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Development and Evaluation of Pantoprazole Sodium Enteric Coated Sustained Release Matrix Tablets

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ABSTRACT

The purpose of this study was to make a comparison of the concentration levels of biopolymers such as xanthan gum, guar gum, and agar, as well as the influence of the physiochemical existence of the active ingredients on the drug release. Pantoprazole sodium tablet approach by providing (F1, F2, F3, F4, F5, and F6) were straightforwardly compacted using biodegradable polymers with microcrystalline cellulose, magnesium stearate talc, as well as PVPK30. Pantoprazole sodium tablets were seal coated (2 percent w/w weight gain) with HPMC E5 and then enteric coated with polymer HPMC-AS for weight gains of 10%, 12%, 14%, 16%, and 18% using an aqueous process. The preparation is available for rapid compression and has been measured in terms of the angle of repose, compressibility index, and sieve results obtained. These findings suggest that Pantoprazole could be used in a controlled-release drug delivery system by designing it to have greater efficacy in the therapeutic range while ignoring dangerously high levels, as is the issue with conventional formulations. These dosage forms can both decrease and increase dosing frequency.

INTRODUCTION

A peptic ulcer is a sore on the lining of your stomach, small intestine, or esophagus. A peptic ulcer in the stomach is called a gastric ulcer. A duodenal ulcer is a peptic ulcer that develops in the first part of the small intestine (duodenum). An esophageal ulcer occurs in the lower part of your esophagus.

Acid Defences in the Stomach

An unexpected elevation amount of H+ in the intestinal mucosa required a substantial shielding method to protect the esophageal and abdomen. The upper esophageal, which safeguards and prevents regurgitation, is the principal gastrointestinal resistance.

Along with the increased proliferation action and oxygen consumption of the mucous membrane, therapies that need adequate circumferential blood flow are performed. The generation of a mucin coating that supports stomach macrophages is one invaluable opportunity. When gastrointestinal mucus pours, it generates an inflexible polymer that protects the mucosal surface of the abdomen, inhibiting ion diffusion and preserving the barrier from lipid membrane injury. Pepsin, for illustration Prostanoids E2 and I2, enhance capillary permeability while ultimately lowering intra - abdominal pressure by parietal cells.

As a response, alcohol, aspirin, and other treatments that suppress gene transcription lower mucus discharge and contribute to acid-peptic sickness. The formation of bicarbonate ions by superficial gas is a further critical part of regular epithelial resistance Carbon dioxide suppresses acid in the mucosal cell upstream end, boosting pH and eliminating acid-mediated damages. [7]

Pantoprazole is a hydrogen-potassium adenosine (HPA) triphosphates H+/K+-ATPase gastric inhibitor. It belongs to the same functional group as additional commonly used proton pump inhibitors (PPIs). The FDA has approved the management of oral mucosa in the short term. PPIs blocked (H+/K+-ATPase) in the enhancing parietal cell's secretory ventricular septum in a specific way. The bioavailability of these substances can be improved by increasing the quantity of time the dosage form spends in the stomach. The gastrointestinal residence period of dosage forms can be enhanced by developing them as floating medicines. Pantoprazole is well-absorbed and has a 77 percent absolute bioavailability when it passes through first-pass metabolism. Almost one hundred tests have been conducted. The pharmacokinetics of these

medicines can be enhanced by increasing the duration spent in the stomach by the prescription form. By developing the dosage forms as floating drug carriers, the digestive residence time of the dosage forms can be extended. Pantoprazole is competently absorbed and has an absolute bioavailability from around seven percent when it crosses first-pass metabolism. Almost one thousand trials have been conducted. 40 mg just once a day for up to eight weeks if you have esophagitis. In patients with gastroesophageal reflux disease that are incompetent to take oral treatment, an i.e. dose of 40 mg given over 15 minutes once a daytime is recommended [1-2].

Matrix Tablets

Tablets with the matrix are a form of well-ordered drug delivery technique in which the medicine is delivered in a steady state via a dissolution and diffusion-controlled process. The medication is disseminated in a swell-able hydrophilic substance, which is surrounded by an insoluble matrix of hard, non-expandable hydrophobic elements or To regulate the release of therapeutic agents with widely different solubility properties, synthetic polymers are used.

Matrix Tablet Benefits

- Simple to prepare; versatile, effective, and affordable
- The sustained release preparations may be able to sustain therapeutic concentrations for longer periods.
- Sustain-release formulations are used to get around high blood levels.
- Increase the patient's willingness to comply.
- Reduce the adverse reaction of the medicine by decreasing its absorption.

