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Formulation, Development and Evaluation of Bilayer Tablets Containing Esomeprazole And Amoxycillin

Prashant G. Bhukan[1], Dr. Satyam Z. Chemate[2],

[1]Department of Pharmaceutics,

[2] Head of Department of Pharmaceutics,

Dr.Vithalrao Vikhe Patil Foundation's College of Pharmacy,

Vilad Ghat, Ahmednagar, India - 414111.

Abstract

The objective of the work is the formulation, development and evaluation of bilayer tablets containing Esomeprazole and Amoxycillin. Esomeprazole in the immediate release layer and Amoxycillin in the sustained release layer, using Crosspovidone, Cross Carmellose sodium as a superdisintegartion for the immediate release layer and the hydrophilic HPMC K100, hydrophobic matrix Ethyl cellulose are used in the sustained release layer. Immediate and sustained release layer tablets were formulated by direct compression method. The bilayer tablets was evaluated for their Precompression parameters, physical characteristics like bulk density, tapped density, compressibility index, Hausner's ratio, angle of repose and post compression parameters like hardness, friability, drug content, % drug release, thickness, disintegration time. The immediate release layer was 97.73±0.19% and 96.98±0.41 in 90min. and sustained release layer was 98.86 ±0.07% and 98.76 ±0.04% in 720min.

Keywords: Esomeprazole, Amoxicillin, Bilayer tablet, Immediate release, Sustained release, Antiulcer, Helicobacter pylori.

INTRODUCTION

Oral drug delivery system is considered to be one of the most convenient and commonly employed drug delivery system as it possesses some specific advantageous characteristics, such as ease of administration, least aseptic constraints and flexibility in the design of the dosage form. Another revolution towards the oral drug delivery is the modified release dosage forms which have advantages over immediate release formulations of the same drug. There are different methods for the designing of this modified dosage form, some of them are film coated pellets, tablets, capsules or more sophisticated and complicated delivery systems such as osmotically driven systems, systems controlled by ion exchange mechanism, systems using three dimensional printing technology and systems using electrostatic deposition technology. The modified release products are usually designed to provide slow and continuous delivery of drug over the entire dosing interval and improve patient compliance and convenience. [1, 2, 3] The popularity of the oral route is attributed ease of administration, patient acceptance, accurate dosing, cost effective manufacturing method and generally improved shelf-life of the product.[4]

The effective oral drug delivery practice depends upon various factors like gastric emptying process, gastrointestinal transit time of dosage form, drug release from the dosage form and site of absorption of drugs.[5] A peptic ulcer is a sore in the lining of stomach or duodenum. The duodenum is the first part of small intestine. Peptic ulcers are found in the stomach are called as gastric ulcers, in the duodenum are called duodenal ulcers. [6]

Helicobacter pylori, previously named Campylobacter pyloridis, are a Gram negative, microaerophilic bacterium found in the stomach. It was identified in 1982 by Barry Marshall and Robin Warren, who found that it was present in patients with chronic gastritis and gastric ulcers, conditions that were not previously believed to have a microbial cause. It is also linked to the development of duodenal ulcers and stomach cancer. However, over 80 percent of individuals infected with the bacterium are asymptomatic and it has been postulated that it may play an important role in the natural stomach ecology. [7]

MATERIALS AND METHOD

Esomeprazole and Amoxycillin Balaji Drugs, Crosspovidone, Ozone International, Mumbai, Cross Carmellose sodium, Yarrow Chem Products, Lactose, Sodium Bicarbonate, Magnesium Stearate, Talc, HPMC K100, Ethyl cellulose, Polyvinyl pyrrolidone, Microcrystalline cellulose from Loba Chemie Pvt. Ltd., Mumbai.

Method:

Preparation Bilayer Tablet using direct compression technique:

Preparation of Esomeprazole (Immediate release layer):

The Tablet was prepared using direct compression method. All the ingredients weigh drug and excipients. After incorporating different super Disintegrants such as, Cross Carmellose sodium, Crosspovidone in different concentration. The ingredients were weighed and mixed in a dry and clean motor. Then the ingredients were passed through mesh #40. Magnesium stearate as lubricant and talc as glidant were added in a final step and mix well with motor pestle. Then 250mg mixture was weight, filled in die cavity and then compressed into tablet using flat punches 8 station Lab tablet press compression machine.

Preparation of Amoxycillin (Sustained release layer):

The Tablet was prepared using direct compression method. All the ingredients weigh drug and excipients. After incorporating different super Disintegrants such as, HPMC K 100, Ethyl Cellulose in different concentration. The ingredients were weighed and mixed in a dry and clean motor. Then the ingredients were passed through mesh #40. Magnesium stearate as lubricant and talc as glidant were added in a final step and mix well with motor pestle. Then 400mg mixture was weight, filled in die cavity and then compressed into tablet using flat punches 8 station Lab tablet press compression machine.

Formulation of Bilayer tablet:

The immediate release layer (Esomeprazole) placed in die cavity and then compressed into tablet using flat punches then sustained release layer (Amoxycillin) placed in die cavity and then compressed into tablet using flat punches, both layers were compressed to form bilayer by using 8 station Lab tablet press compression machine.

Composition of Bilayer Tablets

Table No. 1: Immediate Release Layer of Esomeprazole

Ingredients (mg)	EF1	EF2	EF3	EF4	EF5	EF6
Esomeprazole	20	20	20	20	20	20
Crosspovidone	4	6	8	-	-	-
Cross Carmellose sodium	-	-	-	4	6	8
Lactose	62	60	58	62	60	58
Sodium bicarbonate	150	150	150	150	150	150
Magnesium stearate	5	5	5	5	5	5
Talc	2.5	2.5	2.5	2.5	2.5	2.5
Polyvinyl pyrrolidone	6.5	6.5	6.5	6.5	6.5	6.5
Total weight	250	250	250	250	250	250

Table No. 2: Sustained Release Layer of Amoxycillin

Ingredients (mg)	AF1	AF2	AF3	AF4	AF5	AF6
Amoxycillin	250	250	250	250	250	250
HPMC K100	25	-	50	25	50	75
Ethyl cellulose	50	50	-	25	25	25
Polyvinyl pyrrolidone	12.5	12.5	12.5	12.5	12.5	12.5
Magnesium stearate	10	10	10	10	10	10
Talc	2.5	2.5	2.5	2.5	2.5	2.5
Microcrystalline cellulose	50	75	75	75	50	25
Total weight	400	400	400	400	400	400

Evaluation of Bilayer tablet

General Appearance [8]
The general appearance of a tablet, its visual identity and overall "elegance" is essential for consumer acceptance. Includes in are tablet's size, shape, Colour, presence or absence of an Odour, taste, surface texture, physical flaws and consistency and legibility of any identifying marking.

Size and Shape:
The size and shape of the compressed tablets were examined under the magnifying lens.

Thickness [9]
Tablet thickness is an important characteristic in reproducing appearance and also in counting by using filling equipment. Some filling equipment utilizes the uniform thickness of the tablets as a counting mechanism. Ten tablets were taken and their thickness was recorded using Vernier Calipers. Vernier caliper consists of metric and imperial scales. The main matric scale is read first then read "hundredths of mm" of imperial scale (count the number of division until the lines concedes with the main metric scale. The imperial scale number is multiply with 0.02. Then that number obtained from imperial scale added with main metric scale to get final measurement.

