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Formulation and Evaluation of Orodispersible Tablet of Cimetidine

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ABSTRACT :

The main goal of this study is to create and compare the orodispersible capsules of H_2 blockers using a direct compression method. All of the formulations had been arranged using three super disintegrants. All the formulations have been tested for various parameters like hardness, weight, friability, wetting time, and many others to ensure their quality. The formulations were evaluated in a lab environment and were selected primarily on the basis of their hardness, wetting time, and disintegration time. The final outcomes revealed that the disintegration time decreased as a result of the utilization of exceptional disintegrants, and the drugs also exhibited the desired hardness. This is likely because of the high wicking and capillary action of crosspovidone, as well as its greater gelling tendency compared to sodium starch glycolate and crosscarmellose sodium. Among all the six formulations, the exceptional system was selected as the one to change An extremely efficient disintegrant was used in the creation of a quick-acting medication delivery system for cimetidine.

Keywords : Ulcerprotective Tablet, Orodispersible Tablet ,H_2 blocker .

Introduction

The concept of fast-dissolving capsules objectives to provide sufferers a more conventional technique for administering their remedy. Many individuals, especially the aged and pediatric populations, enjoy dysphasia, that is the difficulty in swallowing, due to numerous physiological adjustments. speedy-dissolving pill formulations that dissolve or disperse in saliva inside the mouth facilitate easier swallowing for severa patients, which includes youngsters, older adults, and adults who decide on the benefit of effortlessly ingestible dosage bureaucracy. those pills hastily dissolve at the tongue, liberating the energetic aspect at a pH of 6.8 in saliva.[1] according to the eu Pharmacopoeia, "rapid dissolving" refers to tablets that ought to dissolve on the tongue in beneath 3 mins after ingestion. whilst strong dosage paperwork are the most prevalent, they frequently present the undertaking of dysphagia. To deal with this difficulty, modern strong dosage forms like speedy-dissolving tablets had been developed, which dissolve swiftly in saliva with out the want for water. This speedy dissolution helps to avoid first-skip metabolism and complements the bioavailability of the lively ingredient. [2]Cimetidine, a commonly prescribed medication, has been utilized for more than four decades in managing gastrointestinal issues caused by excess stomach acid. First introduced in the 1970s, cimetidine transformed the management of peptic ulcer disease, gastroesophageal reflux disease (gerd), and zollinger-ellison syndrome, providing a safer and more effective alternative to previous treatments. The pharmacological properties of cimetidine, such as its ability to compete with histamine for binding to h2-receptors on parietal cells, have been extensively studied and documented.[3]. This mechanism of action is crucial to its effectiveness in reducing gastric acid production, which aids in ulcer healing and provides relief from symptoms related to acid-related conditions. Despite the emergence of newer treatments like proton pump inhibitors (ppis), cimetidine remains a crucial and advantageous choice in certain medical situations. Additionally, ongoing research is uncovering new potential applications for cimetidine, such as its potential use as a supplementary treatment in cancer therapy. The purpose of this paper is to provide a comprehensive analysis of the current literature on cimetidine, examining its pharmacological characteristics, efficacy, safety profile, and medical uses. Furthermore, we will delve into the recent advancements in research regarding the innovative applications of cimetidine, highlighting its potential as a versatile therapeutic tool in contemporary clinical practice.[3,4].

Properties

Physical Properties:

1. Appearance: White or off-white crystalline powder
2. Solubility: Soluble in water and ethanol
3. Melting Point: 140-145°C
4. Molecular Weight: 252.34 g/mol
5. Molecular Formula: C10H16N6S

Pharmacological Properties:

1. Mechanism of Action: Competitive inhibition of histamine binding to H2-receptors on parietal cells
2. Histamine H2-Receptor Antagonism: Reduces gastric acid secretion
3. Antiulcer Activity: Heals and prevents ulcers
4. Antisecretory Activity: Reduces gastric acid secretion

Pharmacokinetic Properties:

1. Absorption: Rapidly absorbed from the gastrointestinal tract
2. Distribution: Widely distributed throughout the body
3. Metabolism: Metabolized in the liver by the cytochrome P450 enzyme system
4. Elimination: Excreted in the urine, with a half-life of approximately 2-3 hours
5. Bioavailability: 60-80% after oral administration

Therapeutic Properties:

