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Research Article

Bilayer Floating Tablet of Amoxicillin with Deglycyrrhizinated Licorice (DGL) Powder for the Treatment of Peptic Ulcer

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ABSTRACT

Peptic ulcer disease is associated with mucosal erosion from an imbalance of gastric acid, pepsin, Helicobacter pylori infection, and weakened mucosal defenses. This study was done to treat Peptic ulcer disease by formulating Amoxicillin, which is a ß-lactam antibiotic that kills bacteria by inhibiting cell wall synthesis. Moreover, Deglycyrrhizinated licorice, an herbal alternative, was added in the formulation to provide mucosal protection and anti-inflammatory activity, aiding ulcer healing without affecting acid secretion and reduceing side effects.

The current study aimed at formulating a bilayer-floating tablet containing amoxicillin and deglycyrrhizinated licorice, and the purpose of this study was to increase gastric retention, increase localised drug delivery, and generate a synergistic anti-ulcerative effect. The floating drug delivery system has been designed to extend the gastrointestinal residence time, and thus, enhance the systemic availability of the drug to act locally in the upper gastrointestinal tract. In addition, the polymers used to make the bilayer tablet a sustained-release tablet were complemented by effusive agents to provide buoyancy and prolonged gastric retention. Wise choices were made on the excipients in order to stabilise the tablet. Based on this, the main objective was to develop a gastro-retentive bilayer tablet enabling the gradual delivery of amoxicillin in combination with the immediate localised activity of deglycyrrhizinated licorice. The findings showed effective floating characteristics and a consistent drug release profile, suggesting its potential as a promising therapy for treating peptic ulcers.

Keywords: Peptic Ulcer Disease, Amoxicillin;, Deglycyrrhizinated Licorice, Bilayer-Floating Tablet, Gastro-Retentive Drug Delivery.

INTRODUCTION

An ulcer is a local defect, or excavation of an organ or tissue's surface, produced by sloughing of inflammatory necrotic tissue. Ulcer is divided into Peptic ulcers, Esophageal ulcers, and Aphthous ulcers [1]. Peptic ulcer disease is a chronic complication of the gastrointestinal tract which is described as the ulceration and erosion of the mucosal lining due to the aggressive action of acid pepsin secretion [2].

Peptic ulcers can be classified into gastric (stomach) ulcers and duodenal ulcers. A duodenal ulcer occurs 4 times more frequently than a gastric ulcer. Gastric ulcers are common in the elderly, on the lesser curve. Normally, the integrity between the duodenal and gastric mucosa is maintained by neutral pH, continuous epithelial cell renewal, and a mucus bicarbonate barrier. All peptic ulcers arise from an imbalance between the normal defenses and aggressive factors [3]. The etiological factors in peptic ulcer are H.pylori, Heredity, NSAIDS, Smoking, Alcohol, Enhanced Gastric Acid Secretion, Comorbidity, Stress, and Diet [1]. There are asymptomatic and symptomatic patients, among symptomatic patients the most common symptoms are epigastric pain which may be similar to dyspepsia, abdominal fullness, nausea, bloating, hematemesis, bloody stools, and fatigue [4]. The non-pharmacologic treatments include the elimination or management of psychological stress, nonselective NSAIDS, including aspirin, and smoking. Restrict certain beverages and foods like alcohol, caffeine, and spicy food. The pharmacological treatment includes H2-receptor antagonists, proton pump inhibitors (PPIs), Triple therapy regimen (PPIs, Amoxicillin, Clarithromycin), and quadruple therapy (PPIs, Tetracycline, Metronidazole, Bismuth salts) [3,4].

Nowadays, novel drug delivery systems are used to treat illnesses. These systems have overcome many hurdles of decreased gastric retention time and fast gastric emptying. Some of them include floating drug delivery systems, swelling and expanding systems, and polymeric bio-adhesive systems. Oral delivery of drug is more favorable over other dosage forms as its

cost effective, good compliance and easy administration. For absorption of the drug in the upper GIT, oral sustained release gastro-retentive dosage forms (GRDFs) are preferred, such as Floating Drug Delivery Systems (FDDS). It enhances the gastric retention time of the drugs by making them float upon the gastric contents and also prolongs the gastric emptying time [5]. This system increases the gastric-retention time by floating in the gastric fluids for a longer period due to having low density. The drug is slowly released over a period of time as it remains in the stomach for a longer duration [6]. In floating drug delivery, the medication is buoyant enough to float over the stomach contents and stay there for an extended period of time [7]. The floating tablet is branched into effervescent and non-effervescent systems. The Effervescent FDDS includes a Gas generating system and a Volatile liquid containing system. Moreover, the Non-Effervescent FDDS comprises of Colloidal gel barrier system, Microporous compartment system, Floating microsphere, and Alginate floating beads. A raft-forming system is also one of its types [6]. This drug delivery system works by swelling up in hydrocolloid when it's exposed to gastric fluids due to the release of CO2. The swellable polymers used in this can be methylcellulose and Chitosan, along with effervescent compounds such as sodium bicarbonate, tartaric acid, and citric acid [6, 8]. These are low density and low specific gravity floating drug delivery systems. They release CO2 in the gastric fluids which gets trapped in the gelatinized hydrocolloid, which causes it to float in the stomach [6, 9]. It consists of a hallow deformable unit having a first and a second chamber, having a non-permeable, pressure-reactive, adjustable bladder in between. The drug is placed in the first chamber, and a volatile liquid like cyclopentane is placed in the other. This volatile liquid produces gas that makes the dosage form float. The drug is mixed with swellable cellulose-type hydrocolloids, polymers like polycarbonate, polymethacrylate, and polystyrene. It swells up and floats on gastric fluid [6]. It contains a drug with highly soluble cellulose-type hydrocolloid such as HPMC, polycarbophil, polystyrene, and polyacrylate, that forms aa gel in the stomach and floats [10]. The drug is encapsulated in the microporous compartment that has porous walls. The peripheral walls are sealed so that no gastric fluid can go inside. The floatation chamber has trapped air that causes it to float on the gastric fluid [11]. It consists of a central hollow space where the drug is loaded, covered by an outer polymer shell. It consists of sodium alginate beads dipped in calcium alginate solution, which are then frozen and dried. They act as porous systems that float on the gastric fluids. CO2 bubbles get trapped in the gel forming a Solution, which swells up and makes a raft layer above the gastric contents and floats on it. Bilayer tablets consist of two different active ingredients in two different layers, which are supposed to be released at different time intervals. One layer is immediately released, and the others layer is released gradually over time, thus acting as a sustained release [12]. The sustained release layer absorbs the gel barrier on its surface. This produces the bulk density lesser than gastric fluid and remains buoyant in the stomach for extended period of time [5].

