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Design, Development and Evaluation of Antacid Used in Peptic Ulcer

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A B S T R A C T

A much larger proportion of individuals administered antacids exhibited a decrease above 50% in ulcer size compared to those receiving a placebo. But, Additionally, full healing, devoid of any signs of inflammation, occurred significantly more frequently in the antacid-treated group compared to the placebo-treated group. Statistically, the antacid group had more people who had their ulcer pain go away than the placebo group. Taking aluminum-magnesium hydroxide tablets as an antacid seems to speed up the healing of ulcers. Smoking cigarettes made ulcers heal more slowly, but starting to have signs of an ulcer at a young age and having too much acid in the body were good for healing. Pantoprazole is a proton pump inhibitor that belongs to the benzimidazole group. Pantoprazole sodium was made by directly compressing microcrystalline cellulose, mannitol, and dicalcium phosphate in different amounts. Crosscarmellose sodium was used as a disintegrating agent, and magnesium stearate and talc were used as a glidant and lubricant, respectively. Direct compression is cheaper than wet granulation because it needs fewer steps. This implies that fewer machines, less electricity, less space, less time, and less work are needed to make tablets, which lowers the cost of making them. The tablets that were made were tested for hardness, weight fluctuation, friability, and drug content consistency, and the findings were determined to meet regulatory criteria. We used enteric coating polymers such cellulose acetate phthalate and Eudragit L100 to coat the pills. We did this by dipping them in the coating.

Keywords: Peptic Ulcer, Pantoprazole, antacid, proton pump inhibitor.

1. Introduction

The stomach connects to the esophagus at the cardiac sphincter and to the duodenum at the pyloric sphincter. It possesses two curvatures. The stomach has three regions: the fundus, the body, and the antrum. The pyloric sphincter, located at the distal end of the pyloric antrum, regulates the entrance between the stomach and the duodenum. When the stomach is inactive, the pyloric sphincter remains relaxed and open; conversely, when the stomach contains food, the sphincter is closed. Temporary storage facilitates the digestive process, including chemical digestion, iron preparation for absorption, and the creation of intrinsic factor essential for vitamin B12 absorption in the terminal ileum, while regulating the transit of stomach contents into the duodenum. Once the chyme is adequately acidified and liquefied, the pyloric antrum propels tiny jets of stomach contents through the pyloric sphincter into the duodenum. The stomach produces around 2.5 liters of gastric juice each day. The primary exocrine secretions include proenzymes like prorenin and pepsinogen produced by chief or peptic cells, as well as hydrochloric acid (HCl) and intrinsic factor released by parietal or oxyntic cells. Mucus-secreting cells are prevalent among the surface cells of the stomach mucosa. Bicarbonate ions are released and retained in the mucus, forming a gel-like protective barrier that sustains the mucosal surface at a pH of 6-7 despite a significantly more acidic environment (pH 1-2) in the lumen. Gastric acid secretion is a multifaceted, ongoing process influenced by several central and peripheral variables culminating in the production of H+ by parietal cells. Neuronal (acetylcholine, ACh), paracrine (histamine), and endocrine (gastrin) agents together modulate acid secretion. Their particular receptors (M3, H2, and CCK2) are located on the basolateral membrane of parietal cells in the gastric body and fundus. The elevated concentration of H+ in the gastric lumen necessitates strong protective systems for the esophagus and stomach. The principal esophageal defense is the lower esophageal sphincter, which inhibits the reflux of acidic stomach contents into the esophagus. The stomach safeguards itself against acid damage by many processes that need sufficient mucosal blood flow, perhaps due to the elevated metabolic activity and oxygen demands of the gastric mucosa. A primary defense mechanism is the production of a mucus coating that safeguards stomach epithelial cells. Gastric mucus is initially soluble upon secretion but rapidly transforms into an insoluble gel that adheres to the stomach's mucosal surface, impeding ion transport and safeguarding the mucosa from injury by macromolecules like pepsin. Prostaglandins E2 and I2 increase mucus formation and directly block stomach acid release by parietal cells. Consequently, alcohol, aspirin, and other substances that suppress prostaglandin synthesis reduce mucus production and increase susceptibility to acid-peptic illness.

