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FORMULATION AND EVALUATION OF PANTOPRAZOLE SODIUM ENTERIC COATED TABLETS USING DIFFERENT SUPER DISINTEGRANTS

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Abstract:
The aim of the present study is to formulate and evaluate the pantoprazole sodium enteric coated tablets using different super-disintegrants in different ratio's and to study the physicochemical properties, drug-excipients compatibility studies and to carry out disintegration, dissolution and stability studies. Pantoprazole is a proton pump inhibitor belongs togroup of benzimidazole. This compound inhibits gastric acid formation and thereby it is very efficientfor the treatment of gastric and duodenum ulcers. An enteric coated pantoprazole sodiumtablets were successfully prepared by directcompression method. Nine formulations ofPantoprazole were developed by preparing coretablets using mannitol as diluent, Aerosil as glidant,Magnesium stearate as lubricant, PVPK30 as binderandkollidone, HPC &Explotab as super disintegrants in 3 different concentrations i.e. 5%7.5%, 10% of which F3 formulation with kollidoneas super disintegrant with concentration of 10% wasselected as best formulation as it has shownmaximum drug release of 100.16% within 45 mins.

Key words: *Pantoprazole, Formulation, Evaluation, Enteric coated tablets*

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INTRODUCTION:

Acidity is a term used for a set of symptoms caused by excess production of acid by the gastric glands of the stomach. The stomach normally secretes hydrochloric acid which is requiredfor the breakdown and digestion of food we eat.Acidity caused symptoms like dyspepsia, heartburn, gastric inflammation and ulcer in the stomach.Acidity is generally a consequence of several external factors like eating habits, fad diets, stress. Sinking and alcoholconsumption, lack of physical activity, irregularities in eating pattern. TheincidenceAcidity is higher in countries where individuals eat more of non-vegetarian, oily and spicy food. Certain medications like non-steroidal anti-inflammatory drugs (NSAID's) also predisposes individualto gastric acidity.People suffering from acidity feel a burn sensation after eating a meal. Sour belching is also seenSometimes, constipation and indigestion is also seen in people having acidity. Acidity can be treatedwith antacid and mainly bymaking changes in eating and lifestyle habits a new technology calledEndostismcanalso provide relief from acid reflux. This section offers some really good home Remedies for acidity which you can try. You can read the importance of having an alkaline diet toReduce the symptoms of acidity [1-2].

Gastroesophageal Reflux disease is a commonRelapsing condition that carries a risk of significant morbidityPotential mortality from resultant complications. While manyPatients self - diagnose, self-treat,and do not seek medicalAttention for their symptoms, other suffer frommoresevereDiseases with esophageal damage ranging from erosive toUlcerative esophagitis. More than 60 million adult American suffer from Herat burn atleast once a month and over 25 million experience Herat burn. The National Ambulance medical care survey found that 38.53 [3-4]

Million annual adult outpatient visits were related to GERD.For Patients presenting with GERD symptoms, 40-50%or more haveReflex esophagitis on upper endoscopy. GERD is morePrevention in pregnant women. And higher complications rateexitsamongtheearly. Patients with GRED generally report. Several studies have demonstrated that on-demand therapy with PPIs is the most cost-effective method for non-erosive reflux disease (NERD). Evidence from numerous randomized controlled trials has shown that PPIs are more effective than both H2RAs and placebo in controlling symptoms from erosive reflux disease (83% compared to 60% and 27%, respectively) over a 4-8 week period. One systematic review compared the efficacy of PPIs and H2RAs and found that a greater number of people improved symptomatically with PPIs, yet the difference was not significant for heartburn remission. One randomized controlled trial showed that at 12 months, significantly more people were still in remission with omeprazole compared to ranitidine. Another randomized controlled trial found that treatment with omeprazole was more likely than ranitidine to improve symptom and psychological well-being scores [5-6]. [Note: ranitidine was removed from the US market by the FDA in April 2020 as part of an investigation of a contaminant known as N-Nitroso dimethylamine (NDMA) in ranitidine products.