Weight Variation [10]
To study the weight variation, twenty tablets were taken and their weight was determined individually and collectively on a digital weighing balance. The average weight of one tablet was determined from the collective weight. Not more than two of the individual weights deviate from the average weight by more than the percentage shown in the following table and none deviate by more than twice the percentage. The mean and deviation were determined. The percent deviation was calculated using the following formula.

$$\textbf{Weight Variation} = \frac{\textbf{Individual weight} - \textbf{Average weight}}{\textbf{Average weight}} x\ 100$$

Hardness [11]
Hardness is done to evaluate the strength of the tablet to withstand the pressure applied. Nature and quantities of excipients and difference between upper and lower punches decide the hardness of formulation. The hard tablet will not disintegrate in the required time and the soft tablet will not withstand the pressure during packaging and transportation. The hardness of the tablet was tested using Monsanto tester. The unit for Hardness is measured in kg/cm^2.

Friability [12]
Friability generally refers to loss in weight of tablets in the containers due to removal of fines from the tablet surface. Friability generally reflects poor cohesion of tablet ingredients. 10 tablets were weighed and the initial weight of these tablets was recorded and placed in Roche Friabilator and rotated at the speed of 25 rpm for 100 revolutions. Then tablets were removed from the Friabilator dusted off the fines and again weighed and the weight was recorded.
Percentage friability was calculated by using the formula.

$$\%\ \textbf{Friability} = \frac{\textbf{Initial weight} - \textbf{Final weight}}{\textbf{Initial weight}} \textbf{x}\ 100$$

Drug Content [13, 14, 15]

Drug content of Esomeprazole: From each batch 3 tablets were weighed each containing 10 mg of tablet powder were taken. Tablets were triturate in motor and quantity of powder equivalent to 10mg of tablet powder was transferred to 100 ml volumetric flask. Sufficient quantity of 0.1 N HCl was added with shaking and volume was made up to the mark and filter through Whatman filter paper. Further dilutions were made in concentration of 2, 4, 6, 8, 10µg/ml. Then absorbance was recorded at different wavelength of drugs such as Esomeprazole at 274 nm against 0.1N HCl as a blank was measured using UV Visible spectrophotometer.

Drug content of Amoxycillin: From each batch 3 tablets were weighed each containing 10 mg of tablet powder were taken. Tablets were triturate in motor and quantity of powder equivalent to 10mg of tablet powder was transferred to 100 ml volumetric flask. Sufficient quantity of phosphate buffer pH 6.8 was added with shaking and volume was made up to the mark and filter through Whatman filter paper. Further dilutions were made in concentration of 2, 4, 6, 8, 10µg/ml. Then absorbance was recorded at different wavelength of drugs such as and Amoxycillin at 232 nm against phosphate buffer pH 6.8 as a blank was measured using UV Visible spectrophotometer. The concentration was obtained from the calibration curve by using the regression equation.

$$\textbf{Concentration}(\mu\textbf{g/ml}) = \frac{\textbf{Absorbance} - \textbf{Intercept}}{\textbf{Slope}}$$

$$\textbf{Drug Content} = \textbf{Conentration x Diluation factor}$$

$$\%\ \textbf{Drug Content} = \frac{\textbf{Drug content}}{\textbf{Labeled claim}}\ x\ 100$$

Disintegration Test [16]

The disintegration time was determined using disintegration test apparatus. The tablets were placed in each of the 6 tubes of the basket and one disc was added to each tube. The 10 mesh screen at the bottom end was taken according to the U.S.P. The assembly was suspended in water maintained at a temperature of 37ºC ± 2ºC and the apparatus was switched ON and moves the basket containing tablet upwards and downwards a frequency of 28 to 32 cycles per minute. The time taken to disintegrate the tablets completely was noted.

In vitro drug release studies [17]

In-vitro dissolution studies of immediate release layer:

The in-vitro dissolution studies were performed using USP-II (paddle) dissolution apparatus at 50 rpm. In-vitro drug testing of the bilayer tablets was done using a rotating paddle dissolution apparatus in 900 ml of 0.1N HCL (pH 1.2) for 1.5 hr. A 2 ml was withdrawn at specific time intervals and same volume of fresh medium was replaced and diluted up to 10 ml with 0.1 N HCL, filtered through a Whatman filter paper no. 41 and analyzed on UV spectrophotometer at 274 nm using 0.1 N HCL as a blank.

In vitro dissolution studies of sustained release layer:

The in vitro release of sustained release layer was carried out for 12 hours using USP type-II apparatus at 50 rpm for the first 60 minute in 900 ml phosphate buffer (pH 6.8) maintaining at 37 ±0.5°C and then at phosphate buffer pH 6.8. A 2 ml was withdrawn at different time intervals and replaced with an equal volume of fresh medium was replaced and diluted up to 10 ml with phosphate buffer (pH 6.8), filtered through a Whatman filter paper no. 41. The samples were suitably diluted with blank dissolution medium, filtered and analyzed on UV spectrophotometer at 232 nm.

Table 3: Procedure for Dissolution Study

Parameters	Conditions
Dissolution media	900ml of 0.1 N HCl
	900ml of phosphate buffer solution pH 6.8
Temperature	37±0.5 ^{O}C
RPM	50
Drug content	Weight of tablet equivalent to 650mg
Volume Withdrawn	2ml
Volume made up to	10ml
Λmax	274nm and 232nm
Dilution factor	5

Stability Study [18]

The tablets are stable over these conditions and thus not require frequent test on storage, unless of course chemical reaction occurs, this changes the nature of the components. ICH recommends carrying out stress testing on the drug substance to establish its inherent characteristics and support the solubility of the proposed analytical procedure. It was also required that analytical method should be validated to demonstrate that impurities unique to new drug substances do not interfere with or separated from specified and unspecified degradation products in the products. The drug was subjected to force degradation and assay to detect the presence of degrades. This is useful while carrying out the assay of stability batch product to identify the degradation. Stability study at room temperature is the method of determining the actual shelf life of the product. Unfortunately it is difficult to make an accurate expiration date prediction accelerated stability studied were carried out at elevated temperature will help to determine shelf life with in a lesser period of time. The prepared tablets were evaluated a period of one to three month as per ICH Guidelines. After determining the drug content, the optimized batches of the tablet were monitored up to 1 month at accelerated stability conditions of temperature and relative humidity (40ºC ± 2ºC and 75% ± 5% RH). Samples were withdrawn after one month and characterized for Appearance, Weight, Thickness, Hardness, drug content, and drug release. The choice of appropriate storage condition during accelerated stability study is necessary to predict the long term stability of bilayer tablet.

RESULTS AND DISCUSSION

Appearance and Color:

Esomeprazole: Yellow colored, odorless powder.

Amoxycillin: White to pale yellow, crystalline powder, odorless powder.

Melting Point

The melting point of the drug matched with the value found in literature.