Amoxicillin is a semi-synthetic, broad-spectrum antibiotic of the class Penicillin, which is used to treat several infections. It is generally more effective against infections caused by gram-positive bacteria than gram-negative ones. Amoxicillin is considered a bactericidal antibiotic. It inhibits the synthesis of mucopeptide of the bacterial cell wall during its division. It performs its action by binding to penicillin-binding proteins (PBPs) and breaking the beta-lactam ring in the cell wall. It stops the synthesis of two linear cross-linked peptidoglycan by inhibition of the enzymes, which in turn stops the final stages of bacterial cell division. Then, autolytic enzymes called autolysins lyse the bacterial cell wall. This leads to formation of weak and easily breakable bacterial cell wall [13, 14]. Amoxicillin is used in the treatment of a number of infections such as tonsillitis, pharyngitis, and otitis. As a part of triple and quadruple therapy, it is used for the removal of H. Pylori infection. It is also used to treat infections of the lower respiratory tract, like acute bacterial sinusitis. Immediate-release amoxicillin is use for the infections of skin and skin structures. Moreover, it is also used to eradicate urinary tract infection [15, 16].

Hydroxypropyl methylcellulose compositions K4M and K100M are used as excipients in the formulation process, and they are commonly used in sustained-release pharmaceutical preparations [17]. When these excipients are exposed to gastric fluids, they form a gel barrier which helps in the controlled release of the active pharmaceutical ingredients over a long period. DGL use Amoxicillin, which is used concomitantly with deglutethionylated

glutathione (DGL) in a bilayer floating tablet design, allows therapeutic control of peptic ulcer disease with increased bioavailability, decreased dosing frequency and improved adherence by patients. Moreover, the physical chemochemical compatibility of amoxicillin with DGL with the excipients was measured using Fourier transform infrared (FTIR) spectroscopy. FTIR spectra of the drug and the excipent components were compared to show that there was no sign of adverse chemical interactions, which confirmed that the drug preserved its structural integrity and that the components of the formulation were compatible [18, 19].

This bilayer floating tablet formulation represents a significant change in the treatment plan of peptic ulcers. The formulation is shown to have the ability to improve the efficacy of current treatment regimens and reduce the need to be dosed repeatedly by adding both DGL and extending the gastrointestinal residence time of amoxicillin to supplementary mucosal protection. The prolonged action of the two active agents is guaranteed by the sustained releases, making the agents to have greater therapeutic activity, which reflects on the enhanced patient outcomes in clinical treatment of peptic ulcer disease [5, 6, 12].

Material and Methods

Materials

To formulate the bilayer-floating tablet formulation, a variety of materials, chemicals, apparatus, equipment, and software were utilized in this research. The major components of the drugs were Amoxicillin trihydrate, which was purchased in City Pharmaceuticals, and Deglycyrrhizinated Licorice (DGL), which was purchased in Herbal Ingredients Expert. A number of excipients and chemicals, such as HPMCK4M, sodium bicarbonate (NaHCO3), citric acid, Avicel, and magnesium stearate, were also included in the formulation that were provided by Novamed Pharmaceuticals and HPMCK100M and Aerosil by Pharmasol (Pvt) Ltd.

Laboratory equipment necessary included a set of beakers, pestle and mortar, spatula, stirrer, sieves, trays, funnel, tripod stand, measuring cylinder, pipette, test tubes, capillary tubes, and a measuring scale; they were needed to prepare and mix the tablet formulation. The instruments used in the research were a Planetary Mixer (HM 40 China), Multi-Station Rotary Tablet Machine (ZP420-3ID, Shanghai Tianfan Pharmaceutical Machinery Factory), Monsanto Hardness Tester (OG-HT101), a Dissolution Apparatus (TDT-21) and a Friabilator, a UV spectrophotometer, a weighing balance (SF-400C), a stopwatch, a Karl Fisher titrator (KFT-4 Software applications, such as MS Word, MS Excel and EndNote were used to process words, analyze data and manage references respectively in order to ease the process of data analysis and documentation. All these resources were used in the overall formulation and analysis of the formulation in this study. The chemicals and ingredients used in this study are demonstrated in Table 1:

Ingredients (mg per tablet)	**T1**	**T2**	**T3**	**T4**	**T5**
Amoxicillin trihydrate	500	500	500	500	500
HPMC K4M	140	180	150	135	120
HPMC K100M	21	27	23	21	18
NaHCO3	120	105	120	120	120
Citric acid	30	30	30	30	30
Avicel	46	25	34	49	49
Magnesium Stearate	15	15	15	15	15
Aerosil	10	10	10	10	10
Second layer					
Deglycyrrhizinated Licorice (DGL)	100	100	100	100	100
Avicel pH5 102	18	18	18	18	18
Color	Q.S	Q.S	Q.S	Q.S	Q.S
Total(mg)	1000	1000	1000	1000	980

Table 1: List of Ingredients

Pre-Formulation

The physical evaluation of Amoxicillin involves assessing its physical properties to ensure quality and purity. It was examined for its organoleptic properties. The melting point apparatus was used to assess the melting point of amoxicillin by the Capillary fusion method. The melting point was measured and contrasted with the standard value. Different solvents like methanol, ethanol, and water, each of 05 mL, were taken in different test tubes to check solubility (See Figure 1). Then a slight amount of drug was added in each test tube and shaken for 05 to 10 mins.

Pre-Compression Parameters

The sieve method is effective for determining particle size. A series of sieves (20, 25, 30, 35, 40, 70 and 100) were stacked above each other, and 150 g of powder was poured on the uppermost sieve and shaken for 15 minutes (See Figure 2 and 3). Then the powder retained on each sieve was collected. The average diameter of the powder was computed by the following equation:

$$\mathbf{d} = \frac{\sum \mathbf{xidi}}{\mathbf{100}}$$

Where, **xi** = upper and lower sieve average size,
di = range [35].