1. Treatment for Zollinger-Ellison syndrome, gastric ulcers, duodenal ulcers, and gastroesophageal reflux disease (GERD)
2. Prevention of: Stress-induced ulcers and aspiration pneumonia
3. Adjuvant Therapy: Cancer treatment [5,6,7]

Advantages

1. Effective in Healing Ulcers
2. Rapid Onset of Action
3. Long Duration of Action
4. Oral and Parenteral Administration
5. Cost-Effective
6. Immunomodulatory Effects
7. Reduced Risk of Ulcer Complications [8]

Disadvantages

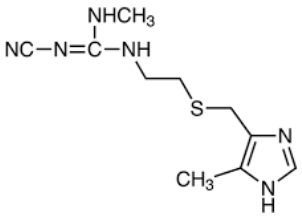
1. Gynecomastia and Impotence
2. Central Nervous System Side Effects
3. Interactions with Other Medications
4. Rebound Hyperacidity
5. Bone Marrow Suppression
6. Hepatotoxicity
7. Renal Impairment[9]

Drug profile : Cimetidine

Generic name : Cimetidine IUPAC Name :

N-cyano-N'-methyl-N''-[2-[[(5-methyl-1H-imidazol-4-yl)methyl]thio]ethyl]guanidine Chemical formula : C10H16N6S

Structural formula :



Molecular weight: 252.34g/mol

Route of elimination : kidney

Mechanism of Action of Cimetidine

Cimetidine a histamine h2-receptor antagonist, exerts its anti-ulcer effects through a specific mechanism of action.), cimetidine competitively inhibits histamine binding to h2-receptors on parietal cells in the stomach, thereby reducing gastric acid secretion [10]. This mechanism of action is supported by the findings of a study that showed cimetidine to effectively inhibit gastrin-stimulated acid secretion in a dose-dependent manner [11]. Clinical implications the mechanism of action of cimetidine underlies its clinical use in treating conditions such as peptic ulcers, gastroesophageal reflux disease (gerd), and zollinger-ellison syndrome. Cimetidine has demonstrated its efficacy in treating duodenal ulcers and reducing the likelihood of their recurrence [12]. Antagonism of Histamine H2-Receptors. Cimetidine's main way of working is by blocking histamine h2-receptors. Cimetidine has a strong affinity for histamine h2-receptors, effectively blocking histamine from binding and triggering acid secretion. This process is unique to histamine h2-receptors and does not impact other receptors or enzymes responsible for gastric acid production.

Excipent profile :

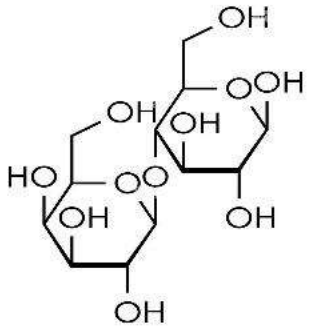
1) Lactose monohydrate

IUPAC Name : 4-O-β-D-Galactopyranosyl-D-glucopyranose monohydrate

Molecular weight : 360.31 g/mol

Molecular formula : C12H22O11·H2O

Structural formula :

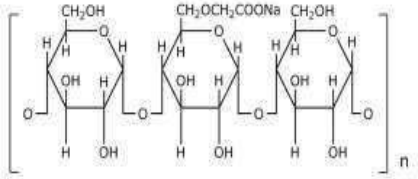


2) Sodium starch glyacolate

IUPAC Name : Sodium (2S,3S,4R,5R)-2,3-dihydroxy-6-[(2R,3R,4S,5R,6R)-3,4,5-trihydroxy-6- (hydroxymethyl)oxan-2-yl]oxyhexanoate

Molucular formula : (C6H9NaO6)n

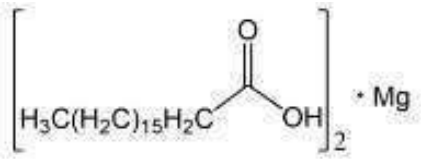
Stuctural formula :



3)Magnesium stearate

Chemical Formula: C36H70MgO4

Structutal formula



Materials and Methods :

Materials: Cimetidine , Microcrystalline cellulose , Crosspovidone , Sodium starch glycolate , Magnesium stearate , Aspartame , Peppermint oil .

