based on their anatomical locations. Peptic ulcer of the stomach is called gastric ulcer. Similarly ulcers of the duodenum are called duodenal ulcer and ulcers of the esophagus are called esophageal ulcer (Tripathi KD, 5th edition; David EG, 2005; Vishnu K, 2007).

Erosion in a segment of the GI mucosa typically in the stomach is called gastric ulcer and the first few centimeters of the duodenum is called duodenal ulcer. That erosion penetrates through the muscularis mucosa (Tripathi KD, 5th edition). A peptic ulcer is

damage to the lining of the stomach, duodenum, or esophagus. This is caused due to corrosion caused by digestive juices secreted by stomach cells (Vishnu K, 2007). The average size of ulcer is between one-quarter and one-half inch in diameter. They develop when digestive juices produced in the stomach, intestines, and digestive glands damage the lining of the stomach or duodenum (Bortoli M, Leonardi G, Ciancia Em, 2007; Gancz H, Jones KR, Merrell DS, 2008). Peptic ulcer patients were treated with fresh cabbage juice. It was observed that this juice contains an antiseptic ulcer factor. This factor (vitamin U) prevents the development of histamine-induced peptic ulcers (Malagelada J-R, KuipersMartin EJ, Blaser J, 2007). Gastritis includes a lot of disorders. It involves inflammatory changes in the gastric mucosa, including erosive gastritis caused by Helicobacter pylori bacterial infections. It also include other infectious gastritises, nonsteroidal anti-inflammatory drugs (NSAIDs), noxious irritants, reflux gastritis from exposure to bile and pancreatic fluids, infectious gastritis, and gastric mucosal atrophy (Philip S, 2008). The stomach produces acid to help with digestion. The lining of the stomach and first part of the small intestine (duodenum) protect themselves naturally from this acid. When these process stop working, then the acid can eat into the stomach lining causing a peptic ulcer (Rang HP, Dale MM, Ritter JM, Moore PK, 2003; Bortoli M, Leonardi G, Ciancia E, 2007; Laine L, Curtis SP, Cryer B, 2007; Moberly JB, Harris SI, Diff DS, 2007). Duodenal ulcers affect about one in 10 people. It usually occurs between the ages of 45 and 65. Stomach ulcers are less common, and usually affect people aged over 65 (Bertram GK, 8th edition; David EG, 2004; Philip S, 2008). Almost all ulcers are caused by Helicobacter pylori infection or NSAID use. It can be diagnosed by endoscopy and testing for H. pylori. Treatment involves acid suppression, eradication of H. pylori (if present), and avoidance of NSAIDs (Philip S, 2008).

Causes risk factors of peptic ulcers

There are various causes for peptic ulcers which include:

Helicobacter pylori

Helicobacter pylori are small, microaerophilic, spiral-shaped, gram-negative bacteria. It causes duodenal ulcer, a type of peptic ulcer (Bortoli M, Leonardi G, Ciancia E, 2007; Kim JI, Cheung DY, Cho SH, 2007). The bacterium slowly destroyed the protective mucous coating of the stomach and duodenum. As a result the acids and bacteria can easily irritate the lining and cause a sore or ulcer (Bertram G K, 8th edition). Helicobacter pylori can easily survive in the strong stomach acid by secreting enzymes. These enzymes neutralize the acid (Bortoli M, Leonardi G, Ciancia E, 2007; Kim JI, Cheung DY, Cho SH, 2007).

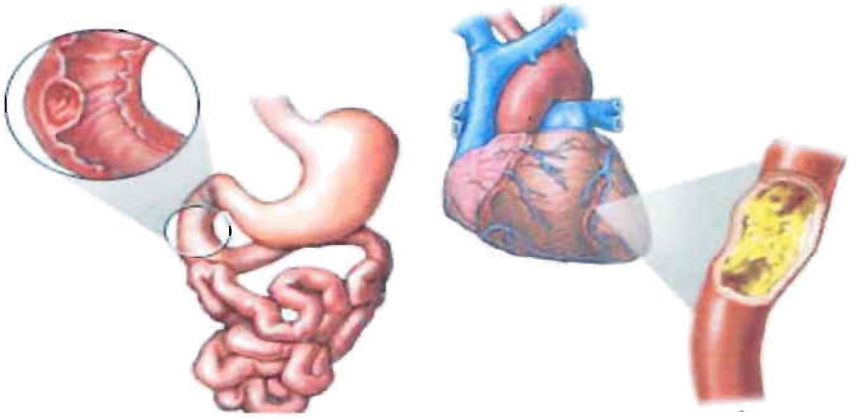
Drugs

Nonsteroidal Anti-Inflammatory Drugs (NSAID's) such as aspirin, ibuprofen (Motrin), naproxen (Naprosyn) and etodolac (Lodine) are painkillers. But they also cause ulcers by interfering with prostaglandins. Prostaglandins help the gut linings from resisting corrosive acid damage (Bertram GK, 8th edition; Rang HP, Dale MM, Ritter JM, Moore PK, 2003; Mercer DW, Robinson EK, 2007).