Figure 2: Sieve Stack for Particle Size

Figure 3: Sieving of Ingredients

Powder was weighed and put into the measuring cylinder. Bulk density (g/ml) was calculated by using this formula:

$$\text{Bulk Density} = \frac{M}{V_0}$$

Where, **M** = Mass of the sample

V_0 = Total amount of space the powder occupies

Powder was weighed and put into the measuring cylinder. The cylinder was tapped every second from a height of 2.5 cm until the volume remained constant (See Figure 4). Tap density was determined by using this formula:

$$\textbf{Tapped Density} = \frac{M}{V_f}$$

Where **M** = mass of the sample

V_f = Tapped volume of sample

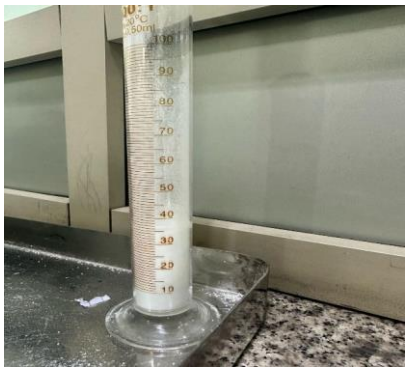

Figure 4: Tapped Density of Amoxicillin

The compressibility index, represented as a percentage, was used to describe the flow properties of powder. It was calculated by using a specific equation:

$$\text{Compressibility index} = \frac{Tapped\ density - Bulk\ density}{Tapped\ density} \times 100$$

Hausner ratio is a way to measure the flow characteristics of powder. It was determined by the formula:

$$\text{Hausner's Ratio} = Tapped\ Density\ /\ Bulk\ Density$$

The fixed funnel method is used to determine the angle of repose of powder. This method involves the preparation of drugs with different excipients. Next, these were weighed and poured into a funnel. The funnel was carefully placed just above the peak of the powder heap. The powder was then allowed to flow freely onto the surface. The height (H) and Radius(R) were calculated (See Figure 2 and Table 5). Angle of repose was determined by the formula:

$$Tan\theta = \frac{H}{0.5 \times D}$$

Where **θ** = the angle of repose.

H = the height of the pile.

D = diameter

Table 2: Flow Properties and Angle of Repose

The Angle Of Repose Value	Flow Properties
>20	Excellent
20-30	Good
30-34	Passable
<40	Very poor

Figure 5: Angle of Repose

Assay

Crush and weigh 20 tablets, take powder equivalent to 500 mg Amoxicillin and transfer into 100ml volumetric flask. Dissolve in phosphate buffer (Ph 1.2) sonicate for 15 minutes to dissolve, and filter through Whatman No. 41 and make up the volume to 100 Ml to obtain a 5000µg/Ml stock solution. Further dilute to prepare working standard solutions in the range of 2–12 µg/Ml. Record the absorbance at 272 nm against blank.

Assay %=((abs.of sample)/(abs.of standard))×concentration

A calibration curve of amoxicillin was formed in this study by measuring its absorbance at 272 nm through a series of known concentrations. The absorbance of known solutions was measured using a UV spectrophotometer and known concentrations of amoxicillin. The analysis of the resulting data showed a regression equation (e.g., y = 0.0507x + 0.0012) and the coefficient of determination (R2), which are used to determine the extent of linear dependence between the absorbance and the concentration. Attenuated total reflectance-Fourier transform infrared (ATR-FTIR) spectroscopy was further employed to evaluate possible molecular interactions between amoxicillin and excipients that are included into the bilayer floating tablet preparation. The spectra obtained from 4000 to 600 -1 were recorded and specific functional-group absorptions (such as the 20 -1770 cm -1 20 -16001640 cm $^{-1}$) were observed. The resulting spectra enabled the identification of any chemical reactions or structural changes that could affect the stability of the formulation or its performance.

Ethics Statement

The study was undertaken in compliance with the ethical principles of the corresponding institutional and regional regulations. Animal trials were all conducted according to the ethical standards of the Committee to the Purpose of Control and Supervision of Experiments on Animals (CPCSEA) and, thus, humane treatment was ensured. To reduce pain and agony, the administration of anesthetics and analgesics was carefully observed. The research processes involving human subjects adhered to the ethical standards provided by the Indian Council of Medical Research (ICMR). The relevant ethics committees were consulted before the study was initiated, and thus the study followed the best practices in ethical research.

RESULTS

Pre-Formulation Studies

Amoxicillin trihydrate was observed for physical state, color, and odor (See Figure 6). During physical examination, Amoxicillin trihydrate was found to be a white, or almost white, crystalline powder having a a slight characteristic odor.

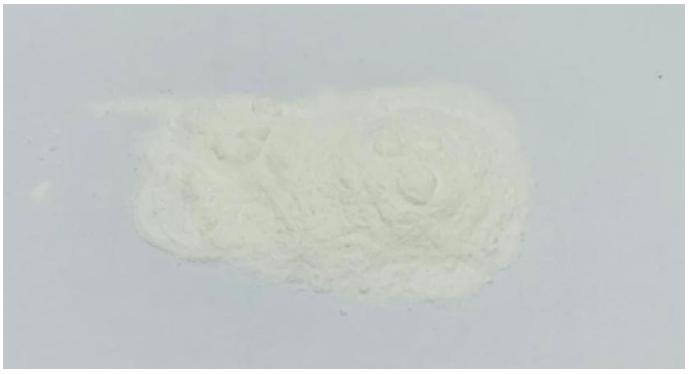

Figure 6: Appearance of Amoxicillin Powder

The melting point of the sample was accurately determined using the capillary fusion method. The substance was finely powdered and meticulously packed into a capillary tube, and heated gradually. The observed melting point was 195°C, indicating a high level of purity, as the range was sharp with no significant deviation. This result is consistent with expected values for a pure compound whose results were shown in Table 3.

Table 3: Melting point of Amoxicillin

Method used	Experimental Value	Literature Value
Capillary fusion method	195 °C	160-200°C

First, we performed the solubility test in which we dissolve the amoxicillin in three different solvents ethanol, methanol and water and shown in table 4 and it was more soluble in water and to some extent it was soluble in ethanol, and it shows poor solubility with methanol (See Figure 7).

