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FORMULATION AND EVALUATION OF CAPSULE CONTAINING ESOMEPRAZOLE GRANULE FOR THE TREATMENT OF GASTRIC ULCER

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ABSTRACT

Proton pump inhibitors (PPIs) are most widely prescribed classes of medications in the primary care treatment of acid-peptic diseases. Esomeprazole is a unique and potent agent for suppression of gastric acid secretion and that's how it mitigate the problem of Ulcer. In this study an attempt was made to formulate granules of Esomeprazole using wet granulation method and then finally they were entrapped in to the Capsule. Two types of granules were prepared immediate release granules and Controlled release granules by using different polymers, For Immediate release granules were prepared by using gas generating agent by sodium bi carbonate, polyvinyl pyrollidon, carboxy methyl cellulose and isopropyl alcohol as a wetting agent. and for sustained release granules hydroxyl propyl methyl cellulose, carboxy methyl cellulose were used. The purpose was to improve the of formulation bioavailability. Prepared granules were evaluated for bulk density, Tapped density, percent compressibility, Hausners ration and prepared formulation were evaluated for entrapment efficiency and In vitro drug release. The maximum drug release was found to be 45% at 180 minutes.

INTRODUCTION

The goal of drug substances is to deliver drug into the body. Consistently sophisticating and advancing pharmaceutical field have led to the development of a variety of drug delivery system. Inspite of all the advancement of drug delivery systems and its administration mode, oral administration via tablets and capsules remains the most convenient, feasible and vitally preferable route for drug delivery due to its ease to administration, non-invasive nature, economical, and patient compliance. Though there are certain limitation of the oral drug delivery like high enzymatic activity of gastrointestinal (GI) tract, acidic environment of the stomach can hinder absorption.[1]

Multi compartment and formulation contain multiunit provide high surface area of drug release and short diffusion way compared to the traditional one-unit single matrix formulations, This in the consequence improve therapeutic efficacy and reduce drug toxicity.

Capsules are unit solid dosage form, in which drug and excipients are enclosed in hard or soft gelatin shell. Hard gelatin capsules are divided into two pieces body and cap. Which are most often obtained from gelatin, sugar and water. Hard gelatin Capsule possesses ability to form non-toxic gel, which is easily soluble in biological fluids and is characterized by strong flexibility.

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Capsules filling might contain of pure active substance, with excipients or multiple units dosage forms. Capsule also have one unique advantage that is it maintain the structure integrity of multiunit forms in capsule shell unlike tablet were during the process of compression, which could destroy structure of multi units forms.[2]

Esomeprazole is a gpod proton pump inhibitor which act by reducing acid secretion through inhibition of the H+ / K+ ATP as in gastric parietal cells.[3]

The drug esomeprazole was selected due to the result of some Early studies which have shown Esomeprazole achieves greater and more sustained acid control than Omeprazole, with a similar safety profile and tolerability. Furthermore, It also shows a more rapid onset of acid-suppression effect than Omeprazole. It was also shown by some studies that it has more effective control of gastric acid at steady state than standard doses of Pantoprazole, Lansoprazole and Rabeprazole in patients with symptomatic gastroesophageal reflux disease (GERD).[4]

In this work an attempt was made to formulate modified release granules containing Esomeprazole drug to improve its bioavailability and to provide desired release profile of drug. The main objective of the study was to enhance oral bioavailability and solubility of the drug.

MATERIAL AND METHOD

Esomeprazole magnesium was obtained from matrix pharmaceutical limited Nasik as Gift sample, Methocel K4M and K50cp ,Sodium carbonate, Microcrystalline cellulose, carboxymethyl cellulose and polyvinyl pyrrolidone mannitol isopropyl alcohol were supplied by DCH limited Delhi.

PREPARATION OF SUSTAINED RELEASE GRANULES

Drug Granules were prepared by wet granulation method. The respective ingredients polymer and additives were passed through a sieve no 60 activation of PVP K-30 was done using isopropyl alcohol and the Prepared granules were dried.

IMMEDIATE RELEASE GRANULES

Fast dissolving granules were prepared by wet granulation method. Granules were prepared by mixing Esomeprazole, polyvinyl pyrollidon, carboxy methyl cellulose, sodium carbonate, using isopropyl alcohol as a wetting agent. The granules were dried at 60°C for 15 minutes in an oven.

