A Novel Analytical Method Development of Esomeprazole Pellet

This dissertation is submitted to the Faculty of Allied Health Sciences, Department of Pharmacy, Daffodil International University, as a partial fulfillment of the requirements for the Masters of Pharmacy (M. Pharm) degree.

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APPROVAL

The thesis titled "A Novel Analytical Method Development of Esomeprazole Pellet" has been submitted to the Department of Pharmacy at Daffodil International University as part of the requirements for the Master of Pharmacy degree. It has been determined to be satisfactory. The thesis has received authorization for both its format and contents.

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CERTIFICATION

This thesis fulfilled the criteria for the Masters of Pharmacy (M. Pharm) degree. I oversaw the completion of the project in my role as an Assistant Professor in the Department of Pharmacy, Faculty of Allied Health Sciences, Daffodil International University. I further affirm that the implementations in this project are completely unique and have not been previously submitted for evaluation in any academic program at this university.

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DECLARATION

I affirm that I am now engaged in this research with the guidance of the Department of Pharmacy, Faculty of Allied Health Sciences, Daffodil International University, and fulfilling the requirements for a Master of Pharmacy (M. Pharm) degree. I proudly declare that this project is my own idea. I hereby affirm that the implementations in this project are unique and have not been previously submitted to any academic program at this university.

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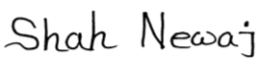

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Above all, I express my gratitude to Allah for granting me the ability to successfully finish my project report and engage in the study of this topic.

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Author

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DEDICATION

I express my gratitude to my parents and professors for their unwavering support in assisting me in attaining my objectives.

ABSTRACT

Proton pump inhibitors (PPIs), also called gastric medicine, are among the most frequently prescribed medications globally. Medications such as Esomeprazole, Omeprazole, Pantoprazole, and others have nearly become ubiquitous in Bangladesh. Although available in various forms on the market, capsules (pellets) are the most prevalent.

Analyzing pharmaceuticals is laborious because only a limited number of pharmaceutical companies produce them internally; the rest purchase granules that have been filled into capsule shells and sold. Thus, only a few in-house methods exist to facilitate the analytical process. The majority of them rely on pharmacopoeial methods such as BP and USP. Although these techniques are widely used, they may only apply to some pharmaceuticals. Therefore, this study is preoccupied with developing a novel technique to facilitate the analysis of PPI pellets.

It is a finished product for a company that has only sold granules; it is a raw material for a purchaser. The analytical technique can, therefore, be identical for both.

For an analyst to analyze these PPI granules, an effective method for both the primary material and the final product must exist. This analysis uses High-Performance Liquid Chromatography (HPLC), the most effective method for separating and identifying mixtures of various components. In addition, distinct reagent and chromatographic conditions are implemented, given that this is a novel methodology.

The ultimate findings exhibit encouraging results. This approach reduces both time and analysis costs, albeit with minor drawbacks.

Esomeprazole, PPI, particle analysis, HPLC, and the development of analytical methods are all keywords.

Keywords: PPI, pellets analysis, HPLC, analytical method development.

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1.1 Introduction

1.1.1 Esomeprazole Medication

Esomeprazole is a medication that reduces gastric acid secretion. This medicine can be used to treat illnesses such as peptic ulcer disease, gastroesophageal reflux disease, and Zollinger–Ellison syndrome. The efficacy of this medication is similar to that of other proton pump inhibitors (PPIs). It is taken either orally or intravenously. The sequence consists of the numbers.

Gastroesophageal reflux disease (GERD) is a medical illness where the stomach's digestive acid comes into contact with the lining of the throat, known as the esophagus. Heartburn is the term used to describe the irritation caused by this illness. Prolonged contact between stomach acids and the esophagus might result in permanent damage to the esophagus. Esomeprazole reduces the formation of digestive acids, hence reducing their influence on the esophagus.