Smoking

Cigarette smoking causes ulcers. It also increases the risk of ulcer bleeding, stomach obstruction and perforation. Smoking also leads to failure in ulcers medication treatment (Tripathi KD, 5th edition; Yuhong Y, Ireneusz TP, Richard HH, 2006).

Tobacco use is associated with increased risk of peptic ulcers and coronary artery disease



(Chey WD, Wong BC, 2007)

Alcohol

Excess drinking of alcohol irritates and erodes the mucous lining of stomach. It leads to increased production of acid consequently causing ulcerations (David EG, 2004; Bortoli M, Leonardi G, Ciancia E, 2007; Kim JI, Cheung DY, Cho SH, 2007; Vishnu K, 2007).

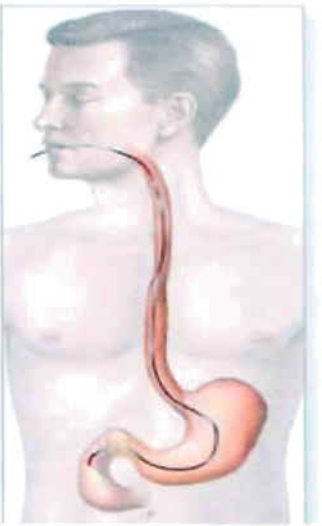
Symptoms of an ulcer

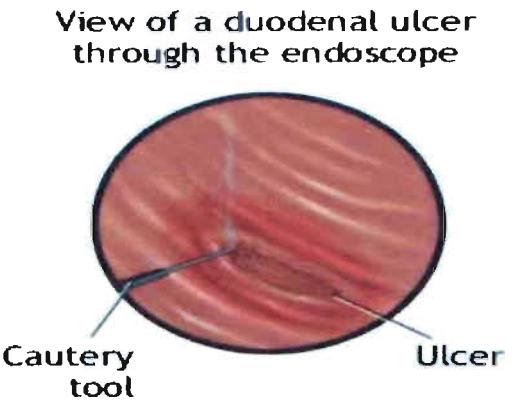
Symptoms of ulcer disease are varied. For ex; many ulcer patients have minimal experienced with indigestion or no discomfort at all. On the other hand, some patients have experienced with abdominal burning or hunger pain one to three hours after meals and in the middle of the night (Bortoli M, Leonardi G, Ciancia E, 2007; Gancz H, Jones KR, Merrell DS, 2008; Yuhong Y, Ireneusz TP, Richard HH, 2006; Philip S, 2008; Mercer DW, Robinson EK, 2007).

Diagnosis of Ulcer

The diagnosis of an ulcer is done by either a barium upper GI x-ray or an upper endoscopy (EGD-esophagogastroduodenoscopy). Barium is visible on x- ray, and outlines the stomach on x-ray film. It is less accurate and may not detect ulcers up to 20%

of the time (Bertram GK, 8th edition; Bortoli M, Leonardi G, Ciancia E, 2007; Gancz H, Jones KR, Merrell DS, 2008; Laine L, Curtis SP, Cryer B, 2007).





(Chey WD, Wong BC, 2007)

But an upper endoscopy is more accurate. It involves sedation of the patient. It is done by the insertion of a flexible tube through the mouth to inspect the stomach, esophagus, and duodenum (Bertram GK, 8th edition). Almost all duodenal ulcers are benign. But gastric ulcers can occasionally be cancerous. In these cases biopsies are often performed on gastric ulcers to stop cancer (Bertram GK, 8th edition).

Ulcer complications

The major problems resulting from ulcers are connected to ulcer complications (Philip S, 2008). Complications include ulcer bleeding, ulcer perforation, and gastric obstruction (Chey WD, Wong BC, 2007; Bortoli M, Leonardi G, Ciancia E, 2007; Gancz H, Jones KR, Merrell DS, 2008). Blood transfusions may require for the patients with persistent or severe bleeding. An upper endoscopy is performed to find the site of bleeding and to stop active ulcer bleeding with the aid of heated instruments (Bertram GK, 8th edition; David EG, 2004; Chey WD, Wong BC, 2007; Gancz H, Jones KR, Merrell DS, 2008). Some patients claim that a sudden onset of extreme abdominal pain, which is worsening by any type of motion. Abdominal muscles become rigid and board-like. In this case, urgent surgery is usually required (Chey WD, Wong BC, 2007; Laine L, Curtis SP, Cryer B,

2007; Vishnu K, 2007; Philip S, 2008; Mercer DW, Robinson E, 2007). Ulcer perforation leads to the leakage of gastric contents into the abdominal (peritoneal) cavity, it is called acute peritonitis (infection of the abdominal cavity).The obstruction usually occurs at or near the pyloric canal (Yuhong Y , Ireneusz TP, Richard HH, 2006).