Table 4: Solubility of Amoxicillin in Different Solvents

Serial No.	Solvents	Solubility
1	Ethanol	++
2	Methanol	+
3	Water	+++

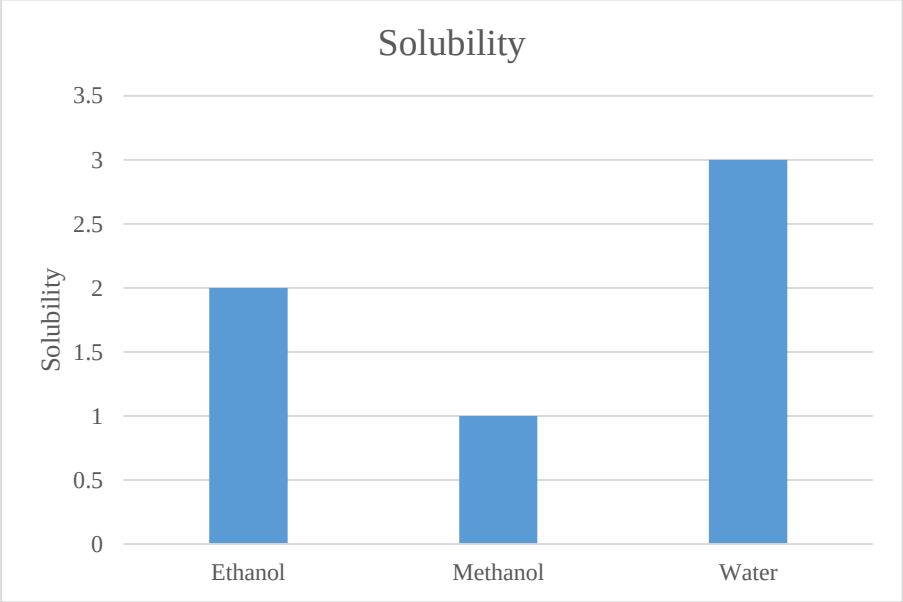

Figure 7: Solubility of Amoxicillin in Different solvents

In the pre-compression studies, particle size analysis was conducted by passing the sample through a series of sieves (20, 30, 40, and 60 mesh) to evaluate the distribution of granule sizes whose results were mentioned in table 3. An average was taken from the values obtained. In the case of F1, the percentages retained was 0.37 on sieve 20, 8.01 on sieve 30, 22.99 on sieve 40 and 34.12 on sieve 60. The values in F2 were 0.31, 8.45, 23.78 and 33.57 respectively. The F3 result was 0.23 percent, F4 was 0.27 percent, 7.56 and 22.19 and 32.80 percent respectively. Lastly, F5 registered 0.33, 8.21, 23.32 and 34.11 (See Table 5). Such reproducible outcomes indicate that the sample has a homogeneous distribution of particles, which is essential in terms of homogeneity of the flow and compression pattern of the sample in the process of tablet formulation.

Table 5: Determination of Particle size

Sieve No.	F1	F2	F3	F4	F5
20	0.37%	0.31%	0.23%	0.27%	0.33%
30	8.01%	8.45%	7.56%	7.78%	8.21%
40	22.99%	23.78%	22.19%	23.02%	23.32%
60	34.12%	33.57%	32.80%	33.11%	34.11%

In the pre-compression evaluation, bulk density was assessed for powder samples to determine their flow properties and compressibility. The test was performed using a graduated cylinder method, the average was taken, and the values obtained were 0.542 g/cm³ for the first sample, 0.568 g/cm³ for the second, 0.537 g/cm³ for the third, 0.534 g/cm³ for the fourth, and 0.542 g/cm³ for the fifth sample, which are shown in Table 6. The results indicate relatively consistent bulk densities across the samples, suggesting uniform particle packing and good

flow characteristics, which are favorable for the tablet compression process. As shown in Table 7, Tap density was determined by performing the test to ensure accuracy and consistency. The recorded average values were 0.7323 g/cm³, 0.7142 g/cm³, 0.7322 g/cm³, 0.7043 g/cm³, and 0.7121 g/cm³. The results showed minor variations, indicating good repeatability and reliable tap density, which reflects the powder's uniform packing behavior under mechanical tapping (See Figure 8).

Table 6: Bulk Density

Formulation Code	Bulk density (g/cm^3)
F1	0.542
F2	0.568
F3	0.537
F4	0.534
F5	0.542

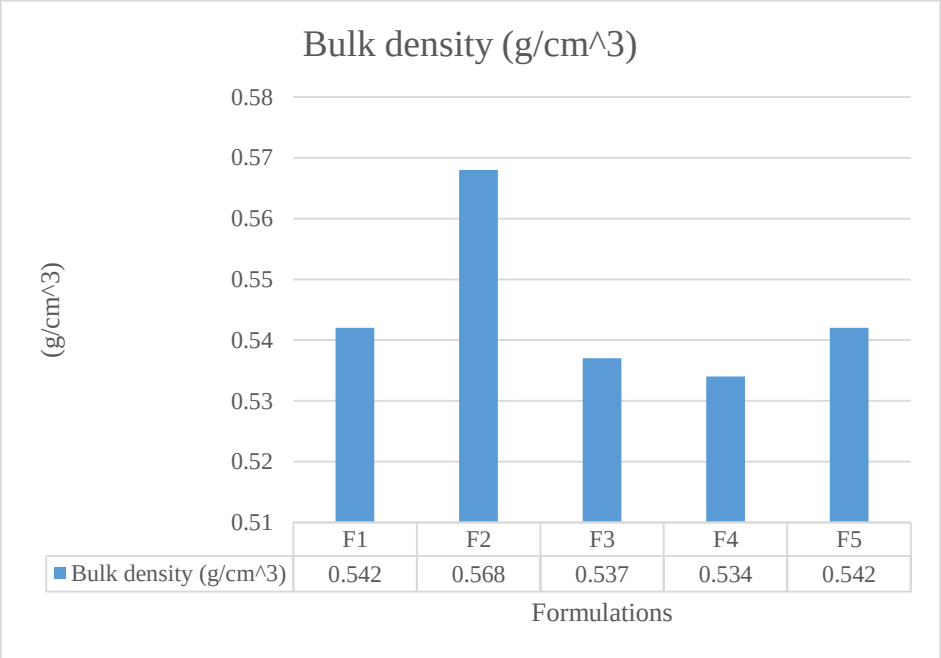

Figure 8: Bulk Density

Table 7: Compressibility

Formulation Code	Cars Index
F1	25.98
F2	20.47
F3	26.22
F4	24.18
F5	23.88

Carr's Index was used to assess compressibility of single powder sample, under well-developed proxy of evaluating flowability as shown in figure 9. The test was replicated to provide some form of reproducibility and the mean values were calculated. Findings produced Carr Index values of 25.98 3, 20.47, 26.22 and 24.18, which are presented in Table 8 and Fig. 10. Such values represent moderate compressibility, which means that the substance has a fair and good flowability and can thus be used in the process of creating tablets.