Table 1.Different composition of Immediate release granules

S. no	Constituents	F1	F2	F3
1	Esomeprazole	19.8	19.8	19.8
2	Mannitol	46	41	36
3	Sodium bi carbonate	30	35	40
4	Polyvinyl PyrrolidoneK 30	6.9	6.9	6.9
5	Carboxymethyl cellulose	16	16	16
6	Isopropyl Alchohol	qs	qs	Qs

Table 2.Composition of Sustained release dose

S. no	Constituents	Quantity
1	Esomeprazole	14.2
2	Microcrystalline cellulose	57.1
3	Polyvinyl Pyrrolidone K30	9.5
4	Hydroxy propyl methylcellulose 50cps	19
5	Isopropyl Alcohol	Q S

EVALUATION OF PREPARED GRANULES

ANGLE OF REPOSE

The angle of repose (a) was determined using funnel method. The blend was poured through a funnel that can be raised vertically to a maximum cone height (h) was obtained. The radius of the heap (r) was measured and angle of repose was calculated.

$$= \tan^{-1}\frac{h}{r}$$

BULK DENSITY (BD)

The bulk density was determined by transferring the accurately weighed blend sample into the 100 ml graduated cylinder by keeping it in a slanting position. The initial volume and weight of granules of Esomeprazole were noted. The ratio of weight of the sample to the volume it occupied was calculated.

TAPPED DENSITY (TD)

Tapped density was determined by transferring the accurately weighed blend sample into 100 ml measuring cylinder which was placed in Electrolab Tapped Density Apparatus. Initial volume (V0) of the cylinder was noted after filling immediate and sustained release granules of Esomeprazole and then the cylinder was tapped for 100 times and the volume was measured. Further additional 500 tapings were made and the volume was noted.

COMPRESSIBILITY INDEX (CI)

Compressibility index (CI) is a measure of the feasibility of a powder to be compressed. It was calculated for Esomeprazole immediate and sustained release granules according to the equation given below,

$$CI = \frac{Tapped\ \ Density - Bulk\ \ Density}{Tapped\ \ Density} \times 100$$

HAUSNER RATIO

Hausner ratio is an indirect index of ease of powder flow. It was calculated by the following formula:

$$Hausners\ \ Ratio = \frac{Tapped\ \ Density}{Bulk\ \ Density}$$

Evaluation of Esomeprazole granules Entrapped Capsules-

ENTRAPMENT EFFICIENCY

Five capsules containing Esomeprazole granules were taken and powder equivalent to 100mg of drug was weighed and was transferred to beaker and 6.8 pH phosphate buffer was added and t was allowed to extract the drug from the granule, finally buffer was added to make the volume up to 100ml and The resultant solution was then sonicated for 15 minutes and filtered through Wattsman fileter paper. Finally a solution was diluted suitably and the absorbance of resultant solution was measured UV Spectrophoto metrically at 301 nm using UV spectro photometer Jasco V 530 against 6.8 pH buffer.

The release rate of the Esomeprazole capsule was determined using reported method in Indian Pharmacopoeia Dissolution test apparatus type – II. The dissolution test was carried out under sink condition. At appropriate time interval 30, 60, 90, 120 and 180 min) 5 ml of sample were withdrawn and was replaced with fresh media to maintain the volume constant. After dissolution and filtration the sample solution was analyzed by UV spectrophotometer at 301nm.

RESULT AND DISCUSSION

Table 3.Characterization of Immediate and Sustained release Granules

Evaluation parameters	F1	F2	F3
Bulk Density g/mL	.38	.45	.42
Tapped Density g/mL	.41	.47	.44
Percent Compressibility	0.005	0.004	0.006
Hausners Ration	1.06	1.04	1.06

GRANULES SIZE ANALYSIS

There are many methods for analyzing the size distribution of granules. for the determination of the size of granules sieving method is used. The mean diameter was found to be 630 micrometer.

Table 4.Percent drug Release in Minutes

Time (Min)	30	60	90	120	150	180
Percent Drug Release	14	28	30	35	41	45

RESULT AND DISCUSSION

A successful attempt was made to formulate granules of Esomeprazole using different concentration of Sodium bicarbonate, Hydroxy methyl cellulose, Polyvinyl Pyrollidone in order to prepare better granules. The prepared granules were subjected to evaluations like Bulk density, tapped density, percent compressibility and Hausners Ratio. Hausners ration below 1.18 considered as best and All the prepared batches showed results within the rage. Percentage compressibility below 0.15 is considered as best and in the prepared granules it was found to be within the range.

Entrapment efficiency of the formulations was found to be 89% which. In vitro release study was conducted for 180 minutes and the percent drug release was obtained was 45%.

CONCLUSION

The aim of the present research work was to enhance the bioavailability anti-ulcerative agent Esomeprazole by modified the release granules by formulating and then to capsules. From the study, it is concluded that, Both the type of granules Immediate and Sustained release granules were prepared successfully.

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