Symptoms and Signs

1. Pain or discomfort
2. Bloating
3. A feeling of fullness. In these case people with severe dyspepsia are unable to drink as much fluid as people with mild or no dyspepsia
4. Hunger and an empty feeling in the stomach, often 1 - 3 hours after a meal
5. Mild nausea (vomiting, in fact, may relieve symptoms)
6. Regurgitation (sensation of acid backing up into the throat)
7. Belching (Bertram GK, 8th edition; David EG , 2004; Chey WD, Wong BC, 2007, Bortoli M, Leonardi G, Ciancia E, 2007; Gancz H, Jones KR, Merrell DS, 2008).

Gastric ulcer

The symptoms pattern of gastric ulcer is not always same. For example, eating sometimes exacerbates rather than relieves pain. This usually occurs in pyloric channel ulcers, which are often associated with symptoms of obstruction (e.g. bloating, nausea, vomiting) caused by edema and scarring (Bertram GK, 8th edition; David EG, 2004; Chey WD, Wong BC, 2007; Bortoli M, Leonardi G, Ciancia E, 2007; Gancz H, Jones KR, Merrell DS, 2008).

Duodenal ulcers

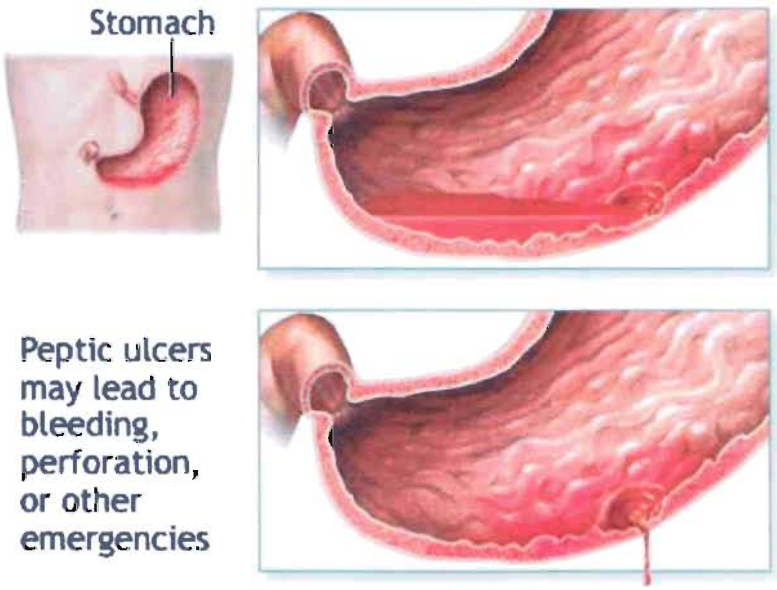
Duodenal ulcers produce more consistent pain. Pain is absent when the patient awakens. But it appears in mid-morning. It is relieved by food. It comes back 2 to 3 h after a meal. Pain awakens the patient at night is common. It is highly suggestive of duodenal ulcer (Vishnu K, 2007).

Emergency Symptoms

The severe symptoms may indicate intestinal obstruction, perforation, or hemorrhage, all of which are called emergencies. Symptoms may include:

1. Tarry, black, or bloody stools
2. Severe vomiting, which may include blood or a substance with the appearance of coffee grounds (a sign of a serious hemorrhage) or entire stomach contents (sign of intestinal obstruction)
3. Severe abdominal pain with or without vomiting or evidence of blood

Anyone who experiences any of these symptoms should go to the emergency room immediately (Bertram GK, 8th edition; David EG, 2004; Chey WD, Wong BC, 2007; Bortoli M, Leonardi G, Ciancia E, 2007; Gancz H, Jones KR, Merrell DS, 2008)



(Chey WD, Wong BC, 2007)

Vomiting of a substance that looks like coffee grounds or the presence of black tarry stools may indicate serious bleeding (Rang HP, Dale MM, Ritter JM, Moore PK, 2003; David EG, 2004; Chey WD, Wong BC, 2007; Bortoli M, Leonardi G, Ciancia E, 2007; Gancz H, Jones KR, Merrell DS, 2008).

Ulcer recurrence

According to the older studies, it occurs in 5 to 12% after highly selective vagotomy and in 2 to 5% after respective surgery. Recurrent ulcers are diagnosed by endoscopy. It generally responds to either proton pump inhibitors or H_2 blockers. The completeness of vagotomy should be tested by gastric analysis, H. pylori eliminated if present, and Zollinger-Ellison syndrome ruled out by serum gastrin studies (Rang HP, Dale MM, Ritter JM, Moore PK, 2003).