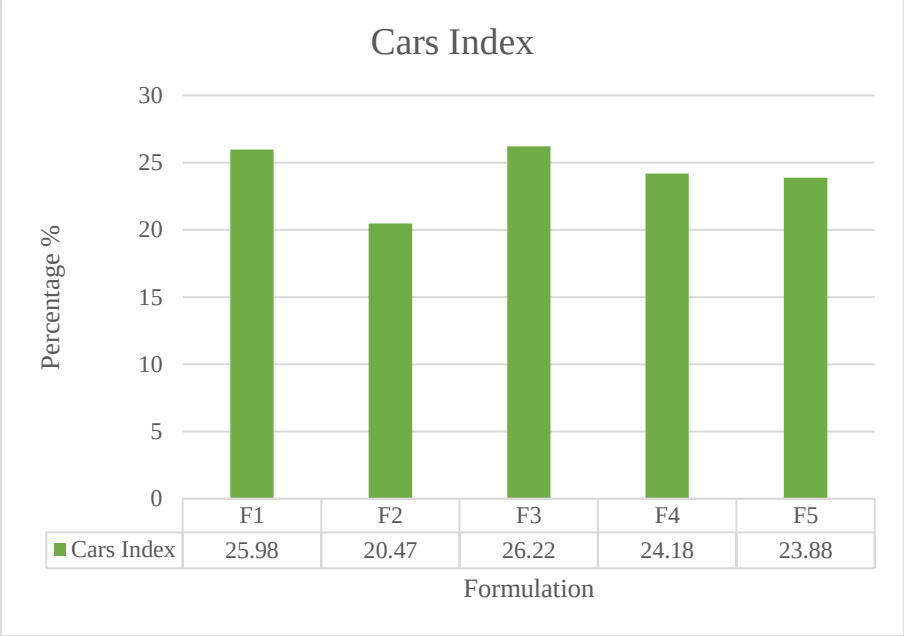

Figure 9: Compressibility

The Hausner Ratio test was also used to further analyze flowability and compressibility. This is done by dividing the tap density by the bulk density as per the formula: Hausner Ratio=Tap Density/Bulk Density. Mean values have been calculated as follows: 1.35 of formulation F1, 1.25 of F2, 1.36 of F3, 1.31 of F4 and F5 which is now given in Table 9 and Fig. 11 (Appendix). These values indicate that the powder has fair to good flow properties, as all readings fall within the acceptable range for pharmaceutical processing.

Table 8: Hausner's Ratio

Formulation Code	Hausner's Ratio
F1	1.35
F2	1.25
F3	1.36
F4	1.31
F5	1.31

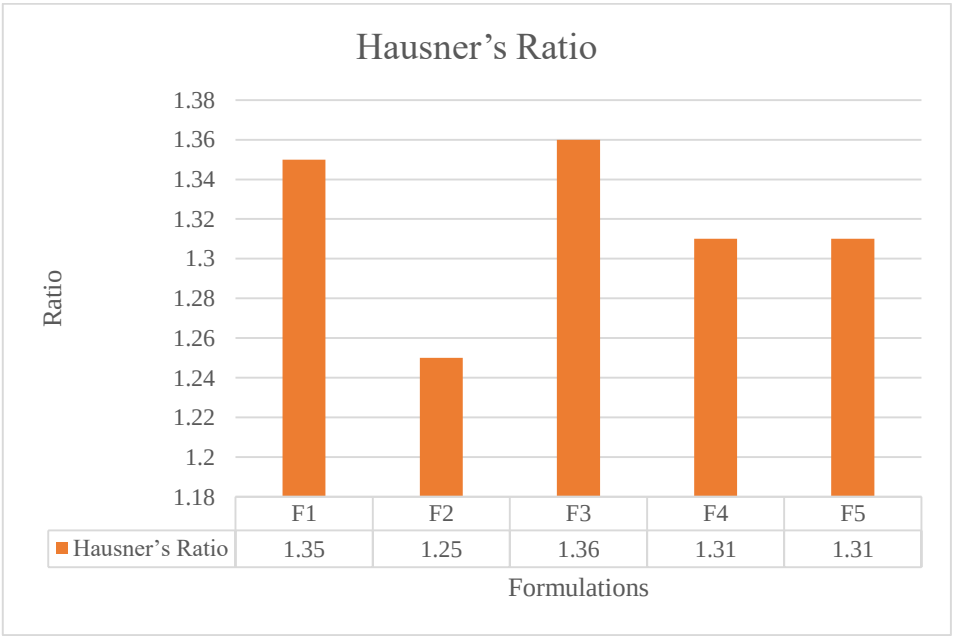

Figure 10: Hausner's Ratio

After that, we performed the Angle of Repose test on a single powder sample to evaluate its flow properties. The test was carried out by allowing the powder to flow through a funnel onto a flat surface, forming a conical heap, and then measuring the angle formed between the surface and the slope of the heap. The angle of repose values obtained were 36.97°, 35.19°, 38.36°, 35.58°, and 36.69°, which are shown in Table 10 and Figure 12. These results indicate that the sample has acceptable flow properties, with all values falling within a moderately flowing range

Amoxicillin trihydrate standard solutions were made in phosphate buffer (pH 1.2) with concentrations ranging from 2 to 12 µg/mL. A UV-visible spectrophotometer was used to analyze these solutions at a wavelength of 272 nm in order to create a calibration curve for quantitative estimation. The absorbance values were noted (See Table 11 and Figure 13).