Sustained Release Matrix Tablets Advantages [17-22]

- Decrease the frequency of you have dosing.
- Steady release profile across time.
- Patient engagement has increased.
- Optimizing accessibility with the shortest possible dose.

- Reduce or eliminate side effects in the surrounding area.
- Minimize or eliminate systemic adverse effects as much as possible.
- Employ chronic doses to prevent drug accumulation.
- Reduces peak-valley concentration variability.

Disadvantage of sustain-release Matrix tablets [17-22]

- Affect the time you take a dose.
- Steady release profile over time.
- Patient involvement has increased.
- Improve accessibility with the shortest dose possible.
- Reduce or eliminate side effects in the immediate vicinity.
- Reduce or eliminate systemic side effects to the greatest possible extent.

Enteric coating

Enteric coating is a coating that controls drug release into the gastrointestinal tract. It safeguards acid-labile drugs from gastric juice (HCl). Enteric-coating tablets rise gastrointestinal tract pH but do not release a drug in the abdomen; however, when enteric-coated medicines reach the top part of the small intestine, they dissolve and release of drug in basic pH. Various types of enteric coating polymers are used in enteric-coated. There are subsequent effects of enteric coating, Enteric coating prevents drug disintegration in gastric acid and protects the release of the drug into the abdomen.

MATERIAL AND METHODS

Pantoprazole was received as a gift sample from Mylan, Hyderabad. Xanthan gum was procured from Serine Formulations private limited. Guar gum, MCC, and PVP K30 were procured from Mylan, International Specialty Product Technologies limited, and BASF Pvt ltd respectively.

PREFORMULATION STUDY

Identification of drug by UV spectrophotometry

Pantoprazole sodium was recognized by UV visible spectrophotometry; an operating standard solution of pantoprazole sodium was manufactured in buffer solution and scanned for UV absorption within the assortment of 200–400 nanometers. The wavelength of supreme absorbance (λmax) of the drug was examined and compared with the reported λmax given in the literature.

Analytical method development

A) Determination *of* λmax of pantoprazole sodium

In a buffer solution, a 1mg/ml dosage of pantoprazole sodium was synthesized and then diluted to take a sample of 10µg/ml concentration. In the case of a buffer as a benchmark blank, the sample was measured in UV spectrophotometry and the wavelength of absorbance values (max) of the medication was established.

B) Calibration curve

Preparation *of standard stock solution*

Pantoprazole sodium (100 mg) was measured in a conical flask with a capacity of 100 mL. A 25ml buffer mixture was prepared, and the mixture was vortex mixed. To acquire a 1mg/ml concentration of pantoprazole sodium, the volume was adjusted to 100ml after the drug was dispersed.

Preparation of working stock solution

A 10 mL standard solution was evacuated and transferred to a 100 mL volumetric flask. The volume is been set to 100 mL with a buffer.

Preparation of calibration sample and validation sample

To obtain 5, 10, 15, 20, and 25 µg/ml solutions, the operating stock solution was diluted again with buffer solution (calibration samples). By adequately diluting the working stock, replicate samples of various concentrations at the top (24 µg/ml), middle (16 µg/ml), and lower (6 µg/ml) concentration levels of the correct range were made from the same functioning

solution.

From the same source of operation by diluting the experimental stock solution with buffer solution, way to solve bleed of three distinct proportions were made at the highest (24 µg/ml), middle (16 µg/ml), and lower (6 µg/ml) concentration levels of the mass customization.

Preparation of calibration curve:

In a UV-visible spectrophotometer, the different concentrations of comparative evaluation samples were estimated against such a buffer solution as a baseline at the maximum (292 nm) of pantoprazole sodium. The measurement equation was then obtained by plotting the acquired absorption spectra against their corresponding times using least-squares linear regression.

PREPARATION OF BLEND

All the constituents are eluded in the following table.

Table 1: Ingredients used in Pantoprazole sodium tablets formulations

Formulation code /compositions	**F1 (mg)**	**F2 (mg)**	**F3 (mg)**	**F4 (mg)**	**F5 (mg)**	**F6 (mg)**
Pantoprazole	40	40	40	40	40	40
Xanthum gum	25	30	-	-	-	-
Guar gum	-	-	25	30	-	-
Agar	-	-	-	-	25	30
Talc	2	2	2	2	2	2
Microcrystalline cellulose	25	20	25	20	25	20
Magnesium stearate	4	4	4	4	4	4
PVPK30	4	4	4	4	4	4

EVALUATIONS OF DRUG BLEND FOR TABLETING

The drug blend for direct compression is evaluated for the following parameters.