Preformulation Studies:

Angle of Repose:

The cimetidine mucoadhesive microspheres' angle of repose was evaluated using a fixed funnel technique. The angle of repose, denoted by the symbol θ, was used to determine the microsphere granules' flow characteristics. The funnel aperture was placed on a level surface covered with paper, and the created microsphere granules were let to pass through. The following is the formula for determining the angle of repose. [14]

$$\theta = \tan^{-1} \times h / r$$Where,

θ = angle of repose

h = height of the pile

r = radius of the pile

Bulk Density (BD):

The homogeneity of particles is measured using bulk density. Particle cohesiveness, particle range, particle size, and particle shape all affected the material's bulk density. With the use of a balance, the test substance was precisely weighed. To find the bulk density of the microspheres, use a dry cylinder apparatus. The amount of material may be altered by adjusting the cylinder device capacity. A cylinder filled with the specified substance was used to precisely measure the material's apparent volume. Without any prior attention, the filled material settled in the cylinder. The bulk density of the specified materials was determined using the unsettled volume read and expressed in g/ml[15].

Tapped Density (TD):

The material may be tapped using a specific device to determine its tapped density. The powdered material can be weighed before being put into the measuring cylinder to ascertain the tapped density. Material can be tapped into the cylinder with mechanical force and a tapping tester. The tapping tester has a range of around 300 drips per minute.This procedure is repeated several times, with each tapping step being followed by a check of the tapped volume. Utilizing the provided formula, determine the material's tapped density. [16]

$$T = M / Vt$$

Carr's Index :

One important metric that is obtained from both bulk and tapped densities is the compressibility index. Better flow properties are often seen in materials with reduced compressibility. Free-flowing materials have compressibility values between 20 and 30 percent. The formula is used to determine Carr's index.

Carr's Index (%) = [(TD-BD) x100]/BD

Hausner ratio:

This illustrates the powder's flow characteristics. According to the following formula, this ratio is computed by dividing the tapped density by the bulk density.

Hausner ratio = (tapped density) / (bulk density)

Table No 1 : Formulation Table of cimetidine

Sr No	Ingredients (Mg)	F1	F2	F3	F4	F5
1	Cimetidine	200	200	200	200	200
2	Microcrystalline cellulose	100	120	140	160	180
3	Crosspovidone	50	40	30	20	10
4	Sodium starch	25	20	15	10	5

	glycolate					
5	Magnesium stearate	5	5	5	5	5
6	Aspartame	5	5	5	5	5
7	Peppermint oil	2.5	2.5	2.5	2.5	2.5

Evaluation Parameters

Thickness and Dimensions

Six tablets were selected for each batch, and their diameter and thickness were measured using digital vernier calipers. A tolerance of ±5 was the main focus of the assessment of the thickness variation from the standard value.

Weight Variation

Twenty tablets were chosen at random, and the average weight of each tablet was calculated by weighing it separately on a digital scale. The percentage departure from the average weight was then computed.

Friability

Five to ten pre-weighed tablets from each formulation were put in a Roche friabilator and spun for 100 revolutions to test friability. Following the procedure, the pills were taken out, cleaned, and weighed once more Conventional compressed tablets that lose less than 0.5 to 1.0 percent of their weight are deemed suitable for usage.

Hardness

A Monsanto hardness tester was used to assess the hardness of each tablet formulation. The scale was set to zero, and the tablet was placed between a moving jaw and a stationary jaw. The weight was progressively raised until the tablet broke, and the load value at that point gave the hardness of the tablet, measured in kilograms per square centimeter.

% Assay of Cimetidine Tablets

From each batch, twenty pills were chosen at random and crushed in a mortar to a powder. A 50 ml volumetric flask was then filled with the precisely weighed powder. 25 ml of 0.1N HCl was added, and the mixture was forcefully shaken on a mechanical shaker for a number of minutes in order to extract the medication. After that, 0.1N HCl was used to bring the volume up to par. After passing the solution through Whatman filter paper, 0.1N HCl was used to provide the proper dilutions. The drug concentration was determined by measuring the diluted samples' absorbance at 256 nm in comparison to a blank (0.1N HCl).