Table 11: Absorbance of Amoxicillin

Concentration (µg/mL)	Absorbance at 272 nm
2	0.301
4	0.361
6	0.421
8	0.481
10	0.541
12	0.605

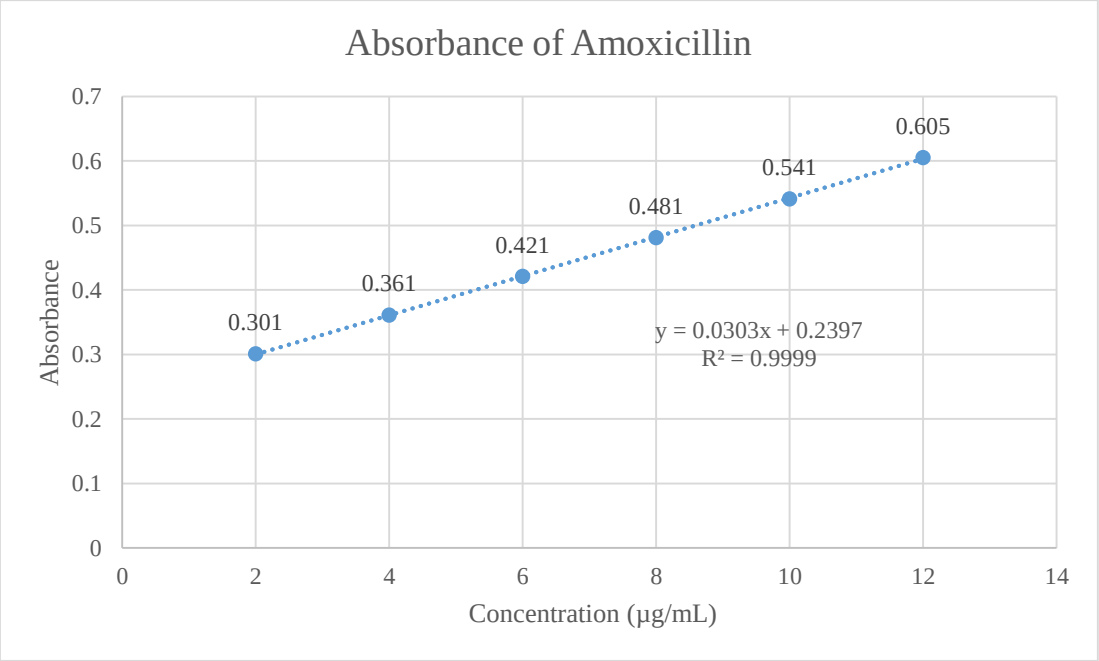

Figure 11: Calibration Curve

According to linear regression analysis, the data showed a strong linear connection between absorbance and concentration. The regression equation that was produced was:

$$Y = 0.0303x + 0.2397$$

Where **x** = Amoxicillin Concentration (µg/mL) and

y = Absorbance at 272 nm

ATR-FTIR

Amoxicillin

Characteristic FTIR absorptions at 1700–1720 cm^{-1} (amide C=O) and broad N-H/O-H stretches (~3300 cm^{-1}) confirm the pure drug's structure as demonstrated in Figure 12. These peaks serve as reference markers for identifying amoxicillin in the formulation (Foschi, Marziale, & Biancolillo, 2022).

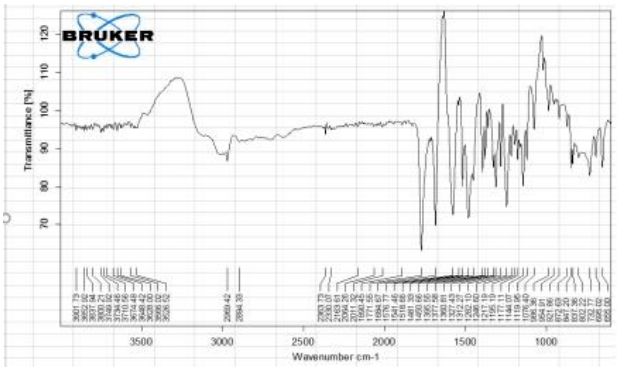

Figure 12: FTIR of Amoxicillin

HPMC Polymer

The spectrum shows dominant O-H stretch around 3395 cm^{-1} and ester-related C-O stretch near 1050 cm^{-1}, typical for hydroxypropyl methylcellulose (See Figure 13). This confirms the polymer's chemical integrity in the formulation (Pan, Svirskis, Waterhouse, & Wu, 2023).

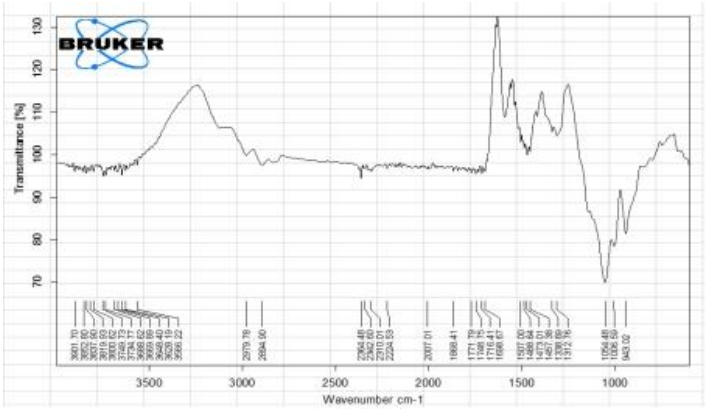

Figure 13: FTIR of HPMC Polymer

Sodium Bicarbonate

Distinct peaks related to bicarbonate and carbonate groups, including bands near 1350–1400 cm^{-1}, verify the presence of sodium bicarbonate as an effervescent agent in the formulation (See Figure 14).

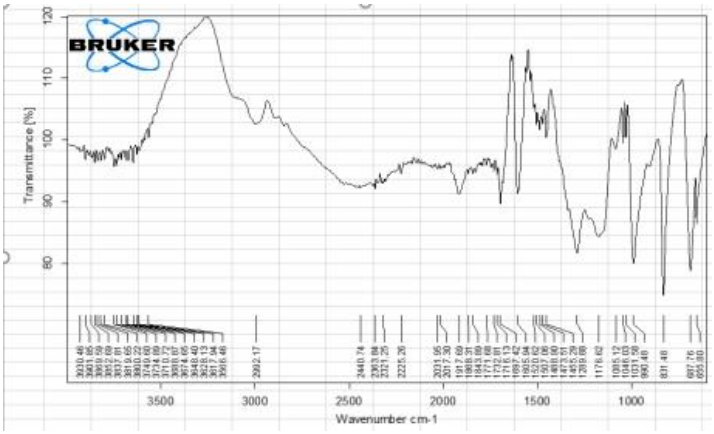

Figure 14: FTIR of Sodium Bicarbonate

Citric Acid

Broad O-H stretching peaks (~3300 cm^{-1}) and sharp carbonyl peaks (~1720 cm^{-1}) confirm citric acid presence, ensuring its role in the tablet's acid-base interaction functionality as demonstrated in Figure 15.