A) The Angle of Repose: The funnel mechanism is used to accomplish this. When measured particles are permitted to smoothly run throughout a funnel, a stack of blend forms on the top.

The angle of repose can be computed using the formula, Tan Ø= h/r

Table 2: Relationship between Angle of repose and flow properties

Flow Property	Angle of repose(degree)
Excellent	25-30
Good	31-35
Fair-aid not needed	36-40
Passable -may hang up	41-45
Poor must agitate, and vibrate	46-55
Very poor	55-65
Very, very poor	>66

Bulk Density: The bulk density is determined by pouring the pre-weighed mixture into a graduated measuring cylinder.

Bulk density = Mass/Bulk volume

It is the method for calculating bulk density

Tapped Density: The measuring cylinder contains a known mass of mix that has been tapped for a set amount of time. Following formula help in the determination of Tapped density.

Tapped density = Mass/Tapped volume

Carr's Index: It is also known as Carr's compressibility index and is a tool for determining granule flow characteristics.

Carr's index = (Tapped density - Bulk density)/Tapped density

Hausner's Ratio: The ratio of tapped density to bulk density is known as Hausner's ratio

Hausner's ratio = Tapped density / Bulk density

Table 3: The optimized Sub-coating of Prepared Core Tablets

Coating parameter	Values	Coating parameter	Values
Inlet temperature	50 °C	Pan RPM	37
Bed temperature	47°C	Gun-to-bed distance	5 cm
Spray feed RPM	2	Atomizing air	1.5 PSI

Table 4: Coating Parameters

Coating Parameter	Values	Coating Parameter
Bed temperature	65 °C	Gun-to-bed distance
Spray feed RPM	1	atomizing air

RESULT AND DISCUSSION

Table 5: Pantoprazole pre-formulation study results

S. No.	Parameter	Inference	Outcome
1.	Organoleptic characteristics		
	Color	yellow colored	**yellow colored**
	Taste	metallic taste	**metallic taste**
	Texture	Smooth	**Smooth**
2.	Solubility	Water-insoluble, somewhat soluble in phosphate buffer pH7.4, & unsolvable in n-hexane	**Water-insoluble, somewhat resolvable in phosphate buffer pH7.4, & insoluble in n-hexane**
3.	pH	9.9 (2% solution)	**9.9 (2% solution)**
4.	Melting Point	197° C	**197 ° C**
5.	Odor	Pungent	**Pungent**
6.	**Particle size analysis**	**Avg Particle size 0.498±0.051**	**Avg Particle size 0.498±0.051**

Table 6: UV Spectroscopic study

Sr. No.	Concentration (µg/ml)	Absorbance (nm)
1.	5	**0.249**
2.	10	**0.353**
3.	15	**0.468**
4.	20	**0.587**
5.	25	**0.702**

Calibration of UV-visible spectroscopy method

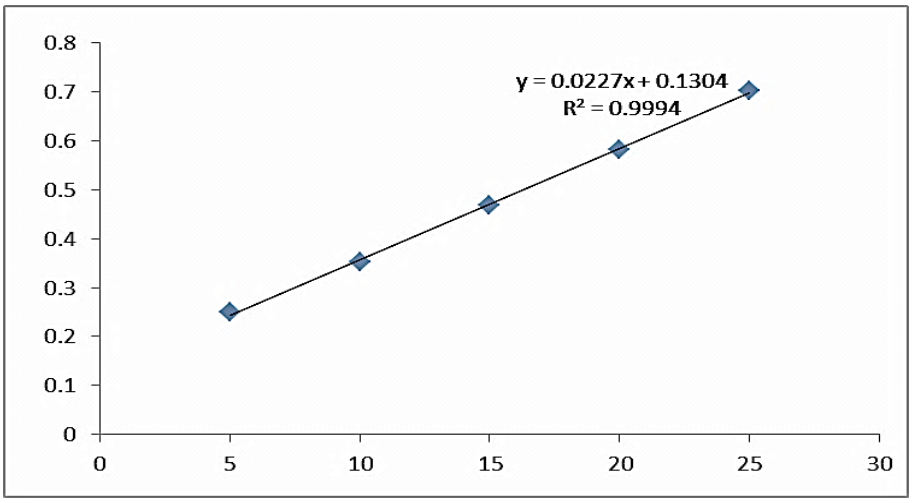

Figure 1: Calibration curve of Pantoprazole

The FTIR spectroscopy studies were carried out for pure drug alone and a combination of drug and polymer. FTIR spectrum of pantoprazole alone and their physical mixture of Guar gum and Xanthum gum.

