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Studies On Different Marketed Antiulcer Drugs.

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ABSTRACT

In recent years scientific and technological advancements have been produced many classes of Antiulcer drugs in the medicinal market, such drugs are used to treat the ulcer as quick remedies in people, so we selected some drugs for our studies and market survey then to find out the fast movable antiulcer drug had a potential of some selected antiulcer drugs and the reasons for most leading sales of antiulcer drugs of various areas of medicinal market. These drugs are evaluated by the physiochemical parameters and selected the best familiar drug based on leads to the sales and evaluated parameters.

Keywords: Helicobacter pylori, Antiulcer drugs, medicinal market, physiochemical parameter

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INTRODUCTION

Peptic ulcer is occurs in that part of the gastrointestinal tract, which is exposed to gastric acid and pepsin, the stomach and duodenum. It results probably due to imbalance between the aggressive (acid, pepsin, bile and *Helicobacter pylori*) and defensive (gastric mucus, bicarbonate, prostaglandins, nitric oxide, high mucosal blood flow, innate resistance of the mucosal cells) factors.

A variety of psychosomatic, humoral and vascular dearrangements have been implicated and the importance of *Helicobacter pylori* infection as a contributor to ulcer formation and recurrence has been recognized [1] [2]

REGULATION OF ACID SECRETION

Gastric acid secretion is regulated through a complex interaction of nerves, hormones, and local or paracrine enterichromafin like cells agents. Gastric acid is produced by specialized parietal cells contained in the fundus mucosa. Parietal cells secrete hydrochloric acid via the secretory canaliculus, and infolding of the plasma membrane which, in turn, communicates with the gastric lumen [2]

BASAL ACID SECRETION

The normal human stomach secretes 2 to 5 mEq of hydrochloric acid per hour in the fasting time. Since vagotomy decreases this basal secretion by some 85%, it has been presumed that vagal tone is important in determining the rate of basal acid secretion by about 80% [1][2]

STIMULATION OF ACID SECRETION

Basic vagal discharge in response to the thought, sight, or smell of food stimulates acid secretion directly by a cholinergic mechanism. Vagal discharge also inhibits gastric somatostatin release. When food enters the stomach, distinction triggers neural refluxes and gastrin release is activated. These estimates range from 15-25 mEq/hr. approximately 75% of maximal response to exogenous gastrin or histamine [1]

INHIBITION OF ACID SECRETION

Inhibitory of regulation of gastric acid secretion is a accomplished through central, vagal, gastric, intestinal, and colonic mechanisms [1]

TYPES OF ULCER

Two types

A) Acute ulcer
B) Chronic ulcer

ACUTE ULCER

Sometimes these acute ulcers may occur following stress, when they are called “stress induced ulcers”. This may occur following hypotension from hemorrhage, endotoxin shock or cardiac infarction.

Sepsis is an important etiological factor. Undrained pus maybe responsible for acute stress ulcers, acute duodenal ulcer may occur which often become chronic ulcer. Patients on steroids may develop acute ulcers, known as “steroid ulcers” [4]

CHRONIC ULCER

It again divided into two types

i) Gastric ulcer

ii) Duodenal ulcer

GASTRIC ULCER

Pyloric duodenal reflux regurgitated bile and other duodenal juices have been taken to be the prime cause of pre-ulcerative superficial gastritis. Mucosal trauma - 85% of gastric ulcers occur along the lesser curve of the stomach. This part of the stomach is exposed to injurious effects of heat and trauma.

DUODENALULCER

Acid hyper secretion - Duodenal ulcer is seemingly simplified at first sight by a clear relationship to over-production of hydrochloric acid by the stomach. Genetic factors is a great number of cases the acid production may be within the high side of the normal range and in these cases ulceration cannot be explained except the diminished mucosal resistance to normal acid secretion [4]

CAUSES OF ULCER

Helicobacter pylori - *H. Pylori,* a bacterial organism, is responsible for most ulcers. Non-steroidal anti-inflammatory drugs - ongoing use of this class of medications is the second most common cause of ulcers. Zollinger-Ellison syndrome, Tumors in the pancreas and duodenum, direct damage to the wall of the stomach or duodenum, such as heavy use of alcohol, radiation therapy, burns, and physical injury [5]

SYMPTOMS

Abdominal pain, Burning pain, buffer stomach acid, vomiting of blood, Dark blood in stools or stools becomes black or tarry, Unexplained weight loss, Appetite changes [6]

DIAGNOSIS

One of two tests will be performed to try to identify an ulcer [4]

A. Upper gastrointestinal (GI) series
B. Endoscopy

RISK FACTOR

Genetic factors may predispose you to developing an ulcer, Chronic pain, from any cause such as arthritis, fibromyalgia, repetitive stress**,** injuries (like carpal tunnel syndrome), or persistent back pain, leading to ongoing use of aspirin or NSAIDs , Alcohol abuse. Diabetes may increase your risk of having *H. pylori* Lifestyle factors, including chronic stress [7]

COMPLICATION

Pregnancy, Prognosis and Complications, Internal bleeding, Infection, Scar tissue [7]

ALLOPATHY [1] [2]

H_2ANTIHISTAMINES:Ranitidine, Cimetidine, Famotidine, Roxatidin.