Tablet No. 4: Melting point of Esomeprazole and Amoxycillin

Sr. No.	Melting Point range	Drugs	
		Esomeprazole	Amoxycillin
1.	Literature	182-191°C	190-196°C
2.	Practical	185°C	194°C

Solubility:

Esomeprazole:

Table No. 5: Solubility of Esomeprazole

Sr. No.	Solvent	Solubility of Esomeprazole
1	Distilled Water	Slightly Soluble
2	0.1 N HCL	Soluble
3	Methanol	Freely Soluble
4	Ethanol	Soluble

Amoxycillin:

Table No. 6: Solubility of Amoxycillin

Sr. No.	Solvent	Solubility of Amoxycillin
1	Distilled Water	Slightly Soluble
2	Phosphate Buffer pH 6.8	Soluble
3	Methanol	Freely Soluble
4	Ethanol	Soluble

Ultraviolet Absorbance spectrum:

Esomeprazole

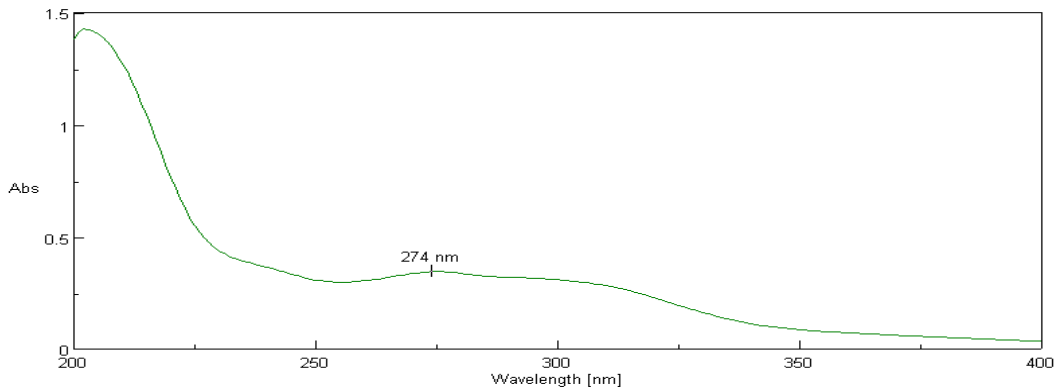

Figure No. 1: UV absorbance spectrum of Esomeprazole in 0.1 N HCL

Calibration Curve of Esomeprazole:

The standard calibration curve of Esomeprazole was obtained by plotting Absorbance vs. Concentration. Table No. 9.5. Displays the absorbance values of Esomeprazole drug. The standard curve is shown in Figure 2. The standard calibration curve shows the slope 0.0342 and coefficient of 0.9994. The curve was found to be linear in the concentration at 10-50 µg/ml and obey Beer – lambert law at λmax 274 nm.

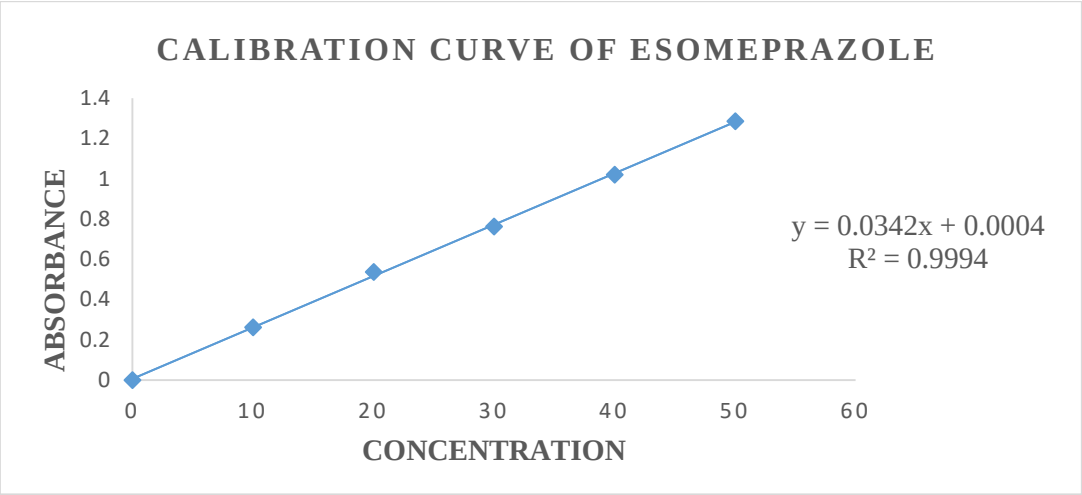

Figure No. 2: Calibration curve of Esomeprazole

Tablet No. 7: Calibration Curve of Esomeprazole 0.1 N HCL

Sr. No.	Concentration (µg/ml)	Absorbance
1.	0	0
2.	10	0.0698
3.	20	0.1358
4.	30	0.2098
5.	40	0.2693
6.	50	0.3448

Tablet No. 8: Data of Calibration curve of Esomeprazole in 0.1 N HCL

Sr. No.	Parameter	Values in 0.1N HCL
1	Absorbance maximum (λ_{max}) in nm	274 nm
2	Slope	0.0342
3	Intercept	0.0004
4	Correlation coefficient	0.9994
5	Equation	y = 0.0342x + 0.0004

Amoxycillin

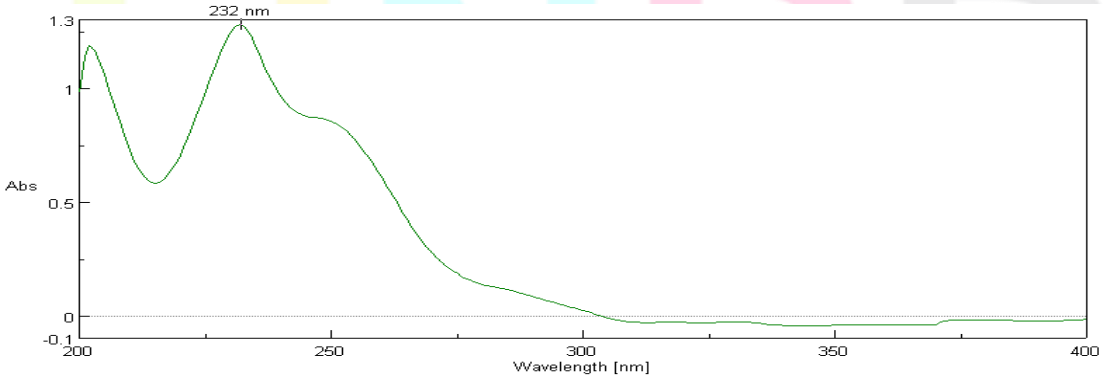

Figure No. 3: UV absorbance spectrum of Amoxycillin in 6.8 pH Buffer

Calibration Curve of Amoxycillin

The standard calibration curve of Amoxycillin was obtained by plotting Absorbance vs. Concentration. Table No. 9.7. Displays the absorbance values of Amoxycillin drug. The standard curve is shown in Figure 9.4. The standard calibration curve shows the slope 0.1276 and coefficient of 0.9995. The curve was found to be linear in the concentration at 2-10 µg/ml and obey Beer – lambert law at λmax 232 nm.