The FTIR spectroscopy studies were carried out for pure drug alone and a combination of drug and polymer. FTIR spectrum of pantoprazole alone and their physical mixture of Guar gum and Xanthum gum are shown in Figure below.

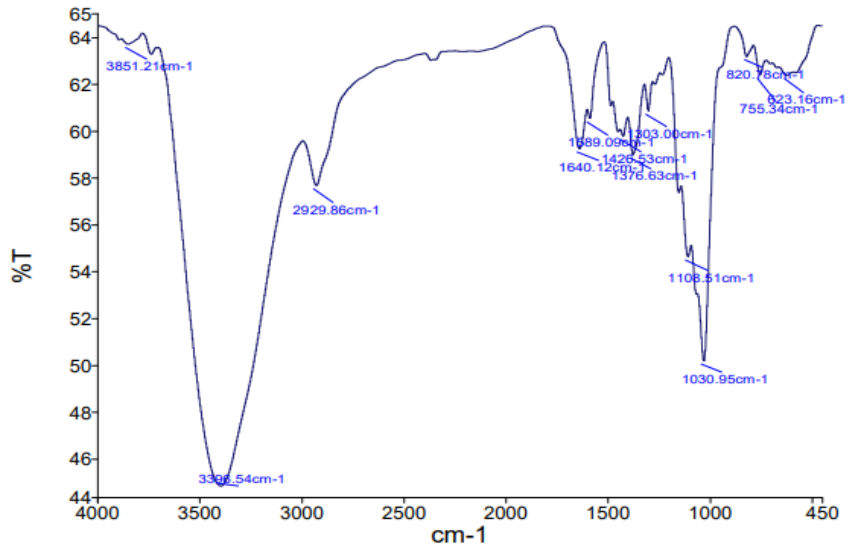

Figure 2: FTIR Spectra of Pantoprazole

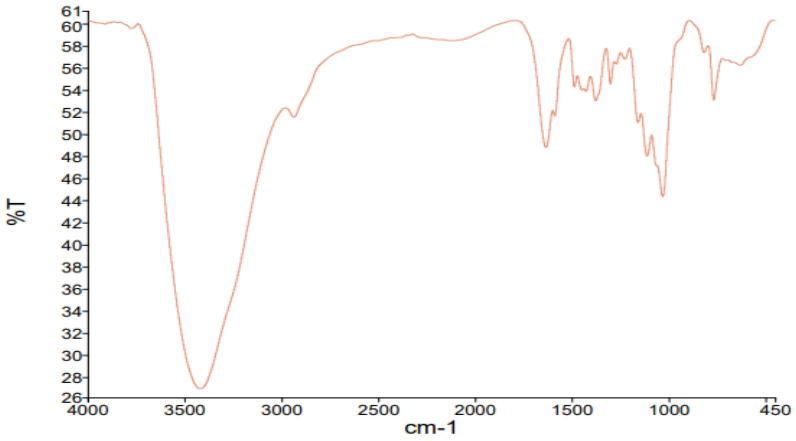

Figure 3: FTIR Spectra

Table 7: Evaluation parameters for uncoated tablets of pantoprazole sodium

Sr. No.	Formulation code/Constraint	Hardness (units)	Weight variation	Friability (%)	Content uniformity
1.	F 1	4.1 ± 0.72	Pass	0.41 ± 0.05	**98.64±2.8**
2.	F 2	4.5 ± 0.03	Pass	0.21 ± 0.02	**99.43±3.1**
3.	F 3	4.3 ± 0.02	Pass	0.45 ±0.03	**99.61±2.6**
4.	F 4	4.9± 0.03	Pass	0.23 ± 0.02	**100.2±3.2**
5.	F 5	4.4± 0.03	Pass	0.24 ± 0.01	**98.24±2.1**
6.	**F 6**	**4.7± 0.05**	**Pass**	**0.15 ± 0.03**	**99.62±1.1**