1.1 Classification of drug delivery system

- Controlled release

- Delayed release
- Extended release
- Sustained release
- Site specific targeting
- Receptor targeting

1.1.1 Extended Release Drug Therapy

A device that delivers the medication continuously for a predefined amount of time with predictable and repeatable kinetics and a known mechanism of release is implied by the phrase "controlled/extended release." This indicates that the medicine is released from a controlled release drug delivery device at a kinetically predictable and repeatable pace from one unit to another. Stated differently, the system aims to regulate the amount of medication present in the target tissue. Because dosage form design is more flexible, there has been increased interest in the oral mode of administration for prolonged release systems. Several interconnected factors of significant relevance influence the design of oral extended release delivery systems, including the kind of delivery system, the condition being treated.

2. Material and Methods

Apparatus and chemicals: Pentoprazole by Reine Life Science, Gujarat, Microcrystalline Cellulose by Ankit pulps chemicals pvt, Maharashtra, Lactose and magnesium stearate by Zytex biotech pvt limited, Gujarat.

Methods: Preparation of matrix tablet.

An optimal blend of granules was immediately compressed into tablets weighing about 200 mg, comprising 40 mg of pantoprazole sodium sesquihydrate, via rotating tablet compression. Riddhi 10 station micro tablet press RDB4-10, manufactured by Rimek in Ahmedabad, India, utilising 8 mm diameter concave punches. The various batches of pantoprazole pills were gathered and kept in airtight containers.

Table 1: Formulation for Pantoprazole Tablet formulation

Composition	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**
Pantoprazole sodium (mg)	40	40	40	40	40	40	40	40	40
Croscarmellose sodium (mg)	2	4	6	2	4	6	2	4	6
Microcrystalline cellulose(mg)	27	25	23	27	25	43	80	50	23
Mannitol (mg)	50	75	100	40	85	80	43	50	75
Dicalcium phosphate (mg)	75	50	25	85	40	25	75	50	50
Talc (mg)	2	2	2	2	2	2	2	2	2
Magnesium stearate (mg)	4	4	4	4	4	4	4	4	4
Total weight (mg)	200	200	200	200	200	200	200	200	200

3. Experimental work

3.1 Preformulation Studies

The study of physicochemical properties, both drug and drug with excipients, is known as preformulation. Preformulation studies aim to identify the physicochemical properties and excipients that may affect the manufacturing process, formulation design, and pharmacokinetic-biopharmaceutical aspects of the final product.

3.2 Determination of Solubility

Solubility was determined by dissolving drug in various solvent like ether, acetone, alcohol and water.

3.3 UV and FTIR Spectroscopy

The wavelength of maximum absorbance was then found by scanning the solution containing 10µg/ml at 274 nm.

The reference standard FT-IR spectra of Pantoprazole and the acquired FT-IR spectrum of Pantoprazole were compared.

4. Result and discussion

4.1 Preformulation Study

4.1.1 Description

Pantoprazole is off-white to white crystalline powder with bitter taste

4.1.2 Result of Solubility

Pantoprazole is soluble in water and ethanol.

4.2 Result of Melting Point

The medicine's melting point was determined to be comparable to the stated value, confirming that the drug samples that were received met the stated specifications. The melting point of a particular pharmacological ingredient will vary depending on any impurities that may be present. Pantoprazole has a reported melting point of 139°C .

4.3 UV Spectroscopy

A peak with an absorbance was seen at 274 nm in a solution of 10µg/ml in methanol. The identity of the Pantoprazole molecule is confirmed by the absorbance maxima at 274 nm, which is one of its hallmarks.

4.3.1 FT-IR Spectroscopy

The drug's infrared spectrum was found to be comparable to Pantoprazole's normal infrared spectrum, indicating that the sample was pure. This validates the Pantoprazole identity.

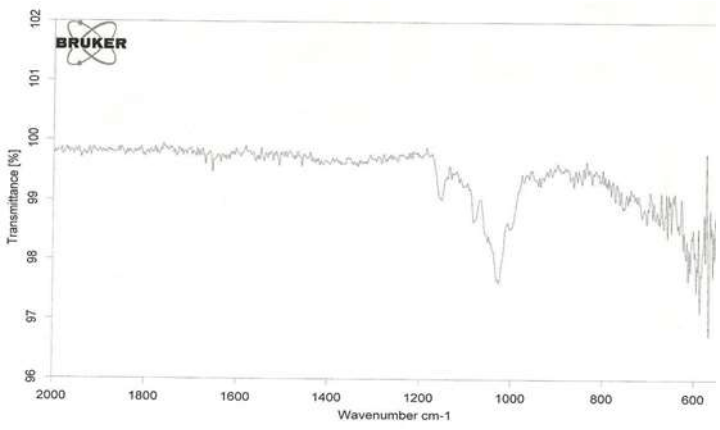

Fig 3. FT-IR of Pantoprazole

4.4 Drug - Excipients Compatibility Study

FT-IR Spectroscopy

The drug and excipients were found to be compatible after FTIR analysis of the physical mixes of the drug and excipients.