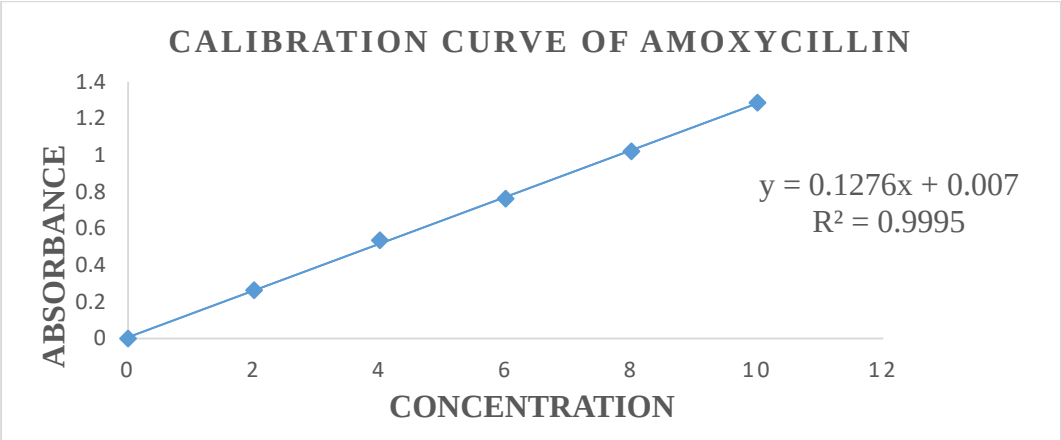

Figure No. 4: Calibration curve of Amoxycillin

Tablet No. 9: Calibration Curve of Amoxycillin in 6.8 pH Buffer

Sr. No.	Concentration (µg/ml)	Absorbance
1.	0	0
2.	2	0.2629
3.	4	0.5367
4.	6	0.7624
5.	8	1.0207
6.	10	1.2861

Tablet No. 10: Data of Calibration curve of Amoxycillin in 6.8 pH Buffer

Sr. No.	Parameter	Values in in 6.8 pH Buffer
1	Absorbance maximum (λ_{max}) in nm	232 nm
2	Slope	0.1276
3	Intercept	0.007
4	Correlation coefficient	0.9995
5	Equation	y = 0.1276x + 0.007

IR Spectroscopy Analysis

The FT-IR were calibrated by preparing KBr pellet. To record the spectra of drug, the same KBr spectra was set as a background graph. FTIR spectra of Esomeprazole and Amoxycillin shows various characteristic peaks for different functional group. All the observed peaks were in compliance with the standard ranges of absorption frequency for function groups. No additional peaks for corresponding functional groups were found. Therefore, we can identify the said API as Esomeprazole and Amoxycillin.

IR Spectrum of Esomeprazole

The IR Spectrum of the drug agree with the chemical structure (RS) - 5- methoxy- 2- [(*S*) - (4-methoxy-3, 5-dimethylpyridin- 2- yl) methylsulfinyl] benzimidazol-1 -ide; dehydrate

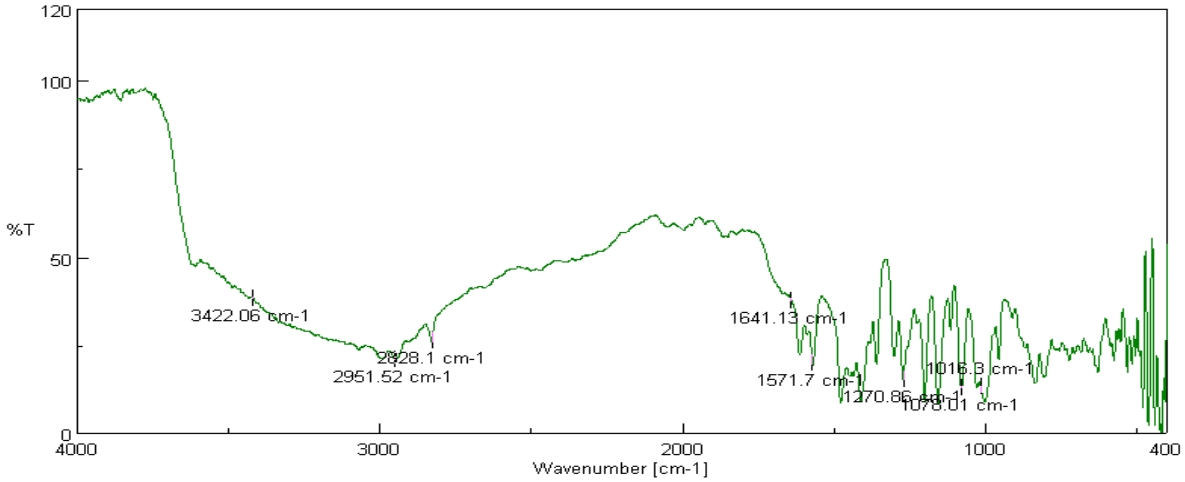

Figure No. 5: IR Spectrum of Esomeprazole

Table No. 11: IR Peaks of Esomeprazole

Sr. No.	Functional Group	Frequency (cm^{-1})
1	-C-H- stretching	2951.52
2	-C-H- stretching in aromatic	2928.1
3	-C-N- stretching	1270.86
4	-N-H stretching	3422.06
5	C-O-C stretching	1078.01
6	-S=O stretching	1016.3
7	-C=C- Stretching	1571.7
8	-C=N-Stretching	1641.13

IR Spectrum of Amoxycillin

The IR Spectrum of the drug agree with the chemical structure (RS) (2S, 5R,6R)-6-[[(2R)-2-amino-2-(4-hydroxyphenyl)acetyl]amino]-3,3-dimethyl-7-oxo-4-thia-1- azabicyclo[3.2.0]heptane-2-carboxylic acid

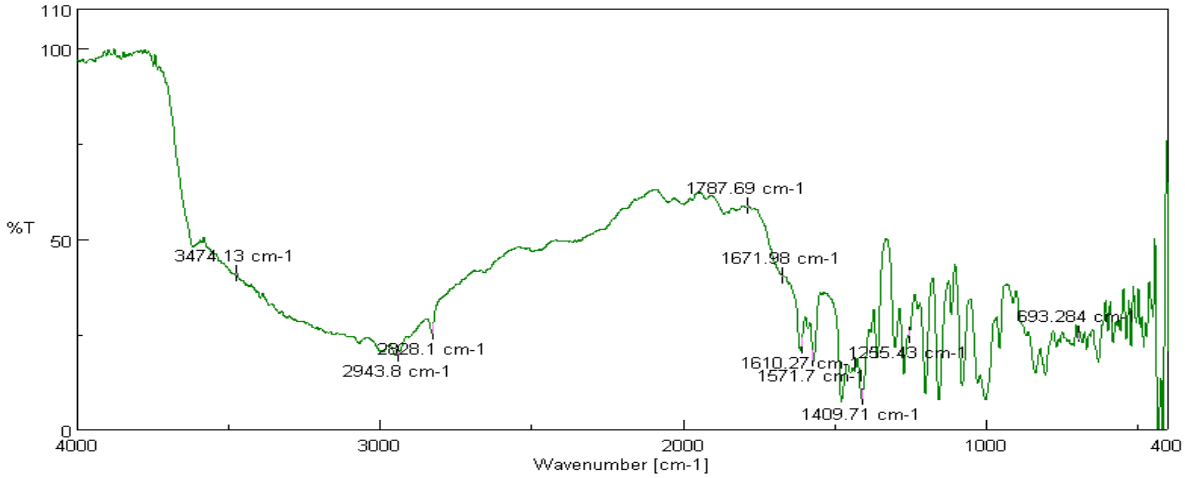

Figure No. 6: IR Spectrum of Amoxycillin

Table No. 12: IR Peaks of Amoxycillin

Sr. No.	Functional Group	Frequency (cm^{-1})
1	-C-H- stretching	2943.8
2	-C-H- stretching in aromatic	1409.71
3	-O-H- stretching	3474.13
4	-COOH- stretching	1787.69
5	-C=C- stretching	1671.98
6	-N-H- stretching	1571.71
7	-C-N- stretching	1255.43
8	-C-S-Stretching	693.28

Differential Scanning Calorimetry (DSC)

The Differential Scanning Calorimetry (DSC) is a thermo analytical technique used for analyzing thermal transitions involving thermal energy with a great sensitivity. The DSC thermo gram of Esomeprazole show a sharped exothermic peak at 211.19 °C. Amoxycillin show a Sharped exothermic peak at 186.37 °C.