HERBS

Herbs are generally a safe way to strengthen and tone the body's systems. As with any therapy, you should work with your health care provider to get your problem diagnosed before starting any treatment. [8]

HOMEOPATHY

Before prescribing a remedy, homeopaths take into account a person's constitutional type your physical

emotional, and intellectual makeup. For the treatment of ulcers, even if you do seek homeopathic remedies as adjunctive care, conventional treatment recommendations must be followed. [7]

ACUPUNCTURE

Acupuncture has been used traditionally for a variety of conditions related to the gastrointestinal tract, including peptic ulcers. A growing body of scientific evidence suggests that acupuncture can help reduce pain associated with endoscopy (the procedure used, as described earlier, to make a diagnosis of ulcer or to treat its complications) [9]

CHIROPRACTICE

Chiropractors report and preliminary evidence suggests that spinal manipulation may benefit some individuals with uncomplicated gastric or duodenal ulcers. [7]

SURGERY

Once hospitalized, if bleeding from our ulcer does not stop by using medication and supportive care (like fluids and possibly blood transfusion)It can almost always the stopped via endoscopy.

HOME REMEDY

The most effective home remedy for treating peptic ulcer is like eat bananas every day, Having cold milk, without sugar, Prepare a paste of 10 grams drumsticks leaves and water and so [7]

RANITIDINE

N-(2-(((5-(Dimethylamino) methyl)2-furany)thiol)ethyl-N-methyl-2-nitro-)1,1 ethanediamino.

Molecular formula $C_{13}H_{22}N_4O_3S$ and the molecular weightis about 314.40. It is white or almost white or White to pale yellow crystalline powder. It having melting range at about 70^0C-72^0C . It is a H_2 Receptor blocking agent. It is well absorbed in oral route, oral biavailability is 60-80% due to first pass metabolism. It is metabolized in the liver by the enzymeCYP450and it is excreted unchanged in urine and bile. The plasma half life of Ranitidine is 2-3 hours and it acts by the inhibition of cAMP mediated ca^{2+}channel opening of H_2 receptor [1] [2] [10] [11]

LANSOPRAZOLE

2((methyl-4, (2, 2, 2 triflouro ethoxy)-2 pyridyl methyl) sulfinyl) benzimidazole.

Molecular Formula $C_{16}H_{14}F_3N_3O_2S$ and the molecular weight are about 369.36. It is white or almost white to half white crystal having melting range at 166^0C. It is freely soluble in Dimethyl Formamide, Methanol. It is a proton pump inhibitor. It is well absorbed in oral route, its oral bioavailability is about 50% due to acid liability. It is metabolized in the liver by the enzyme CYP2C19 and CYP3A4 and it's eliminated through the urine. The half Life of lansoprazole is about 1-1.5 hour. It is rearranged to two charged cations that react covalently with SH groups of the H^+K^+ATPase enzyme inactivates irreversibly, especially the two molecule of drug react with one molecule of enzyme [2] [10] [11]

PANTAPRAZOLE

5(Diflouro methoxy)-2((3,4 Dimethoxy-2-pyridinyl)methyl sulfinyl)1H benzimidazole**.**

Molecular formula is $C_{16}H_{14}F_2N_3O_4S$ and the molecular weight is 432.37. It is White to half white solid having melting point at about 136^0C. It is Freely soluble in water, Slightly soluble in pH 7 phosphate buffer. It is a Proton pump inhibitor . The pantaprazole is well absorbed in oral route, oral bioavailability is about 50% due to acid lability. It is metabolized in the liver by the enzyme CYP2C19 and CYP3A4 and it's eliminated through the urine. The half Life of pantaprazole is 2.8 hours. It is rearranged to two charged cations that react

covalently with SH groups of the H^+K^+ATPase enzyme and inactivates it irreversibly, especially the two molecule of drug react with one molecule of enzyme [1] [2] [10] [12]

RABEPRAZOLE

2(4-(3-Methoxy propoxy)-3 methyl-2-pyridiyl)methyl sulfinyl)-1H-benzimidazole.