When the IR spectra of Pantoprazole, excipients, and their combination are compared, all of the Pantoprazole's distinctive bands are discovered to be intact.

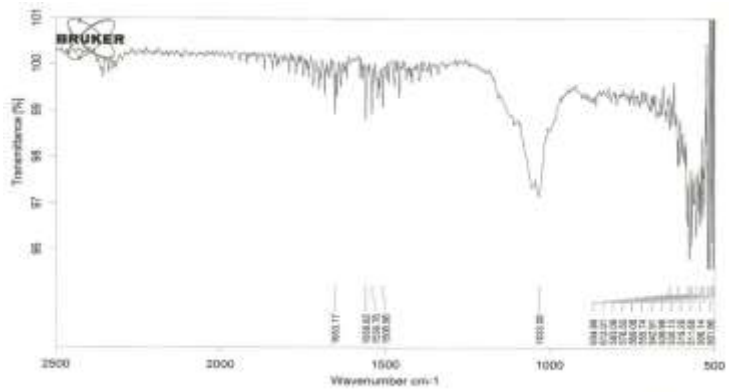

Figure 3 FT-IR Spectra of Pantoprazole and Excipients

4.5 Evaluation of Matrix Tablet

4.5.1 Pre compression parameters

Table.No.:2. Evaluation parameters of powder blend.

Formulation	Bulk density (g/ml) ± SD	Tapped density (g/ml) ± SD	Carr's index	Hausner's Ratio	Angle of repose(θ)
F1	0.357±0.03	0.384±0.05	7.03±0.09	1.075±0.04	28.31±0.26
F2	0.312±0.04	0.335±0.02	6.86±0.15	1.073±0.05	27.20±0.14
F3	0.306±0.03	0.326±0.03	6.13±0.12	1.065±0.02	29.13±0.34
F4	0.312±0.03	0.334±0.06	6.58±0.14	1.070±0.06	26.13±0.26
F5	0.306±0.03	0.334±0.05	8.38±0.17	1.091±0.08	26.78±0.18
F6	0.384±0.04	0.429±0.05	10.48±0.20	1.117±0.07	25.79±0.24
F7	0.358±0.05	0.385±0.04	7.01±0.13	1.075±0.03	29.52±0.14
F8	0.286±0.05	0.313±0.04	8.62±0.07	1.094±0.03	26.95 ±0.15
F9	0.348±0.08	0.328±0.05	5.74±0.13	1.06±0.08	26.13±0.26

Table.No.:3. Physical Parameters of Pantoprazole Matrix Tablets

Formulation	Weight variation**	Disintegration time*	Hardness (kg/cm2)	Friability (%)	Drug content*
F1	199 ± 0.12	10.6± 0.62	5.80 ± 0.12	0.69 ± 0.015	96.28 ± 0.15
F2	206 ± 0.24	8.26± 0.56	5.56 ± 0.24	0.51 ± 0.017	97.62 ± 0.27
F3	201 ± 0.17	5.38± 0.23	5.83 ± 0.08	0.48 ± 0.014	99.51 ± 0.36
F4	208 ± 0.20	11.48± 0.15	4.93 ± 0.15	0.64 ± 0.015	98.17 ± 0.16
F5	203 ± 0.16	9.32± 0.18	5.73 ± 0.25	0.71 ± 0.016	98.92 ± 0.42
F6	206 ± 0.14	6.13± 0.25s	5.12 ± 0.34	0.68 ± 0.026	100.34 ± 0.13
F7	199 ± 0.22	10.54± 0.43	5.66 ± 0.17	0.54 ± 0.026	98.50 ± 0.48
F8	204 ± 0.18	9.12± 0.71	6.20 ± 0.35	0.49 ± 0.025	98.41 ± 0.34
F9	198 ± 0.15	6.02± 0.21	5.60 ± 0.24	0.42 ± 0.018	99.08 ± 0.35

4.5.7 In-vitro release of study

The dissolution release profile of different formulations was examined in vitro. The formulations F1 through F9 were shown to dissolve in vitro based on the findings of controlled release tests. Formulation F8, which has a 12-hour release profile, was chosen to formulate the matrix tablet.