Discontinuing PPIs such as esomeprazole quickly might lead to a rebound effect and stimulate excessive secretion. In order to prevent the rebound effect, it is advisable to gradually decrease or taper the doses of esomeprazole before discontinuing it.

2.1 Aim of Study

- To design an innovative and efficient technique applicable to all esomeprazole pellets as a primary substance.
- To devise an innovative and applicable approach for the production of esomeprazole pellets as a finalized product.
- To develop an Efficient HPLC analytical method.
- To understand the effect of new reagents in analytical procedures.
- Stability study of new solvent mixture.
- To reduce the cost of analysis.
- To reduce the time of the analytical method.

We have done the following studies:

a. Good source of Esomeprazole pellets collected with proper documentation.
b. A working standard with proper documentation.
c. Developed a new method
d. New reagents for analytical procedure introduced.
e. Linearity study of the new method.

3.1 Materials & Methods

3.1.1 Source of Materials

Name: Esomeprazole Pellets 22.5% w/w

Batch: F&D/ESM/P/2/202303007

Reference: USP

Manufacturing Date: March-2023

Expired Date: February - 2026

Source: Metrochem API Private Ltd, India.

3.1.2 Working Standard Details

Name: Esomeprazole Working Standard

Batch: WS/ESM-2304001

Reference: USP

Manufacturing Date: 13-04-2023

Expired Date: 12-04-2024

Potency: 92.8%

Source: Metrochem API Private Ltd, India.

3.1.3 Used Regents

SN	Name	Batch	Expired Date	Source
1.	Potassium Dihydrogen Phosphate	AM1590277 108	N/A	Supelco, Germany
2.	Sodium Hydroxide	B20333198	30-03-2027	Merck, Germany
3.	Type -1 Water	N/A	N/A	In-house
4.	Acetonitrile	1157030 126	30-06-2024	Supelco, Germany

These reagents were collected from a reputed pharma. They ensured the quality and proper storage conditions.

3.1.4 Used Instruments

SN	Name	Model	Origin
1.	Micro Balance	Cubis® II	Sartorius, Germany
2.	Semi-Micro Balance	MS105	Metller Toledo, Switzerland
3.	HPLC	LC-2050, PDA	Shimadzu, Japan
4.	pH Meter	S-230	Metller Toledo, Switzerland
5.	Ultrasonic Bath	UB-32543	Isolab, Germany

All these instruments are calibrated and validated with proper documentation.

3.1.5 Chromatographic Conditions

Column: C18, 250 x 4.6 mm, 5µm

Flow Rate: 1.0 ml/min

Wavelength: 285 nm

Injection Volume for Chromatography: 20 µL

Run Time for Chromatography: 15 min

Detector: PDA

Tailing Factor: NMT 0.5

The acceptable threshold for the relative standard deviation of the absorbance of the system is 2% or less.

3.2 Preparation of pH 7.4 buffer

A solution was prepared by dissolving 7 grams of potassium dihydrogen phosphate and 2 grams of potassium hydroxide in 1 liter of water. The use of 2 M sodium hydroxide involved changing the pH to 7.4.

3.2.1 Preparation of 100 ml, 2 M sodium hydroxide solution:

In a 100 ml volumetric vessel, 8 grams of sodium hydroxide granules were combined with 50 ml water and sonicated for three minutes, ultimately attenuating to the extreme.

3.2.2 Preparation of Mobile Phase

Isocratic

Ratio of buffer solution pH 7.4 and AR Acetonitrile: 65 : 35

650 ml buffer : 350 ml acetonitrile

Filtered and sonicated.

3.2.3 Preparation of Standard:

A 100 ml volumetric vial was filled with 20 mg of Esomeprazole working standard. Then, 40 ml of a 0.1 N sodium hydroxide solution was added to the vial. The vial was subjected to sonication for five minutes at maximum volume while ensuring complete mixing. A 50 ml solution was poured into a volumetric flask, and then 5 ml of the diluted mobile phase was added.