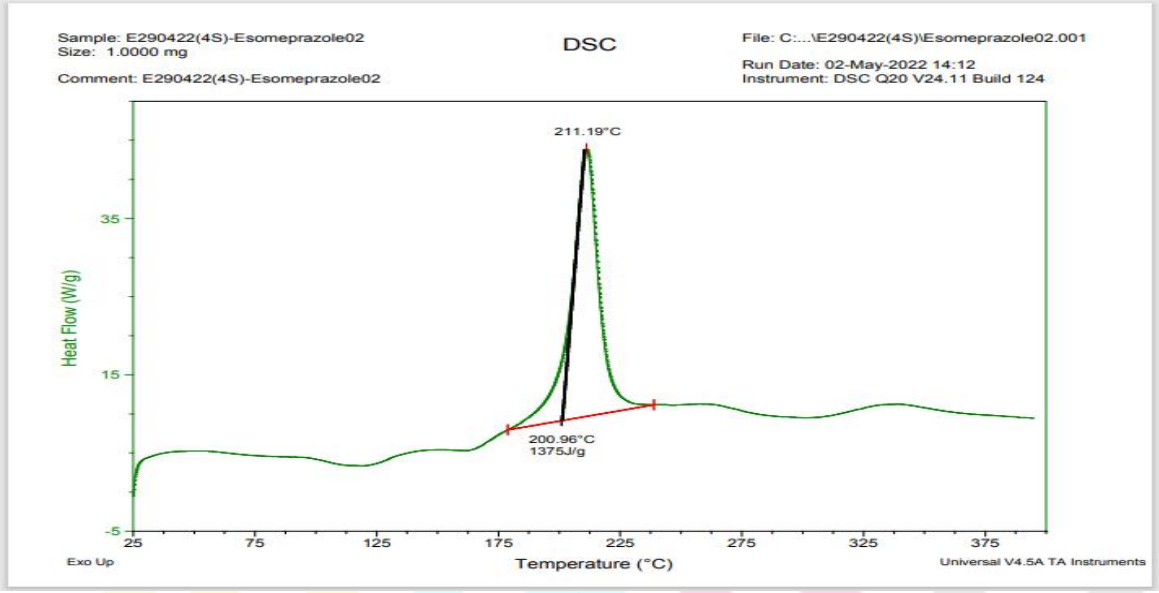

Figure No. 7: DSC Graph of Esomeprazole

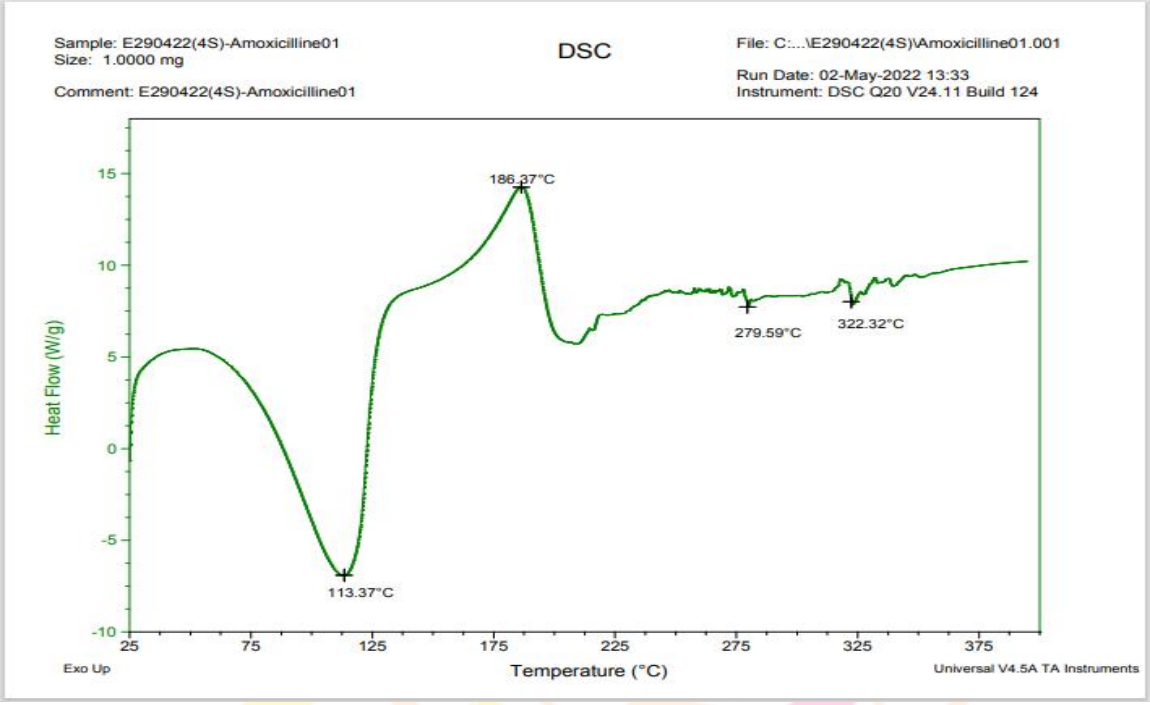

Figure No. 8: DSC Graph of Amoxycillin

Evaluation of Precompression Study

Bulk Density:

Bulk Density of Esomeprazole optimized batch F3 was found to be 0.71±0.03 g/cm^3 and optimized batch F5 was found to be 0.64±0.06 g/cm^3 and Amoxycillin optimized batch F3 was found to be 0.66±0.03 g/cm^3 and optimized batch F5 was found to be 0.69±0.02 g/cm^3 .

Tapped Density:

Tapped Density of Esomeprazole optimized batch F3 was found to be 0.75±0.06 g/cm^3 and optimized batch F5 was found to be 0.69±0.06 g/cm^3 and Amoxycillin optimized batch F3 was found to be 0.72±0.09 g/cm^3 and optimized batch F5 was found to be 0.75±0.02 g/cm^3.

Carr's Index:

Carr's Index of Esomeprazole optimized batch F3 was found to be 5.33±0.03 % and optimized batch F5 was found to be 7.24±0.05 % and Amoxycillin optimized batch F3 was found to be 8.33±0.03 % and optimized batch F5 was found to be 8.00±0.02 %.

Hausner's Ratio:

Hausner's Ratio of Esomeprazole optimized batch F3 was found to be 1.05±0.04 and optimized batch F5 was found to be 1.07±0.02 and Amoxycillin optimized batch F3 was found to be 1.09±0.09 and optimized batch F5 was found to be 1.08±0.02.

Angle of Repose:

Angle of Repose of Esomeprazole optimized batch F3 was found to be 30°. 58' and optimized batch F5 was found to be 23°. 53' and Amoxycillin optimized batch F3 was found to be 22°. 33' and optimized batch F5 was found to be 26°. 77'.