Molecular Formula is $C_{18}H_{20}N_3O_3S$ and molecular weight is 381.42. it is a white crystals having melting point at about 100^0-140^0C. It is very soluble in water or methanol and it is freely soluble in ethanol, chloroform and ethyl acetate. It is a proton pump inhibitor. Rabeprazole is orally well absorbed and its oral bioavailability is about 80% due to acid lability. It is metabolised in the liver by the enzyme CYP2C19 and CYP3A4 and eliminated through the urine. The half Life of rabeprazole is 1-2 hours. It is rearranged to two charged cations that react covalently with SH groups of the H^+K^+ATPase enzyme and inactivates irreversibly, especially the two molecule of drug react with one molecule of enzyme [1] [2] [10] [11]

MARKETED SURVEY

We select the best moving drug in market among the four marketed antiulcer drug, for the reason we taken market survey on 125 medical shop from different areas like Thirunelvelli, Tirupur, Vellore, Villupuram districts and Pondicherry union. The result of market survey given in following table no.1 and following figure 1.

PHYSIOCHEMICAL PARAMETERS

The marketed antiulcer drugs are evaluated and select the best drug among the four marketed antiulcer drugs by comparing the evaluation parameter. The following parameters were evaluated. Hardness, Friability, Weight variation and Disintegration [13] [14]

EVALUATION OF HARDNESS

The resistance of the tablet to chipping, abrasion or breakage under condition of storage, transportations and handling before usage depends on its hardness.

Different instrument are available for testing of hardness of tablets

- ✓ Monsanto hardness tester
- ✓ Pfizer hardness tester
- ✓ Strong cobb hardness tester
- ✓ Erweka hardness tester
- ✓ Schleuniger hardness tester

Among the hardness tester most commonly used is Monsanto and Pfizer hardness. But we use Pfizer hardness test apparatus because it was very simple and rapid determination of hardness of tablet compared to Monsanto.

The tablet to be evaluated was placed in between the jaws of the Pfizer apparatus. Then the pressure was applied and the help of handling unit to break a tablet. The reading on the pressure dial corresponds to the pressure applied to break the tablets. The force was measured in kilogram/cm^3.

EVALUATION OF FRIABILITY

Friability test was carried out to find out the ability of the tablet to withstand abrasion in packaging, handling and shipping by using Roche's friabilator. Previously 20 tablets were weighed and placed in a plastic chamber of apparatus and allowed to rotations for 25rpm for 4 minutes. After the tablets were de dusted and they were reweighed. The friability was calculated by following formula

$$\% \text{ Friability} = [(I-F)/I] \times 100.$$

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I-Initial weight
F-Final weight

EVALUATION OF WEIGHT VARIATION

20 Tablets were selected and weighed at random and the average weight was determined. The individual weight of tablet should not deviated from any weight by more than twice its percentage as per standard value of I.P ,the limits of weight variation given by table: 2.

EVALUATION OF DISINTEGRATION TEST

As per the individual monograph, the tablets were placed in each tube of the basket. The disc was kept above the tablet in each tube of the basket. The disintegration test was carried out in distilled water and maintained at temperature of $37^0 \pm 2^0$C. The basket was lifted from the liquid and the tablets were observed. The evaluated results are given by table no:3.

TABLE-1: COMPARATIVE STUDIES OF MORE SALES ANTIULCER DRUGS

S. No	Name Of The Antiulcer Drugs	Ranking of 125 Pharmacies	Grade
1	Ranitidine	64	I
2	Pantaprazole	40	II
3	Rabeprazole	14	III
4	Lansoprazole	07	IV

The above tabular column gave the experimental results while which drug was moved rapidly in the market, and the above pie diagram represents the more sales of antiulcer drugs in the maket level declared as for the market research followed by us.