Table 8: Evaluation of Enteric Coated Tablets

Formulation	Mean thickness(mm)	Mean hardness (Kg/cm2)	Mean diameter (mm)	Weight(mg)
F1	4.90	4.8±7.2	5.1±2.1	**134 ±2.9**
F2	5.01	5.1±0.04	5±1.8	**136± 2.5**
F3	5.08	4.7±0.02	5±2.8	**138.1 ± 3.1**
F4	5.11	5.3±0.02	5±3.9	**139.2±2.6**
F5	5.18	4.9±0.04	5±5.1	**137 ±3.4**
F6	**5.24**	**4.6±0.07**	**5±6.3**	**139±3.4**

Table 9: In-Vitro dissolution studies

Time(hr)	F1(%)	F2(%)	F3(%)	F4(%)	F5(%)	F6(%)
0.5	31	32	26	22	36	32
1	43	38	38	32	43	41
2	52	46	46	41	55	51
3	64	58	52	48	67	63
4	67	66	64	56	74	69
5	82	72	76	62	85	82
6	89	85	83	69	92	89
7	93	92	88	74	94	93
8	98	94	92	82	98	95
9			95	90		97
10			98	93		
11				97		
12				99		

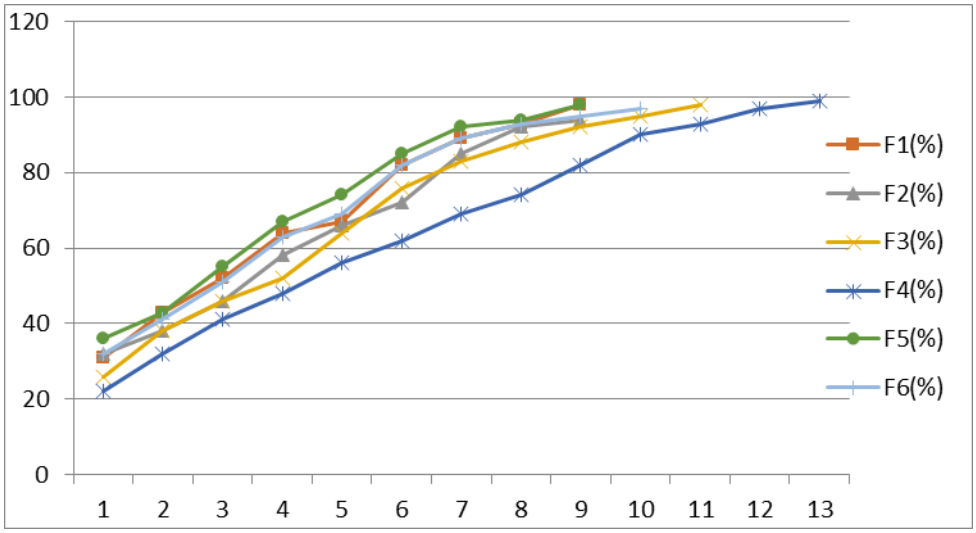

Figure 4: Cumulative % drug release

CONCLUSION

The purpose of this study was to make a comparison of the concentration levels of biopolymers such as xanthan gum, guar gum, and agar, as well as the influence of the physiochemical existence of the active ingredients on the drug release.

Pantoprazole sodium tablet approach by providing (F1, F2, F3, F4, F5, and F6) were straightforwardly compacted using biodegradable polymers with microcrystalline cellulose, magnesium stearate talc, as well as PVPK30. Pantoprazole sodium tablets were seal coated (2 percent w/w weight gain) with HPMC E5 and then enteric coated with polymer HPMC-AS for weight gains of 10%, 12%, 14%, 16%, and 18% using an aqueous process. The preparation is available for rapid compression and has been measured in terms of the angle of repose, compressibility index, and sieve results obtained.

These findings suggest that Pantoprazole could be used in a controlled-release drug delivery system by designing it to have greater efficacy in the therapeutic range while ignoring dangerously high levels, as is the issue with conventional formulations. These dosage forms can both decrease and increase dosing frequency.

The methodology used in the preparatory work of matrix systems, direct compression, is highly practical and expensive in the economic system. When trying to compare too many other formulations, the tablet usually contains Guar gum as an enduring polymer at an

accumulation of 50% had good sustainability, with >80% release profile for 12 hours. F4 will be used to conduct additional product development research.

The dissolution data from the augmented formulation were exposed to release kinetics; the release kinetics outcomes indicate that the composition accompanied the Higuchi drug release rate.

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