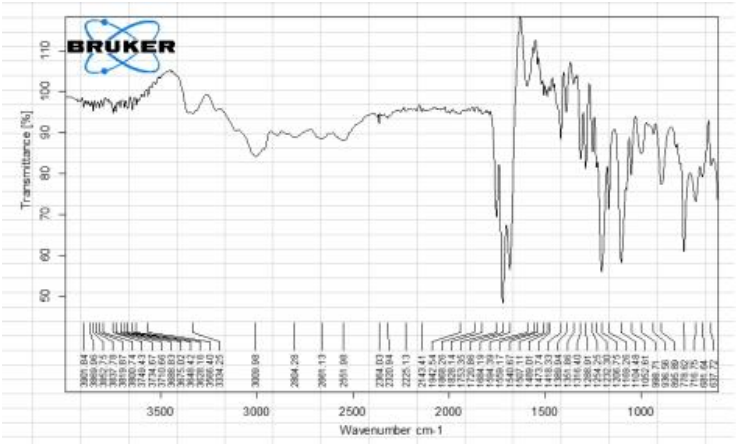

Figure 15: FTIR of Citric Acid

Avicel PH 102

Typical microcrystalline cellulose peaks include broad O-H stretches (~3400 cm^{-1}) and C-O-C vibrations (~1050 cm^{-1}), confirming the excipient's identity and physical stability within the formulation (Figure 16).

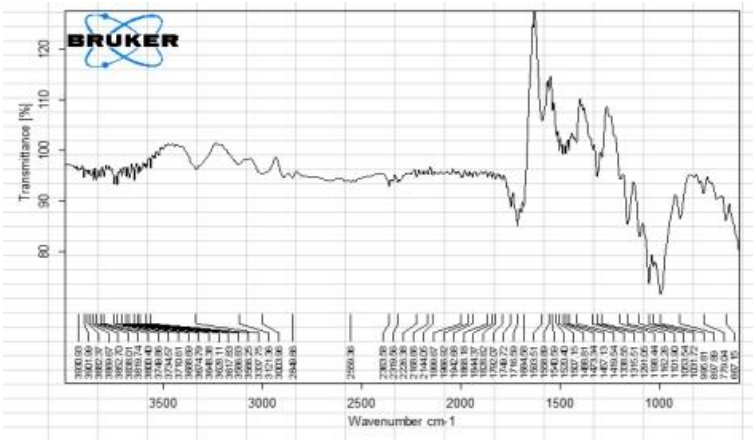

Figure 16: FTIR oF Avicel PH102

Magnesium Stearate

Characteristic carboxylate peaks near 1600 cm^{-1} and 1400 cm^{-1} reflect stearate groups bound to magnesium, supporting the correct inclusion of this excipient in the formulation (See Figure 17).

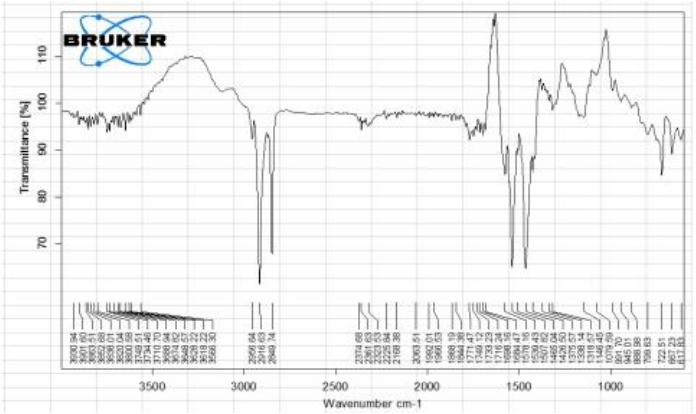

Figure 17: FTIR of Magnesium Stearate

Aerosil - Fumed Silica

Broad peak around 3400 cm^{-1} due to surface hydroxyl groups and Si-O-Si stretching near 1100 cm^{-1} confirm the presence of Aerosil as a glidant with maintained structural features as demonstrated in Figure 18.

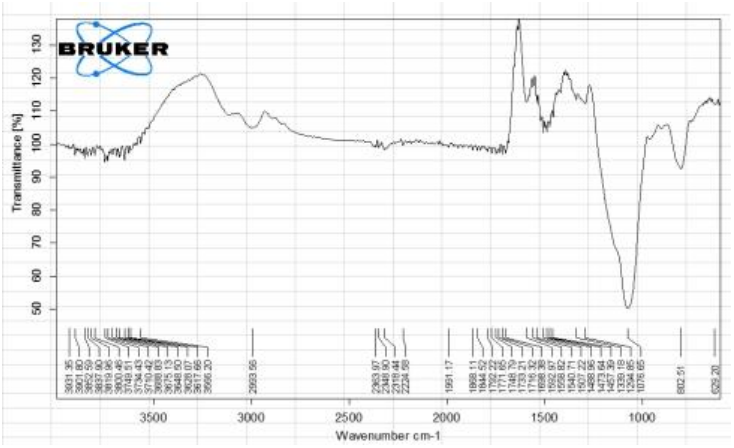

Figure 18: FTIR of Aerosil-Fumed Silica

Deglycyrrhizinated Licorice

Broad O-H stretching (3400 cm^{-1}) and aromatic C=C stretches (~1600 cm^{-1}) indicate key phenolic and flavonoid groups in licorice, affirming its incorporation as a bioactive agent (Figure 19).