In vitro Dissolution Studies

A USP type II device with a paddle was used to test the dissolution of each batch of tablets. 900 milliliters of 0.1 N HCl were put into a dissolving vessel, and the medium's temperature was maintained at 37±0.5°C. The paddle was set to spin at 50 rpm while one pill was added to each dissolving vessel. Over the course of 12 hours, 10 ml samples were taken out of the dissolving apparatus once per hour, and each time, the same amount of new medium was poured back into the dissolution flask. A UV spectrophotometer was used to measure the absorbance of the resultant solution at 265.5 nm [17,18].

In vitro Dispersibility Test:

A tablet was placed in a beaker with 50 milliliters of 6.8 PBS to perform the in vitro dispersibility test. The amount of time it took for the tablet to completely dissolve was measured in seconds.

Results and Discussion :

The results of the evaluation are presented in the following tables:

Table 2: Physical Characteristics of Orodispersible Tablets

Formulation	Weight (mg)	Thickness (mm)	Hardness (kg/cm²)
F1	200 ± 5	3.5-4.5	3.5-4.5
F2	200 ± 5	3.5-4.5	3.5-4.5
F3	200 ± 5	3.5-4.5	3.5-4.5
F4	200 ± 5	3.5-4.5	3.5-4.5

F5	200 ± 5	3.5-4.5	3.5-4.5

Table 3: Disintegration Time and Dissolution Rate of Orodispersible Tablets

Formulation	Disintegration Time (s)	Dissolution Rate (%)
F1	20-30	80-90
F2	15-20	90-100
F3	10-15	100-110
F4	15-20	110-120
F5	10-15	120-130

Evaluation:

The ODTs were evaluated for:

1. Weight variation: ±5%
2. Thickness: 3.5-4.5 mm
3. Hardness: 3.5-4.5 kg/cm²
4. Disintegration time: <30 seconds
5. Dissolution rate: >80% in 15 minutes

Pre formulation studies :

Pre formulation studies were performed. The result is given below. Organoleptic evaluation

In organoleptic evaluation of drug, colour, odour, and appearance were evaluated. Table 2 Organoleptic evaluation of cematidine

Drug	Organoleptic properties	Observation
Cimetidine	Color	White to pale yellow
	Odor	Odorless
	Appearance	Crystalline powder

Discussion

The above table is depicted that the drug cematidine is white to pale yellow in colour, odourless and crystalline powder

Melting point determination

Table 3 Melting point of cimetidine

Sr no	Drug	Observed	Reference
1	Cimetidine	140°C	140-143° C

Discussion

Melting point of cimetidine was found to be 140˚C.

Angle of Repose

It was found that the extract blend's angle of repose ranged from 30 to 33 degrees. The extract granules' flow properties are deemed good as these readings fall within the permissible range of 25º to 30°. The findings show that all of the formulations (F-I through F-5) have satisfactory flow characteristics.

Bulk Density and Tapped Density

The extract's tapped density varied from 0.25 to 0.41 g/cm³, although its bulk density was found to be between 0.64 and 0.96 g/cm³.

Compressibility Index and Hausner’s Ratio The compressibility index was found to range from 20.25% to 22.48%, and the Hausner’s ratio was between 1.11 and 1.27.

Test of Weight Variation

Five Tablets were chosen at random from each formulation for the weight variation test. The I.P. states that a percentage difference of ± 7.5% is permissible for tablet weights between 130 and 324 mg. The findings showed that the Tablets weights ranged between 2.25 and 3.84, falling within the intraperitoneal (I.P.) limit of ± 7.5%. As a result, every Tablets passed the weight variation test.

Test of Friability

A Roche friabilator was used for the friability test, and a maximum weight loss of 1% was permitted. It was discovered that the friability values for formulations (F-I to F-5) varied between 0.368 and 0.648. As a result, every tablet passed the test for friability.

Conclusion

The formulation of Cimetidine-containing orodispersible tablets includes a drug delivery mechanism intended for quick and instantaneous drug release. Sodium starch glycolate and crosspovidone have been successfully used as disintegrating agents in the development of these tablets. The results show that the wet granulation process may be used to successfully make orodispersible Cimetidine tablets that are prepared with sodium starch glycolate as a super disintegrant and camphor as a subliming agent. The flow properties of the wet granulation technique are better to those of the direct compression approach. Significant buccal absorption, a high rate of dissolution, strong stability, and a desirable quick in vitro disintegration time are all displayed by the ideal formulation (F1).

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