3.2.4 Preparation of Sample

A volume of powdered Esomeprazole granules precisely weighed at 20 mg (88.88 mg) was transferred into a 100 ml volumetric vessel. 40 ml of a 0.1 M sodium hydroxide solution was added to this. Ultrasonicated for fifteen minutes at maximum volume while thoroughly mixed. Twenty milliliters of this solution were filtered through a Whiteman filter. A volumetric flask containing 50 ml solution was filled with 5 ml of the diluted mobile phase.

3.2.5 Calculation Formula

$$\frac{A\ of\ SP}{A\ of\ WS} \times \frac{Wt\ of\ WS}{100} \times \frac{5}{100} \times \frac{100}{SP\ Wt} \times \frac{50}{5} \times \frac{100}{LC} \times Potency\ of\ WS$$

Where,

$A\ of\ SP$ = Area of Sample

$A\ of\ WS$ = Area of Working Standard

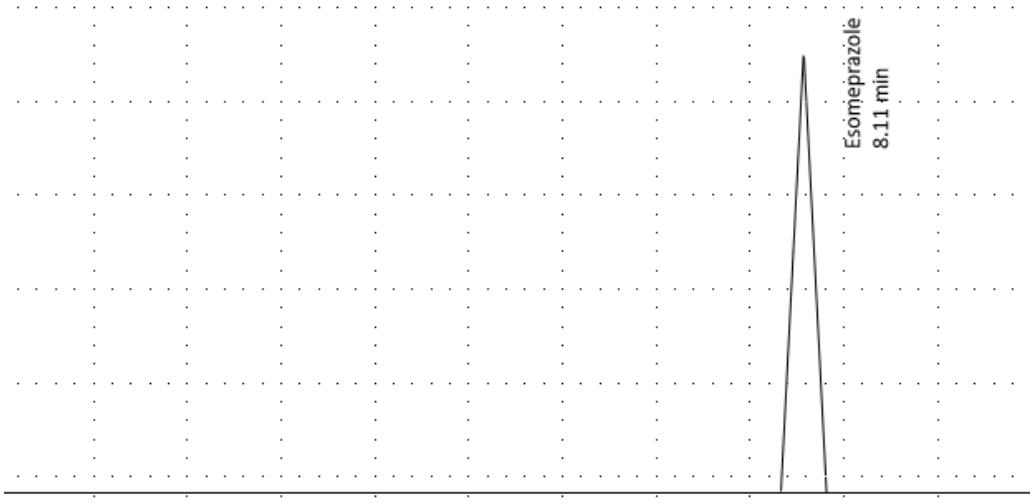
$Wt\ of\ WS$ = Weight of Working Standard

$Wt\ of\ SP$ = Weight of Working Sample

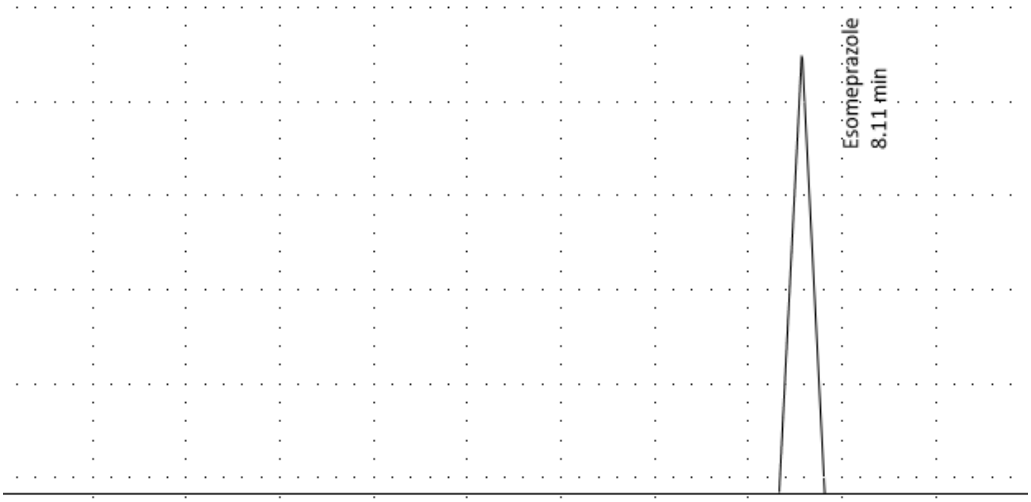
LC = Lebel claim 22.5%

3.2.6 Batch Table for HPLC

Sample	**Injection**
Blank - 1	1
Blank - 2	1
System Suitability Standard	5
Standard	2
Sample	2
End Standard	1
Wash	1