2. Purpose

The purpose of this study is to determine the market feasibility study of Dexlansoprazole. The mechanism of action of all proton pump inhibitor is same. So the study is done depending on its (Dexlansoprazole) indication and clinical response comparing with other proton pump inhibitor. Usually the main aim is to develop a hypothesis on Dexlansoprazole. It can be done by considering the market analysis of all proton pump inhibitor and to make a proposal about the market growth rate of it. For example, whether the market growth rate of Dexlansoprazole will be increased or not and provide an exact reason behind this.

3. Hypothesis

Market superiority of Dexlansoprazole will be increased in comparison to other Proton Pump Inhibitor.

4. Method

The following methods were used to prepare the paper:

1. Many website were used to collect all information about the drug. For example, Google.com, Pubmed.com etc.
2. MS Excel was used to calculate market growth and to plot graph.
3. International Market Strategy (IMS) data was used to determine the market size.
4. Many books, journals, articles were also used to know efficacy and safety profile of drugs.
5. This paper was prepared with authorized person and their publishing year.
6. Comparison of Dexlansoprazole with other Proton Pump Inhibitor was done on the basis of their efficacy and market strategy.

5. Result and Discussion

5.1. Efficacy

Dexlansoprazole has higher Cmax and AUC value. Its half life ($T_{1/2}$) is 1-2 hours. That leads to prolonged plasma concentration of Dexlansoprazole. It is almost double of Lansoprazole. Dexlansoprazole results in extended drug exposure compared to Lansoprazole (Zhang W, Wu J, Vakily M, 2008). Extended duration of Dexlansoprazole causes a progressive increase in the pharmacodynamic response (Vakily M, Zhang W, Wu J, Atkinson SN, Mulford D, 2009). Dexlansoprazole is highly effective in healing erosive oesophagitis and offers benefits over Lansoprazole, particularly in moderate-to-severe disease (Sharma P, Shaheen NJ, Perez MC, Pilmer BL, Lee M, Atkinson SN, Peura D, 2009). Dexlansoprazole MR 30 and 60 mg are superior to placebo in providing 24-h heartburn-free days and nights in NERD patients (Fass R, Chey WD, Zakko SF, Andhivarothai N, Palmer RN, Perez MC, Atkinson SN, 2009). Dexlansoprazole administration results in moderate increases in PG, similar to Lansoprazole (Zhang W, Wu J, Atkinson SN, 2009). The Dexlansoprazole Duel Delayed release formulation may improve acid suppression and offer benefits over conventional single release PPI formulations (Metz DC, Vakily M, Dixit T, Mulford D, 2009). It is more effective in GERD, NERD, erosive oesophagitis and peptic ulcer than other proton pump inhibitor.

5.2. Market Scenario

Market values of total Pharma market, Antiulcerant Drug, Acid Pump Inhibitor and their year to year growth.

Table 1:

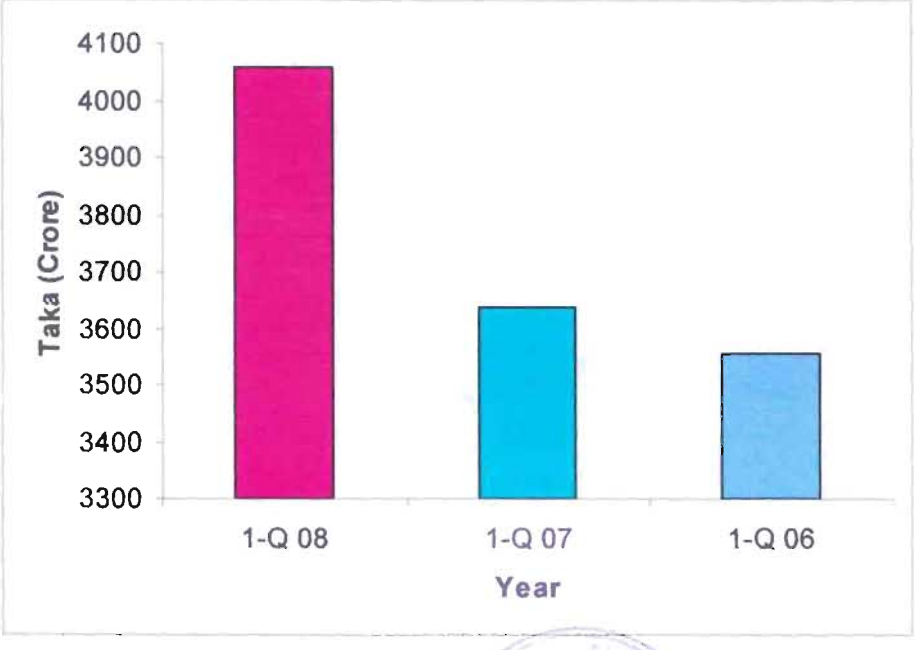
		1-Q 2008 MAT Value TK.	1-Q 2007 MAT Value TK.	1-Q 2006 MAT Value TK.
Total Market	Total Value	40,587,191,000	36,369,963,671	35,574,308,870
	Increased %	11.60	2.24	
Antiulcerant	Total Value	5,630,812,000	4,497,446,717	4,570,457,243
	Increased %	25.20	-1.60	
Acid Pump Inhibitor	Total Value	2,887,017,108	2,601,900,191	2,446,267,349
	Increased %	10.96	6.36	