Table No. 13: Esomeprazole Immediate Release Layer

Formulation	Bulk Density (g/cm^3)	Tapped Density (g/cm^3)	Carr's Index (%)	Hausner's Ratio	Angle of Repose (Degree)
F1	0.63±0.07	0.68±0.05	7.35±0.09	1.07±0.06	25°. 39'
F2	0.65±0.05	0.71±0.03	8.45±0.06	1.09±0.05	26°. 61'
F3	0.71±0.03	0.75±0.06	5.33±0.03	1.05±0.04	30°. 58'
F4	0.66±0.04	0.73±0.02	9.58±0.07	1.10±0.03	22°. 36'
F5	0.64±0.06	0.69±0.06	7.24±0.05	1.07±0.02	23°. 53'
F6	0.70±0.03	0.77±0.01	9.09±0.04	1.10±0.02	24°. 27'

S. D = Standard Deviation n =3

Table No. 14: Amoxycillin Sustained Release Layer

Formulation	Bulk Density (g/cm^3)	Tapped Density (g/cm^3)	Carr's Index (%)	Hausner's Ratio	Angle of Repose (Degree)
F1	0.67±0.04	0.75±0.05	10.66±0.07	1.11± 0.02	27º. 29'
F2	0.75±0.08	0.80±0.03	6.25±0.06	1.06±0.02	24º. 81'
F3	0.66±0.03	0.72±0.09	8.33±0.03	1.09±0.09	22º. 33'
F4	0.78±0.06	0.84±0.05	7.14±0.09	1.07±0.01	25º. 16'
F5	0.69±0.02	0.75±0.02	8.00±0.02	1.08±0.02	26º. 77'
F6	0.71±0.06	0.78±0.05	8.97±0.05	1.09±0.05	24º. 29'

S. D = Standard Deviation n =3

IR Spectrum of Formulation

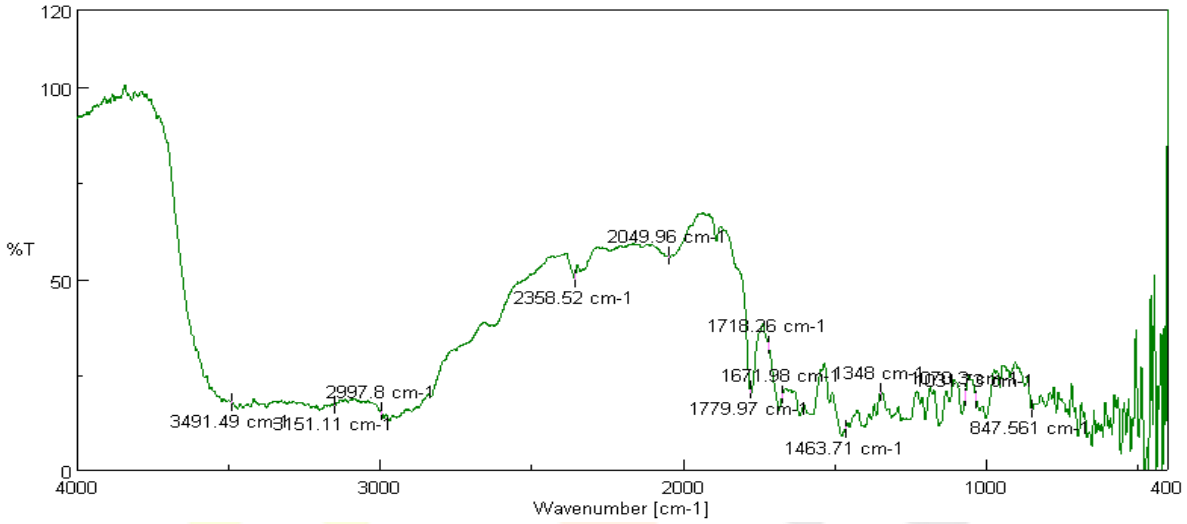

Figure 9: IR Spectrum Formulation Batch B3

Table No. 15: IR Peaks Formulation of Esomeprazole+ Amoxycillin + Crosspovidone + HPMC K100

Sr. No.	Functional Group	Frequency (cm^{-1})
1	-C-H- stretching	2997.8
2	-C-H- stretching in aromatic	1463.71
3	-O-H- stretching	3491.49
4	-COOH- stretching	1779.97
5	-C=C- stretching	1671.98
6	-N-H- stretching	1348.71
7	-C-N- stretching	1255.43
8	-C=O-Stretching	1718.26
9	-C-S- Stretching	847.56

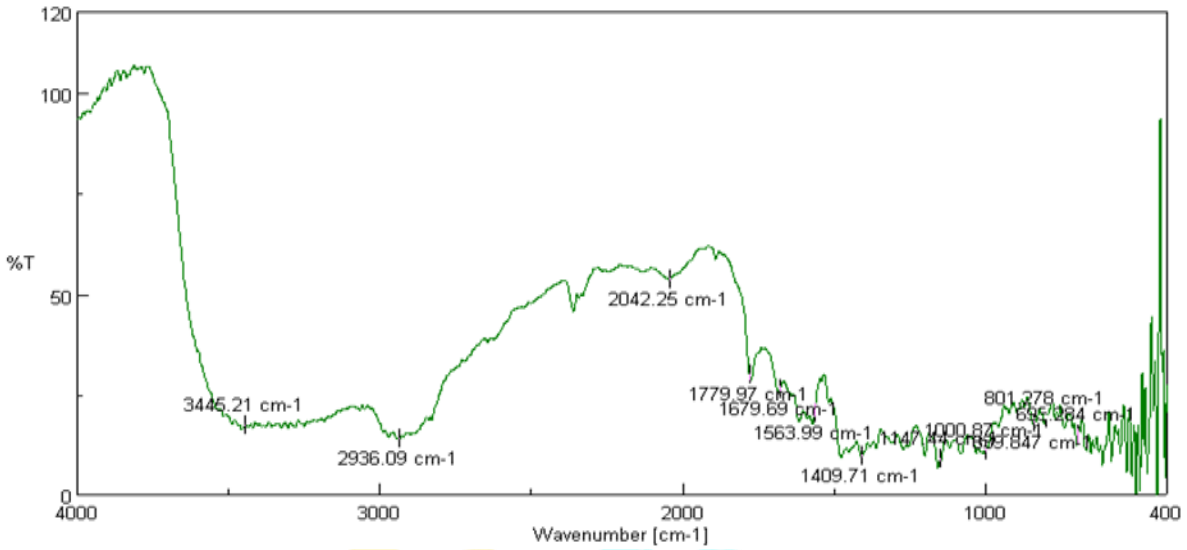

Figure No. 10: IR Spectrum Formulation Batch F5

Table No. 16: IR Peaks Formulation of Esomeprazole + Amoxycillin + Cross Carmellose + HPMC K100 + Ethyl Cellulose

Sr. No	Functional Group	Frequency (cm^{-1})
1	-C-H- stretching	2936.09
2	-C-H- stretching in aromatic	1409.71
3	-O-H- stretching	3445.21
4	-COOH- stretching	1779.97
5	-C=C- stretching	1679.69
6	-N-H- stretching	1563.99
7	-C-N- stretching	1000.87
8	-C=O-Stretching	1768.26
9	-C-S- Stretching	801.27

Differential Scanning Calorimetry (DSC) of Formulation

The Differential Scanning Calorimetry (DSC) is a thermo analytical technique used for analyzing thermal transitions involving thermal energy with a great sensitivity. The DSC thermo gram of Formulation Batch B3 (Esomeprazole + Amoxycillin + Crosspovidone + HPMC K100) show a sharped endothermic peak at 120.89ºC, 153.52 ºC, 198. 46 ºC. Formulation Batch B5 (Esomeprazole + Amoxycillin + Cross Carmellose + HPMC K100 + Ethyl Cellulose) show a sharped endothermic peak at 153.74ºC, 153.52 ºC, 197.66 ºC.