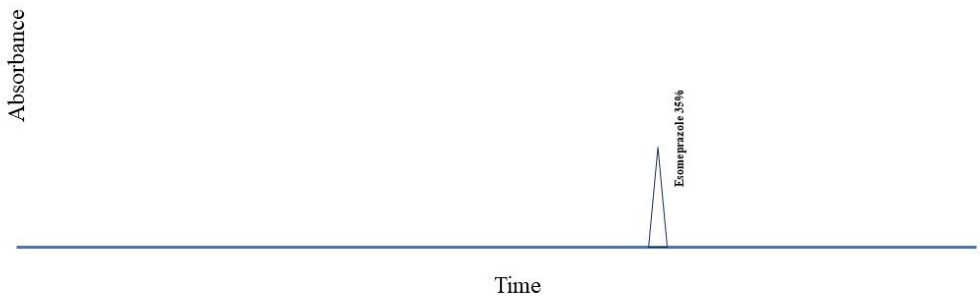
HPLC Chromatogram of Standard



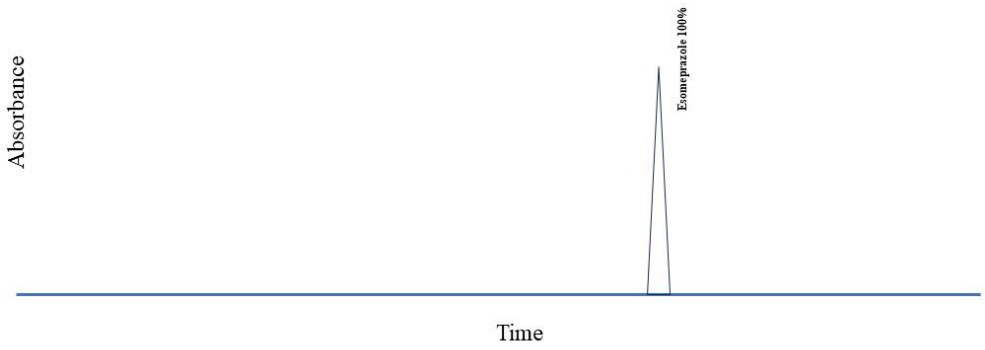
HPLC Chromatogram of Sample

4.1 Linearity Study

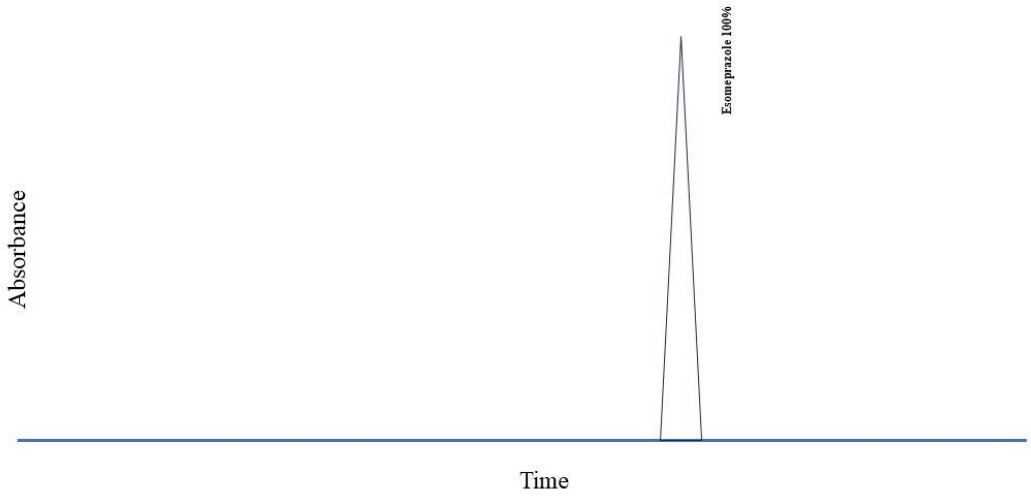
35%, 70% and 100% Sample solution used for this study sample were prepared by dilution method.