(Source: IMS Data)

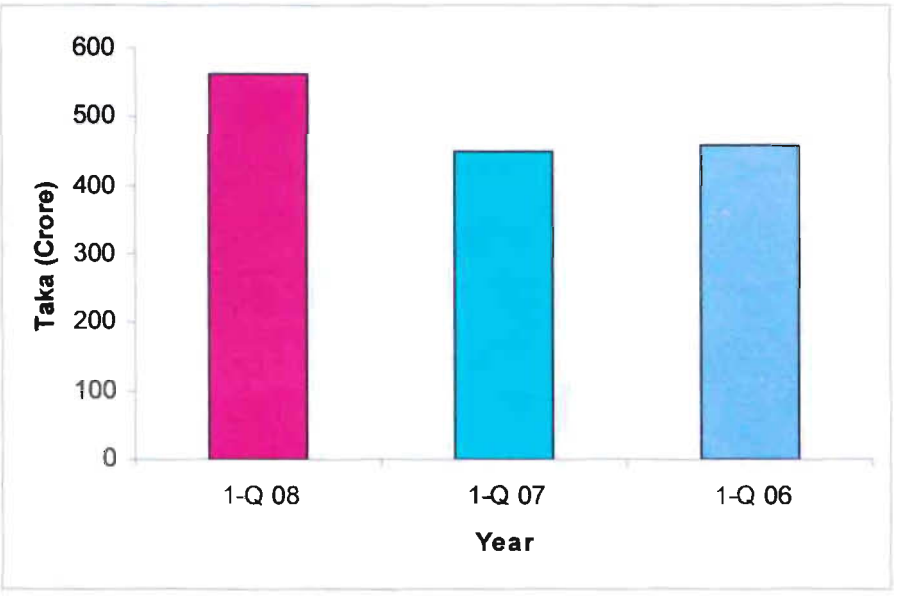
From this table we get that, total Pharma market is changing in every year. The growth rate is 2.24% in year 2007 but in year 2008 it has been increased and the rate is11.60%. The antiulcerant drug cover cover12.85% in year 2006, in year 2007 cover 12.36% and in year 2008 cover 13.87% of the total Pharma market. That means there is no significant change. It is a large market value in over all Pharma market. The total antiulcerant market value is also varying in every year. For example the growth rate is -1.60% in year 2007 but there is huge increase in 2008 to 25.20%. That means market value of total antiulcerant drugs is significantly reduced in year 2007. From this table we also can see that, the Proton Pump Inhibitors cover 6.87% in year 2006, 7.15% in year 2007 and 7.11% in year 2008 of the total Pharma market. The Proton Pump Inhibitors also cover 53.52% in year 2006, 57.85% in year 2007, 51.27% in year 2008 of the total Antiulcerant market. So the Proton Pump Inhibitors have covered a large market all over the Antiulcerant Drug. The Growth rate of Proton Pump Inhibitor is 6.36% in year 2007, 10.96% in year 2008. It is huge increased in the PPI market.

From the table 1 we can plot following graphs:

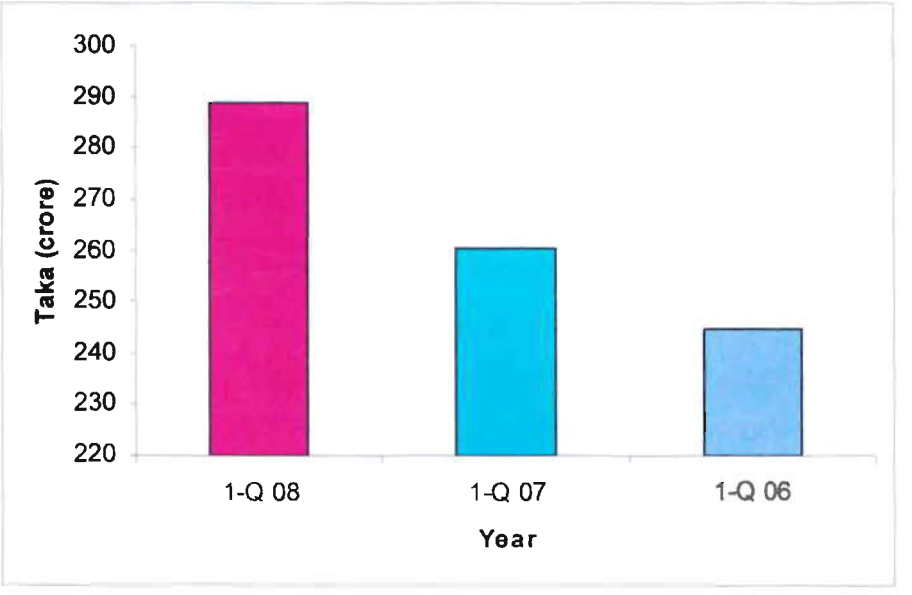
Graph 1: Graphical Presentation of Total Pharma Market Size in last three years.



Graph 2: Graphical Presentation of Total Antiulcerants Market Size in last three years.



Graph 3: Graphical Presentation of Total Proton Pump Inhibitors Market Size in last three years.



Total market values of all Proton pump market Inhibitor and their growth.

Table 2

		1-Q 08 MAT Value TK	1-Q 07 MAT Value TK	1-Q 06 MAT Value TK
Omeprazole	Total Value	1,791,153,108	1,760,463,166	1,783,963,913
	Increased %	1.74	-1.32	
Pantoprazole	Total Value	510,828,000	405,361,198	278,442,595
	Increased %	26.02	45.58	
Esomeprazole	Total Value	422,014,000	295,593,153	250,653,316
	Increased %	42.77	17.93	
Lansoprazole	Total Value	96,841,000	96,563,144	106,638,952
	Increased %	-0.74	-8.51	
Rabeprazole	Total Value	66,181,000	42,919,530	26,568,572
	Increased %	54.20	61.54	

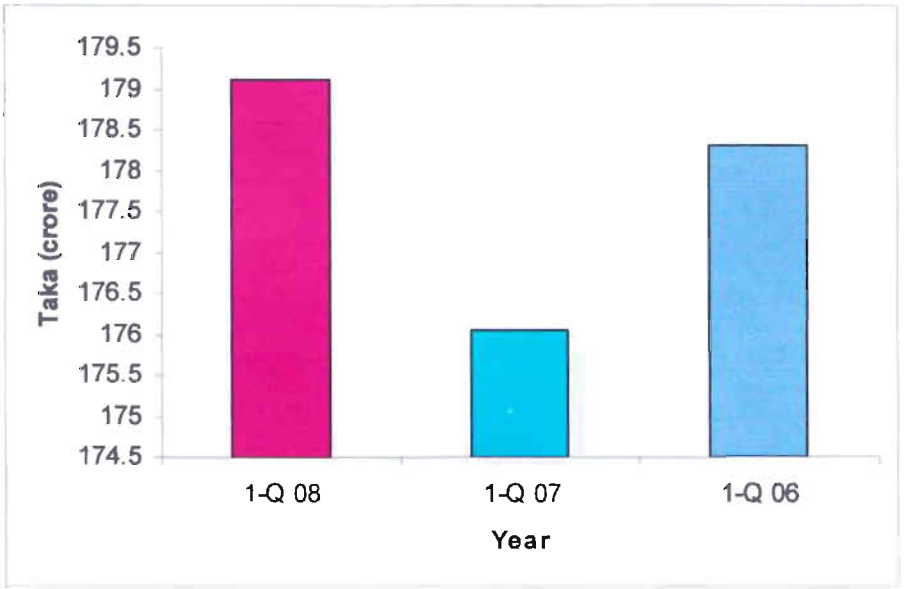
(Source: IMS Data)

From this table we find that, the growth rate of Omeprazole in year 2007 has been decreased to -1.32 but it is very minutely increased to 1.74%. It cover 72.92% in year 2006, 67.66% in year 2007, 62.04% in year 2008 of the total PPI market. So it covers the highest market of the total PPI market. The growth rate of Pantoprazole is 45.58% in year 2007 but it has been reduced to 26.02% in year 2008. It cover 11.38% in year 2006, 15.57% in year 2007, 17.69% in year 2008 of the total PPI market. The growth rate of Esomeprazole is 17.93% in year 2007 but the growth rate of Esomeprazole has been improved to 42.77% in year 2008. That means it take over the Pantoprazole market. It cover 10.25% in year 2006, 11.36% in year 2007, 14.62% in year 2008 of the total PPI market. The growth rate of Lansoprazole is -8.51% in year 2007 although it has been increased to -0.74 but it is not a very high market value. It cover 4.36% in year 2006, 3.71% in year 2007, 3.35% in year 2008 of the total PPI market. The growth rate of Rabeprazole is 61.54% in year 2007. It is a very large market value though it is reduced