Pantoprazole is a proton pump inhibitor, belongs to group of benzimidazole, Pantoprazole sodium were prepared by direct compression method using different concentration of, microcrystalline cellulose as filler, mannitol and dicalcium phosphate as diluents, crosscarmellose sodium as disintegrating agents, magnesium stearate and talc was used as a glidant and lubricant respectively. Direct compression is economic compare to wet granulation since it requires fewer unit operations [7].

This means less equipment, lower power consumption, less space, less time and less labor leading to reduced production cost of tablets. The prepared tablets were evaluated for hardness, weight variation, friability and drug content uniformity and it was found that the results comply with official standards. The prepared tablets were coated using enteric coating polymer such as cellulose acetate phthalate, Eudragit L100 and by dip coating method. The aim of the present study is to formulate and evaluate the pantoprazole sodium enteric coated tablets using different super-disintegrants in different ratio’s and to study the physicochemical properties, drug-excipients compatibility studies and to carry out disintegration, dissolution and stability studies.

MATERIAL AND METHODS:

Formulation of Pantoprazole sodium enteric coated tablets:

Pantoprazole sodium enteric coated tablets were prepared by geometric mixing, all the ingredients were weighed according to the formula mentioned in the table no:1. Such that 3 super-disintegrants (Explotab, Kollidon, HPC) are added at 3 different concentrations such as 5%, 7.5%, 10%. The obtained blend was then punched into tablets weighing about 200 mg containing 40 mg of Pantoprazole, by following direct compression method using a single stage tablet punching machine, among all the formulations optimized formulation is selected

followed by an enteric coating using 3 different enteric coated polymers (Eudragit L100, PVAP, Eudragit RS100) in 3 different ratio's such as 4%, 6%, 8% mention in the table 1 by the spray coating method [8].

Evaluation [9-13]:

Thickness:

Three tablets were picked from each formulation randomly and thickness was measured individually. It is expressed in mm and standard deviation was also calculated. The tablet thickness was measured using dial-caliper (Mitutoyo, Japan).

Hardness:

For each formulation, the hardness of five tablets was determined using the Monsanto hardness tester (Cadmach) and measured in terms of kg/cm^2.

Weight variation:

Twenty tablets were selected randomly from each formulation and average weight was determined. The tablets were weighed individually and compared with average weight. The U.S Pharmacopoeia allows a little variation in the weight of a tablet.

Friability:

A sample of twenty randomly selected tablets were accurately weighed and placed in a Roche friabilator. The friabilator was operated for 4 min at a speed of 25 rpm. The tablets were removed from the friabilator, de-dusted and reweighed. The percent loss in weight due to abrasion and impact was calculated as,

%Friability= (Loss in weight/ Initial weight) x 100

Hardness test:

The hardness of tablet was measured by Pfizer hardness tester and results were expressed in Kg/cm^2**.**

Uniformity of drug content:

Twenty tablets were taken and amount of drug present in each tablet was determined. The tablets were crushed in a mortar and the powder equivalent to 100mg of drug was transferred to 100ml standard flask. The powder was dissolved in 50 ml of 7.2 pH Buffer and made up to volume with of 7.2 pH Buffer. The sample was mixed thoroughly and filtered through a 0.45µ membrane filter. The filtered solution was diluted suitably and reacts with dye and analyzed for drug content by UV spectrophotometer at 7.2 pH Buffer as blank.

***Invitro*buoyancy studies:**

*Invitro*buoyancywasdeterminedbyfloating lag timeasperthe standard method.Thetabletswere separately ina100 mlglassbeakercontaining simulated gastricfluid,pH1.2asperUSP.Thetime necessaryforthetablettoincreasetothe outside and float was determined as floatinglagtime.

Dissolution rate studies:

In vitro drug release of the sample was carried out using USP- type II dissolution apparatus (Paddle type). The dissolution medium, 900 ml 7.2 pH Buffer was placed into the dissolution flask maintaining the temperature of 37±0.50ºc and rpm of 75.One tablet was placed in each basket of dissolution apparatus. The apparatus was allowed to run for 10 hours. Sample measuring 5 ml were withdrawn after every 1 hour up to 10 hours using 10ml pipette. The fresh dissolution medium (37^{0}C) was replaced every time with the same quantity of the sample. From this take 0.5 ml and dilute up to 10 ml with 7.2 pH Buffer and take the absorbance using spectroscopy.