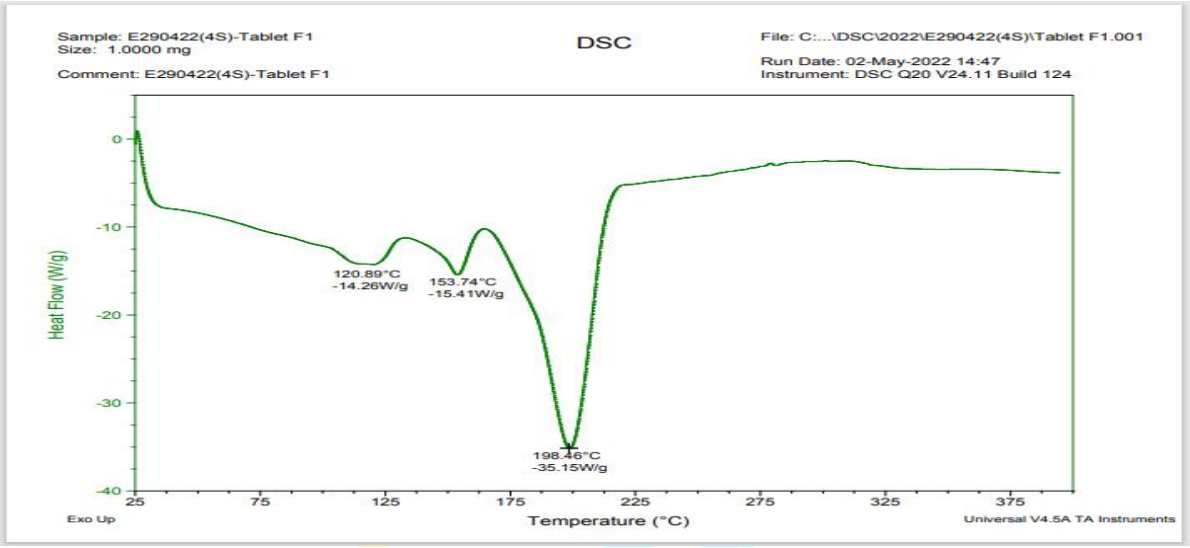

Figure No. 11: DSC of Formulation Batch F3

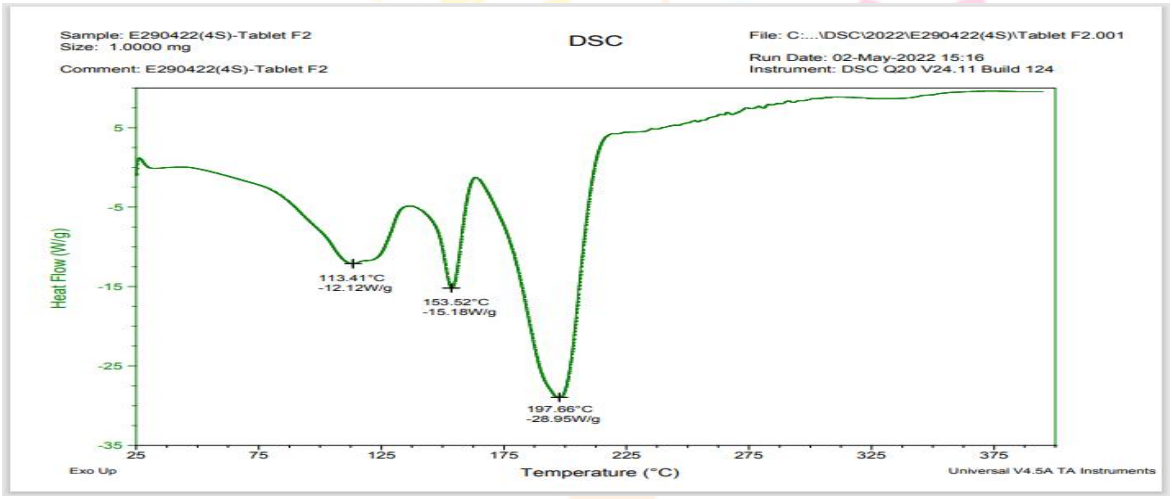

Figure No. 12: DSC of Formulation Batch F5

Evaluation of Post Compression of Bilayer Tablets

Table No. 17: Evaluation of post Compression of Bilayer Tablets

Formulation	Thickness (mm)	Hardness (kg/cm^2)	Weight variation (mg)	Friability (%)	Disintegration Time (min)
F1	4.49±0.82	5.2±0.36	642±0.53	0.51±0.13	90±0.90
F2	4.30±0.65	5.7±0.26	646±0.48	0.57±0.42	75±0.97
F3	4.46±0.36	5.3±0.58	648±0.78	0.41±0.36	110±0.94
F4	4.45±0.29	5.1±0.22	651±0.98	0.58±0.46	115±0.85
F5	4.43±0.62	5.6±0.38	649±0.65	0.45±0.35	105±0.79
F6	4.54±0.45	5.8±0.43	645±0.24	0.75±0.37	120±0.75

S. D = Standard Deviation n =3

Table No. 18: Evaluation of post Compression of Bilayer Tablets

Formulation	Diameter (mm)	Drug Content Esomeprazole (%)	Drug Content Amoxicillin (%)
F1	10.00±0.68	95.89±0.88	93.42±0.26
F2	10.00±0.65	92.22±0.65	94.68±0.46
F3	10.00±0.15	97.14±0.97	98.27±0.98
F4	10.00±0.14	94.42±0.27	95.62±0.65
F5	10.00±0.52	96.28±0.89	97.22±0.95
F6	10.00±0.24	93.64±0.87	95.52±0.66

S. D = Standard Deviation n =3

Table No. 19: In Vitro Dissolution Study of Immediate Release Tablets

Time (min)	% Drug Release					
	F1	F2	F3	F4	F5	F6
0	0	0	0	0	0	0
10	21.50±0.98	19.24±0.42	31.66±0.94	36.41±0.67	30.57±0.25	35.60±0.33
20	27.17 ±0.72	31.22±0.69	42.64±0.22	45.22±0.54	49.10±0.34	46.97±0.39
30	39.26±0.63	40.41±0.40	50.76±0.36	56.12±0.59	56.35±0.45	56.58±0.47
45	48.17±0.40	51.27±0.84	61.04±0.13	66.17±0.64	69.33±0.44	65.68±0.44
60	66.87±0.73	62.02±0.72	78.92±0.75	79.80±0.35	78.75±0.49	70.41±0.39
75	73.44±0.33	85.82±0.93	87.52±0.91	84.58±0.67	89.08±0.24	81.47±0.44
90	91.28±0.33	93.26±0.83	97.73±0.19	95.56±0.88	96.98±0.41	94.43±0.44