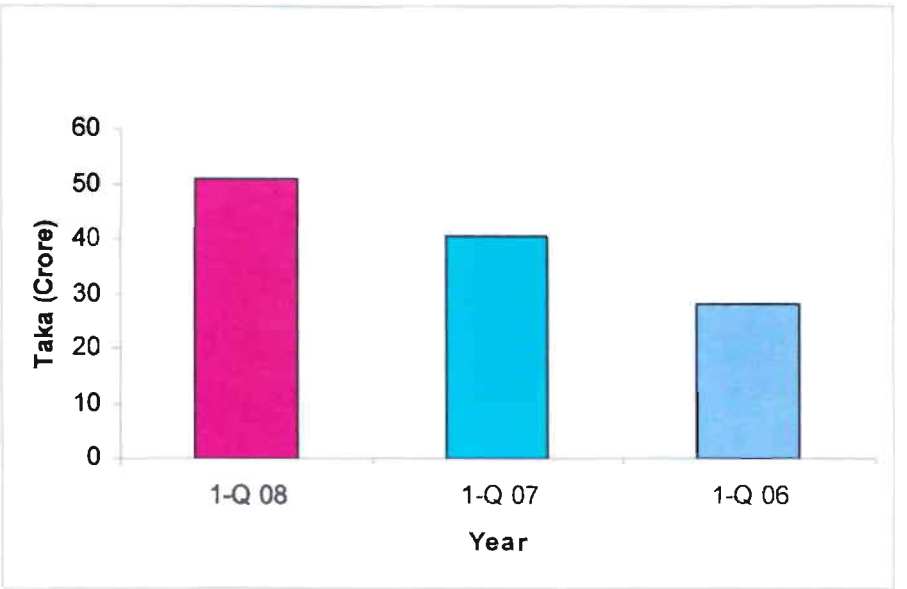
to 54.20% in year 2008. It cover 1.09% in year 2006, 1.65% in year 2007, 2.29% in year 2008 of the total PPI market.

From table 2 we can plot following graphs:

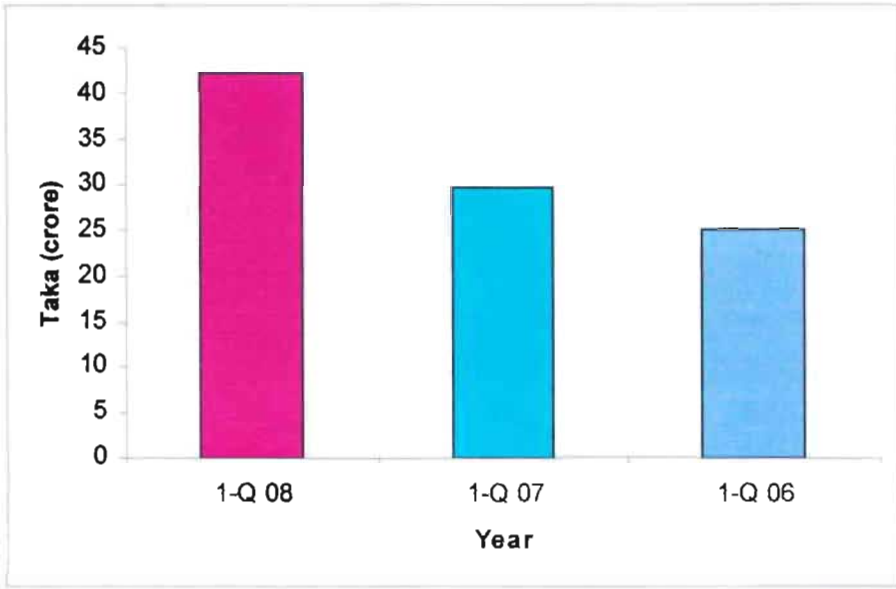
Graph 4: Graphical Presentation of Total Omeprazole Market Size in last three years.