RESULTS AND DISCUSSION:

Pantoprazole is a proton pump inhibitor belongs togroup of benzimidazole. This compound inhibitsgastric acid formation and thereby it is very efficientfor the treatment of gastric and duodenumulcers. An enteric coated pantoprazole sodiumtablets were successfully prepared by directcompression method. Nine formulations ofPantoprazole were developed by preparing coretablets using mannitol as diluent, Aerosil as glidant,Magnesium stearate as lubricant, PVPK30 as binderandkollidone, HPC &Explotab as super disintegrants in 3 different concentrations i.e. 5%7.5%, 10% of which F3 formulation with kollidoneas super disintegrant with concentration of 10% wasselected as best formulation as it has shownmaximum drug release of 100.16% within 45 mins.

Table 1:Formulation Ingredient of Pantoprazole sodium enteric coated tablets

Formulation(mg)	F1	F2	F3	F4
Pantoprazole	40	40	40	40
Explotab	-	10%	-	-
Kollidon	-	-	10%	-
HPC	7.5%	-	-	10%
PVPK30	4%	4%	4%	4%
Mannitol	qs	qs	qs	qs
Aerosil	2.5%	2.5%	2.5%	2.5%
Magnesium stearate	2%	2%	2%	2%

Total weight	200	200	200	200

Table 2: Composition formula for Enteric coating polymers (EC1-EC4)

Ingredients	EC1	EC2	EC3	EC4
EudragitL100(%W/W)	-	-	-	-
PVAP(%W/W)	8%	-	-	-
EudragitRS100(%W/W)	-	4%	6%	8%
PEG	1.5	1.5	1.5	1.5
Acetone	QS	QS	QS	QS

Table 3: Evaluation parameters for (core tablet)

Formulations	Weight variation (mg)	Hardness (k/cm^2)	Thickness (mm)	Friability	Disintegration time	Assay %(w/w)
F1	202	3.45	2.2	0.32	1min	99.4
F2	201	3.48	2.6	0.18	48sec	100.6
F3	199	3.51	2.1	0.16	10sec	100.2
F4	201	3.51	2.0	0.28	1min 44sec	99.5

Table 4: Evaluation parameters for enteric coated tablet

EC Formulations	Weight variation (mg)	Hardness (k/cm^2)	Thickness	Friability (%)	Disintegration time	Acid resistance time	Assay %(w/w)
EC1	217	3.40	2.3	0.45	1 min 30 sec	2 hrs	98.4
EC2	205	3.41	2.7	0.48	1min 18sec	2hrs	101.6
EC3	213	3.52	2.2	0.46	1min 10sec	2hrs	101.2
EC4	216	3.52	2.1	0.48	3 min 44sec	2hrs	99.3

Table 5: Dissolution study for enteric coated tablet
Enteric coated Formulations in cumulative % drug release in 0.1N HCl Acidic Buffer

Time (hrs)	EC1	EC2	EC3	EC4
1 hr	0	0	0	0
2 hr	0	0	0	0
6.8 pH phosphate buffer				
15min	47.04	31.30	50.28	46.49
30 min	70.47	72.41	85.56	74.17
45min	85.56	84.82	100.16	83.90
60 min	92.69	91.58	100.16	93.25
120 min	100.2	98.9	100.16	100.6

CONCLUSION:

The F3 core formulation was selected and coated with three different enteric coating polymers i.e. Eudragit RS 100, Eudragit L 100 and PVAP in three different concentrations each of 4%, 6% and 8%. EC 3 formulation with Eudragit RS100 as an entericcoating polymer with concentration of 6% wasoptimized. Tablets were tested for Weight Variation,Hardness, Friability, Thickness, Disintegration Test, Assay and Dissolution. The EC3 was found to be thebest of all the enteric coated formulations. Further theEC3 formulation was subjected to comparison with marketed formulation (Aciban). Hence EC3 shows better release profile.

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