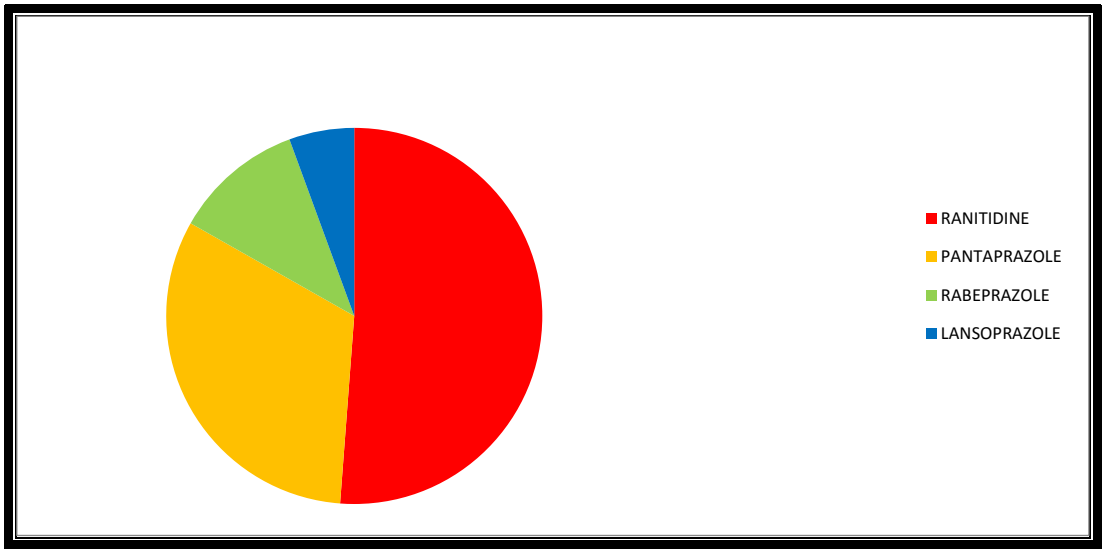

Figure No 1: Pie Diagram of More Sales Antiulcer Drugs

TABLE NO.2: LIMITS OF WEIGHT VARIATION IN I.P.

Weight Variation	Percentage Deviation
130mg Or Less	± 10
130 – 324mg	± 7.5
More Than324mg	± 5.0

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The Evaluation Results Were Given In the Following Table No.3

Tablets/Tests	ardness	Friability	Weight Variation	Disintegration
Ranitidine	6.38	0%	0.59%	15
Rabeprazole	8.88	0%	1%	24
Pantaprazole	3.84	0%	0.92%	115
Lansaprazole	0.7	14.26%	0.69%	13

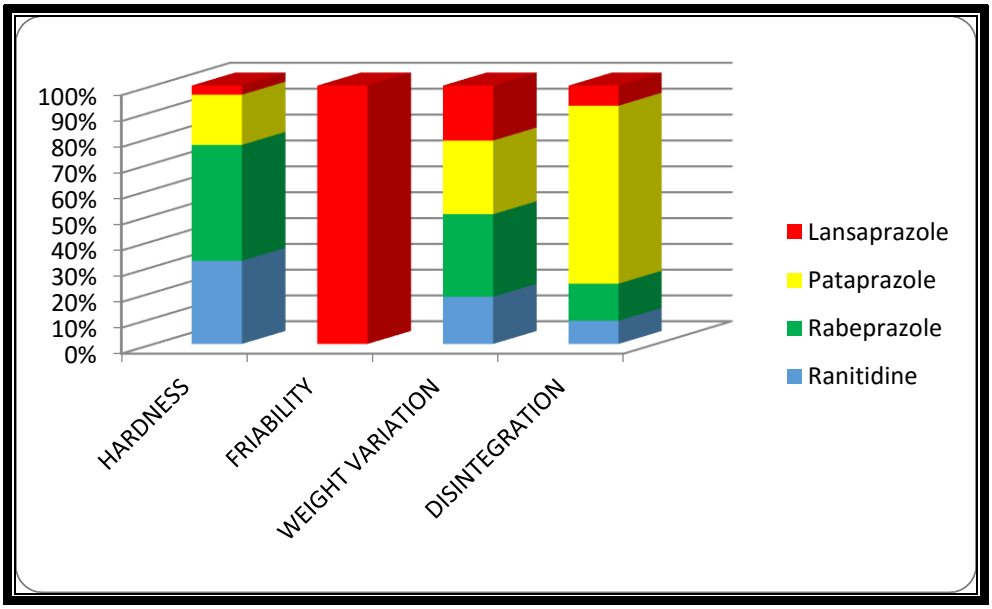

Figure no.2: Bar diagram of evaluation results of marketed Antiulcer drugs

CONCLUSION

The Ranitidine, Rabeprazole, Pantaprazole, and Lansaprazole drugs were commonly used in the treatment of ulcer. The Ranitidine showed highest one in sales among the four antiulcer drugs from the 125 pharmacies and it got grade 1 by based on sales. All marketed product of Antiulcer drugs were evaluated by Hardness, Friability, Weight Variation and Disintegrationtests. The Pantaprazole, Rabeprazole and Lansoprazole, grade II, III, IV Respectively. From the evaluation parameters we concluded that the drug Ranitidine and Pantapraole were best as compared to Lansoprazole and Rabeprazole. So we concluded that according to marketed survey Ranitidine was selected best one compared to other product and based on physical evaluation parameters the Ranitidine and Pantaprazole were best one compared with other marketed products.

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