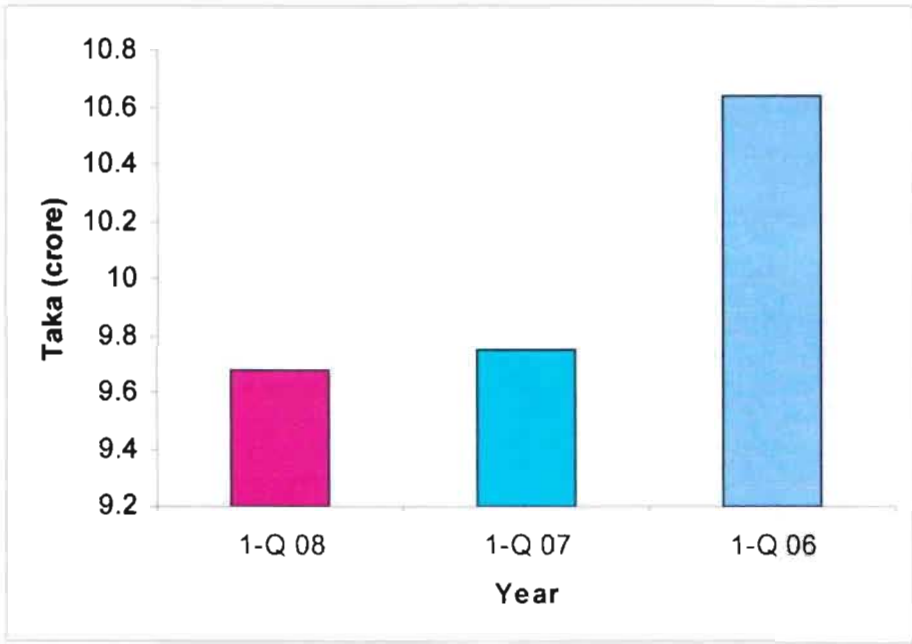
Graph 5: Graphical Presentation of Total Pantoprazole Market Size in last three years.



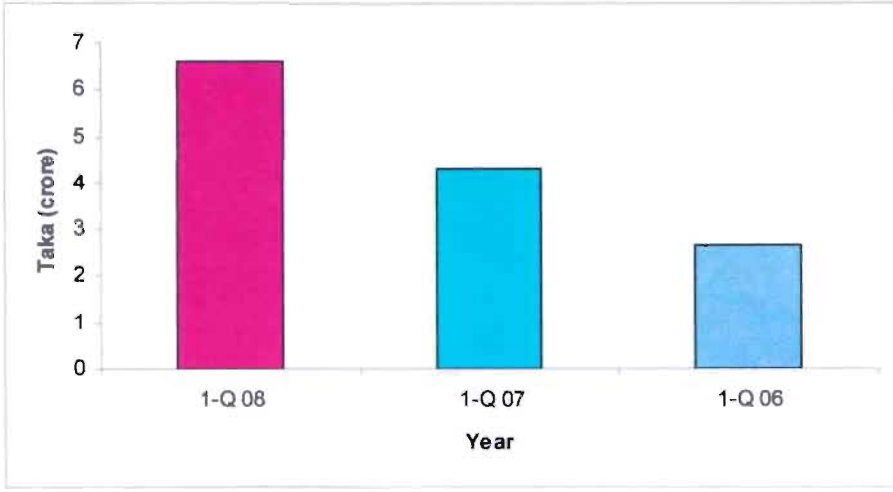
Graph 6: Graphical Presentation of Total Esomeprazole Market Size in last three years.



Graph 7: Graphical Presentation of Total Lansoprazole Market Size in last three years.



Graph 8: Graphical Presentation of Total Rabeprazole Market Size in last three years.



From the given table, we can see that growth rate of Lansoprazole was very low in the last three years. On the other hand, the growth rate of Esomeprazole, Rabeprazole and to some extent Pantoprazole is significantly high. That means the market of Lansoprazole is largely captured by Rabeprazole and Esomeprazole but very minutely by Pantoprazole. So to improve the market value of Lansoprazole should improve its efficacy than the other PPI. This criterion can be fulfilled by the new product Dexlansoprazole. From the clinical study results we get that, it gives prolonged action which is almost double than Lansoprazole. It shows better efficacy in erosive oesophagitis, GERD, NERD than the other proton pump inhibitor. So the total market size of Dexlansoprazole will be increased and it will capture the Rabeprazole, Esomeprazole and Pantoprazole. The estimated market size for Dexlansoprazole is 11.0 crore taka and the estimated growth rate for Dexlansoprazole is 10-12% in the next year.

6. Conclusion

Dexlansoprazole is a proton pump inhibitor which shows better efficacy in GERD, NERD than the other proton pump inhibitors. I think, its market size will increase in the next year and soon it will earn the market superiority than the other Proton pump inhibitors.

7. Limitation

There are some limitations of this study. These are given below:

1. Only web site is not perfect to collect data.
2. Practically no clinical trial was done.
3. No survey study was done.
4. Comparison was done only on the basis of clinical study.
5. No confidential result was found.

8. Significance of the study

The significances of this research are many. These are given below:

1. From this study we know how to launch a new product in a competitive market.
2. It gives a brief knowledge about the whole Pharma market.
3. All information about the nearest competitive product can easily be known.
4. We can get an idea about market position of any drugs.
5. It gives an idea about the limitation of any drugs in the market.
6. We can also know how a product can improve its market position.

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