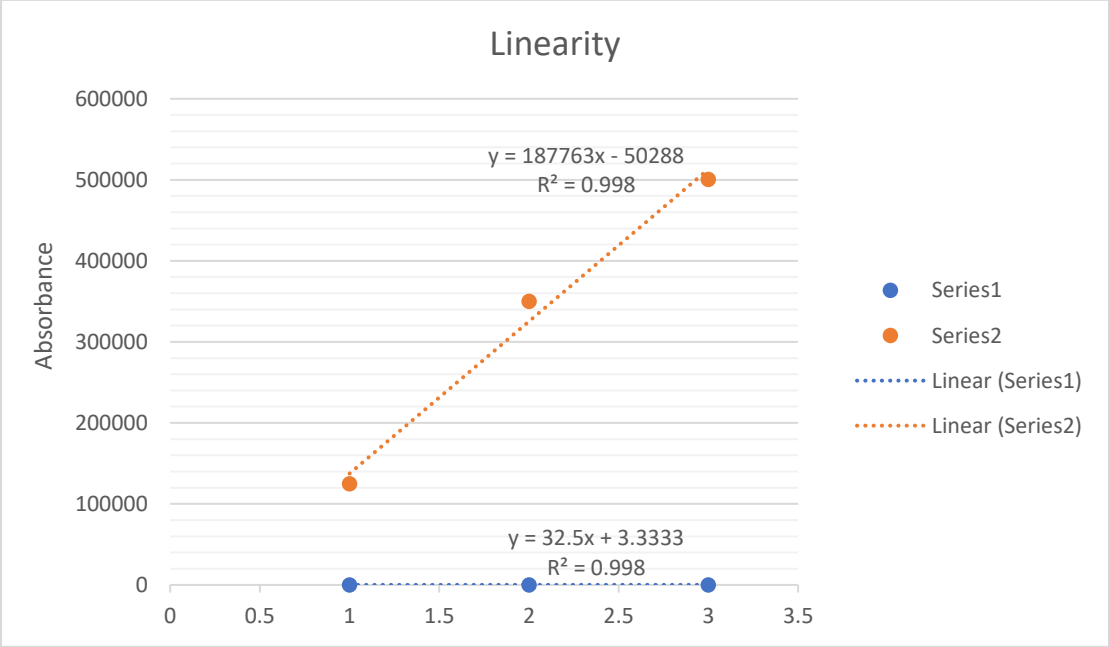
HPLC Chromatogram of Sample 35%



HPLC Chromatogram of Sample 70%



HPLC Chromatogram of Sample 100%



Linearity curve

5.1 Conclusion

Gastritis is a highly widespread health condition in our country. Consequently, esomeprazole, a kind of proton pump inhibitor (PPI), is highly favored and widely used. It is usually challenging to test esomeprazole pellets in a quality control or research and development/product development lab; however, we now have a technology that can assess pellets in both their raw material and finished product states.

The findings of this approach are comparable to those obtained by the USP method of esomeprazole analysis, with a standard deviation of less than 0.5 percent. However, this method requires less time, and the cost of this analytical procedure is also decreased.

There is the potential for this technology to be validated, and any pharmaceutical company may utilize it for their routine analysis.

The analysis can be done more quickly, with less effort, and at a lower cost.

****Abbreviations:**

QC = Quality Control

R&D = Research and Development

PD = Product Development

M = Molar.

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