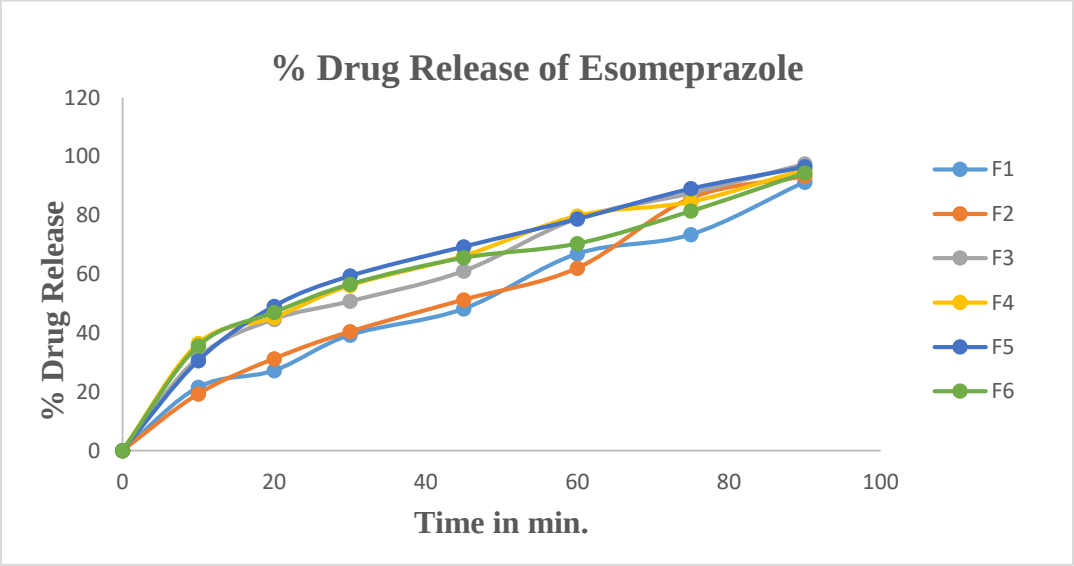

Figure No. 13: % Drug Release of Esomeprazole

Table No 20: In Vitro Dissolution Study of Sustained Release Tablets

Time (min)	% Drug Release					
	F1	F2	F3	F4	F5	F6
0	0	0	0	0	0	0
60	26.06 ±0.67	15.52 ±0.87	26.78 ±0.67	21.61 ±0.45	27.09 ±0.87	24.98 ±0.91
120	34.62 ±0.44	27.54 ± 0.75	38.77 ±0.99	31.23 ±0.34	35.37 ±0.37	29.09 ±0.81
180	48.43 ±0.45	37.68 ±0.78	43.78 ±0.88	39.45 ±0.54	40.71 ±0.31	35.64 ±0.48
240	58.67 ±0.46	40.59 ±0.98	53.37 ±0.56	42.51 ±0.67	52.51 ±0.16	38.95 ±0.43
300	63.52 ±0.28	52.85 ±0.34	66.56 ±0.77	49.91 ± 0.72	60.62 ±0.19	41.62 ±0.56
360	69.73 ±0.33	54.11 ±0.76	70.52 ±0.98	52.60 ±0.58	64.74 ±0.44	45.01 ±0.92
420	72.89 ±0.39	59.08 ±0.98	76.96 ±0.88	57.75 ±0.47	69.47 ±0.57	54.12 ±0.27
480	78.41 ±0.37	67.19 ±0.56	80.30 ±0.56	64.15 ±0.76	77.42 ±0.47	65.21 ±0.38
540	83.45 ±0.57	70.73 ±0.23	89.84 ±0.87	71.89 ±0.35	83.57 ± 0.27	70.86 ± 0.39
600	86.04 ±0.37	81.63 ±0.35	90.71 ±0.56	76.60 ±0.93	87.98 ±0.74	75.93 ±0.30
660	92.27 ± 0.58	85.84 ±0.56	94.55 ±0.45	87.78 ±0.75	90.70 ±0.79	82.23 ±0.39
720	94.74 ±0.12	92.49 ±0.56	98.86 ±0.07	90.08 ±0.46	98.76 ±0.04	91.31 ±0.3

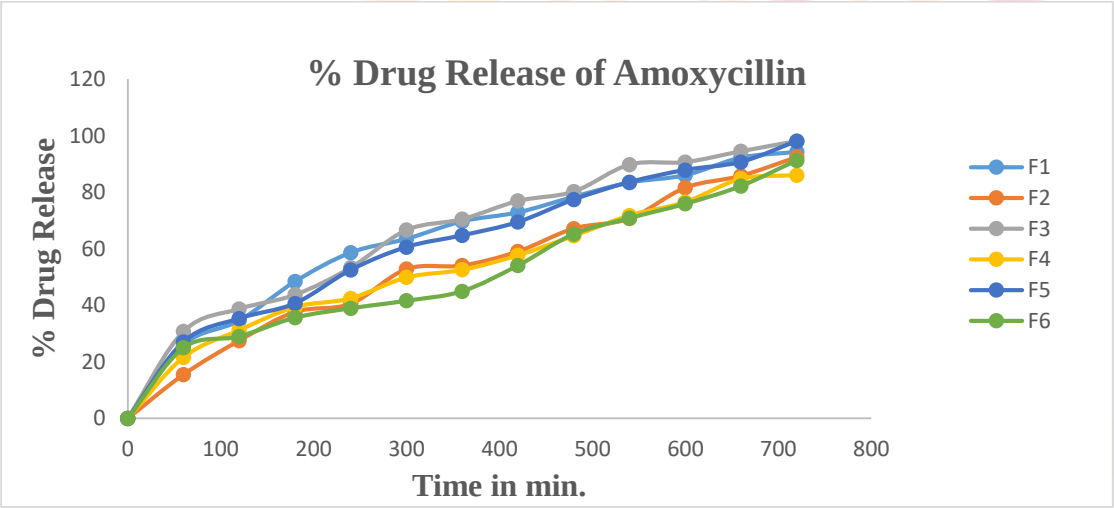

Figure No. 14: % Drug Release of Amoxycillin

Stability Study

Physical Appearance

Colour: Unchanged

Table No. 21: Stability Parameters of Batches F3 and F5 for 0, 30, 60 Days

Formulation	Study Conditions Specification	Months	Drugs Name	% Drug Content	% Drug Release
F3	40°C ±2° C/ 75±5% RH	Initial	Esomeprazole	97.14±0.97	97.73±0.19
			Amoxycillin	98.27±0.98	97.73±0.19
		30 Days	Esomeprazole	97.46±0.67	97.45±0.13
			Amoxycillin	98.67±0.56	98.59±0.91

		60 days	Esomeprazole	95.76±0.34	96.65±0.09
			Amoxycillin	96.89±0.76	97.41±0.43
F5	40°C ±2° C/ 75±5% RH	Initial	Esomeprazole	96.28±0.89	96.98±0.41
			Amoxycillin	97.22±0.95	98.76 ±0.04
		30 Days	Esomeprazole	96.18±0.46	96.56±0.56
			Amoxycillin	97.16±0.36	98.67±0.07
		60 Days	Esomeprazole	96.03±0.74	95.65±0.34
			Amoxycillin	96.45±0.74	97.87 ±0.02

Conclusion

- FTIR and DSC studies indicated that the drug is compatible with all the excipients.
- The bilayer tablets were prepared using the selected immediate release layer and sustained release layer. The prepared tablets were found to be good and free from chipping and capping.
- The hardness of the prepared tablets was found to be in the range of 5.1 to 5.8 kg /cm^2.
- The low values of the standard deviation of average weight of the prepared tablets indicate weight uniformity within the batches prepared.
- The friability of the prepared tablet was found to be less than 1%.
- Drug content of both the drug is calculated using UV spectrophotometer and content was calculated in percentage highest drug content was recorded for formulation at with optimized batches F3 immediate release 97.14±0.97% and sustained release98.27±0.98. F5 immediate release 96.28±0.89% and F5 sustained release 97.22±0.95%.
- In vitro dissolution study of immediate release tablets F397.73±0.19 and F5 96.98±0.41. Sustained release tablets F3 98.86 ±0.07 and F5 98.76 ±0.04gives satisfactory percent release. F3and F5 formulation was kept under stability condition to check the whether the prepared formulation is stable. Results obtained after 60 days were compared with initial reading of this gives complete idea about the stability of drug product. So, we can conclude the formulation F3 and F5 is stable and can be packaged in plastic container.
- The result revealed that the F3 and F5 batches shown the best performance.

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