Table.No.:5. In vitro Dissolution profile Pantoprazole Tablet release tablets

Time in min	**Absorbance**	**Conc.**	**Conc. In 900 ml**	**Loss**	**Cumulative loss**	**Cumulative drug release**	**Cumulative percentage drug release**
0	0	0	0	0	0	0	0
60	0	0	0	0	0	0	0
90	0	0	0	0	0	0	0
105	0.024	0.6469	5.822	0	0	5.822	14.62+0.52
120	0.06	1.6172	14.555	0.0064	0.0064	14.561	36.58+0.40
135	0.091	2.3884	21.496	0.0161	0.0226	21.518	54.05+0.90
150	0.121	3.1758	28.582	0.0238	0.0465	28.629	71.91+0.39
165	0.142	3.7270	33.543	0.0317	0.0782	33.621	84.46+0.17
180	0.162	4.2519	38.267	0.0372	0.1155	38.383	96.42+0.40

4.6 Stability Studies of best Formulation

Table.No.:6. Stability studies of optimized formulation F9

Parameters	**Initial**	**1st Month**	**2nd Month**	**3rd Month**
Physical Appearance	White colour tablets	No Change	No Change	No Change
Hardness (kg/cm2)	6.3 ± 0.14	6.2 ± 0.56	6.2 ± 0.64	6.2 ± 0.26
Drug Content (%)	98.54 ± 0.12	98.36 ± 0.52	98.16 ± 0.36	98.07 ± 0.28

5. Conclusion

This research use both polymers as enteric coating agents, identifying the optimal composition. CAP and Eudragit L100 were utilised in concentrations of 6% and 8%, respectively, yielding the optimal formulation. The dissolving experiments indicated that the enteric-coated polymer remained intact for 2 hours in a pH 1.2 buffer. The optimal formulation is C2F9, designated as formulation number 9, and is coated with 8% CAP. The study demonstrated that pantoprazole enteric-coated tablets are effective for treating ulcers and gastro-oesophageal reflux disorder (GERD). Hence, formulation of pantoprazole as an enteric coated tablet may solve the stability problem of drug in the stomach and release the drug in the intestine. Following satisfactory pre-compression and post-compression results of the core tablets, the tablets were coated with an appropriate coating material to enhance the dosage form, therefore mitigating drug degradation caused by gastrointestinal enzymes and the acidic environment of the stomach.

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References

1. Leon Lachman, Herbert A. Lieberman, Joseph L. Kaing, “The theory and practice of industrial pharmacy”, Verghese Publishing, Indian edition, 3rd edition, 1987, Pg. No.293- 345.

2. Donald, I.Wise. “ Hand book of pharmaceuticals controlled release technology”, Marcel Dekker 1st edition, 2005, Pg. No. 211-253.

3. Anne W, Allison G, in Ross, Wilson. Anatomy and Physiology in Health and Illness. 9th Ed: Churchill Livingstone, Spain; 2001; 296.

4. Rang HP, Dale MM, Ritter JM, Morre PK . Pharmacology. 5th Ed: Churchill Livingstone, 2005; 374.

5. Laurence L, John S, Keith L, in Goodman & Gilman's The pharmacological basis of therapeutics. 11th Ed, McGraw-Hill, 2006: 623- 634.

6. Tripathi KD. Essential of Medical Pharmacology. 5th Ed. Jaypee Brothers Medical Publishers (P) Ltd. New Delhi: 2003; 631

7. Joseph T, Robert L, Gary C, Gary R, Barbara G, L. Michael. Pharmacotherapy: A Pathophysiologic Approach, 6th Ed. 613-615.

8. Nicole GM. Clinical effects of proton pump inhibitors. Erasmus University.2010;1-2.

9. Richard F, Michelle A, Luigi X. Lippincott's Illustrated Reviews: Pharmacology, 4th Ed. Lippincott Williams & Wilkins. 2009; 331.

10. Bertram GK, Susan B. Masters, Anthony J. Trevor. Basic & Clinical Pharmacology, 11th Ed. by The McGraw-Hill Companies, 2009; 1479.

11. Jayesh P, Manish R. Tablet Formulation Design And Manufacture: Oral Immediate Release Application. Pharma Times April 2009; 41(4): 22.