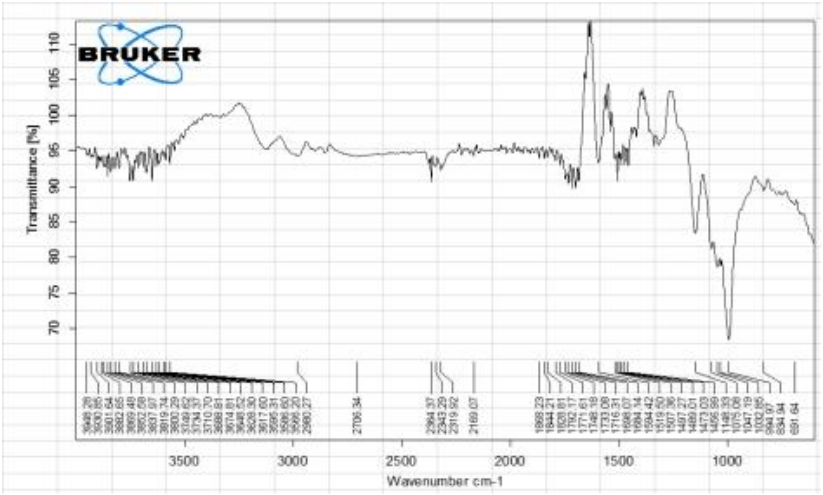

Figure 19: FTIR of Deglycyrrhizinated Licorice

Final Formulation

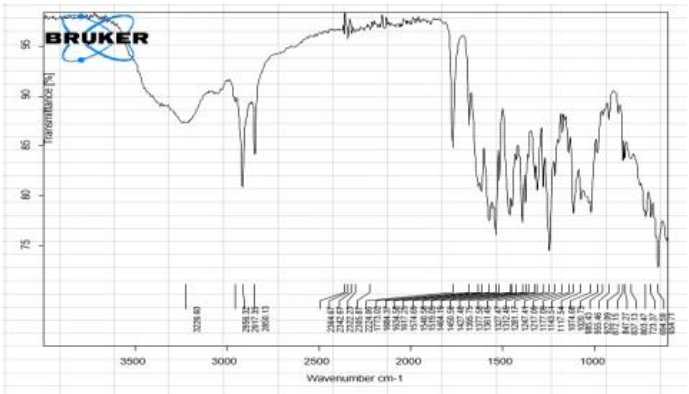

Figure 20: FTIR of Final Formulation

The observed peaks in the FTIR spectrum above correspond to specific molecular bond vibrations, such as stretching and bending, and offer insight into the chemical integrity and compatibility of the formulation components (Figure 20). All major functional groups of Amoxicillin were preserved in the final formulation, including β-lactam C=O, amine N–

H, and carboxyl C=O. No significant shifts, disappearance, or new peaks were observed in the formulation spectrum compared to the individual components, suggesting no chemical interaction or drug degradation during formulation. The presence of excipients (e.g., HPMC, DGL, or $NaHCO_3$) was confirmed by characteristic O–H, C–H, and C–O stretches, aligning with known spectral fingerprints.

Hardness

The observed range was found to have a correlation coefficient (R2) equal to 0.999 thus indicating a high degree of linearity which indicated the accuracy and consistency of the UV spectrophotometric procedure in the quantitative analysis of amoxicillin concentrations in pharmaceutical preparations (Figure 21). Typical FTIR absorptions at 17001720 cm -1 (amide C=O) and the wide range of N-H/O-H abs of the solution at 3300 -1 support the chemical structure of the pure drug, and are used as reference markers to identify amoxicillin in the formulation (Foschi, Marziale, and Biancolillo, 2022).

Table 9: Hardness

Formulation Code	Hardness
F1	5.242
F2	6.589
F3	5.084
F4	5.143
F5	4.326

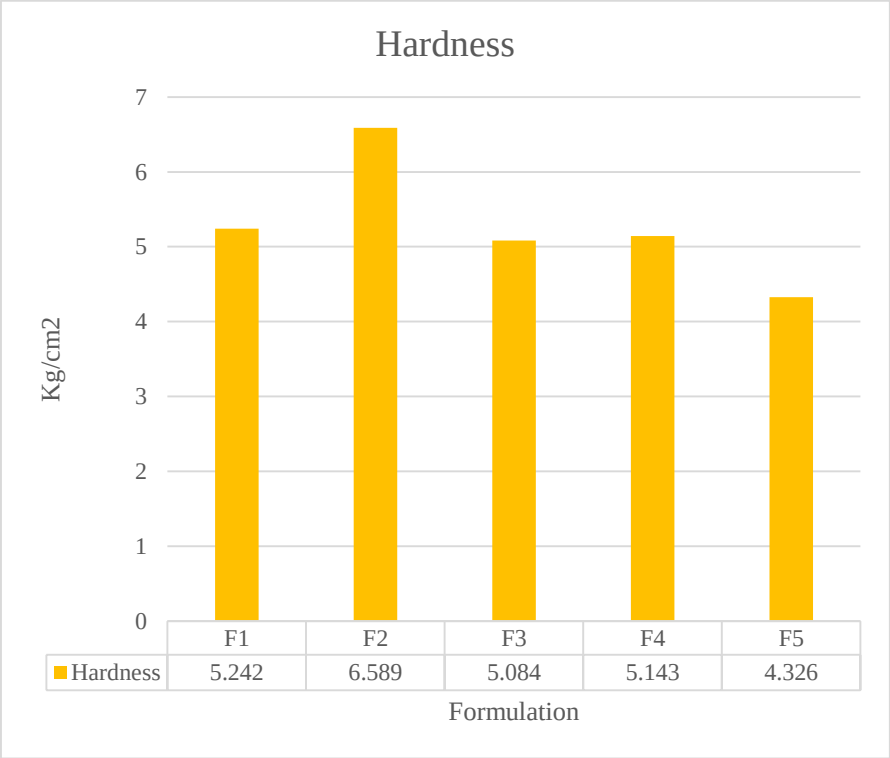

Figure 21: Hardness

The spectrum shows a strong OH stretching band at 3395 cm to 3395 cm -1 and an ester -like C O stretching band at 1050 cm -1, characteristic of hydroxypropyl methylcellulose, thus indicating the chemical integrity of the polymer in the formulation. The presence of sodium bicarbonate in the formulation as an effervescent agent is confirmed by distinct bicarbonate and carbonate groups spectral bands at 13501400 cm -1. The presence of citric acid is determined by broad OH stretching (3300cm -1), sharp carbonyl bands (1720cm -1) that of citric acid, thus confirming its functional presence in the acidbase interaction of the tablet [24].

A common microcrystalline cellulose peak (including broad OH peaks (~3400 cm -1) and C-O-C bonds (~1050cm -1)) indicates the identity and physical stability of the excipient in the formulation (Fouad et al., 2020). Typical

carboxylate absorptions at around 1600 cm -1 and 1400 cm -1 indicate groups of stearates to magnesium, indicating the appropriate inclusion of this excipient. The presence of aerosil in the form of a glidant and the structural characteristics of Aerosil were ensured with a broad peak at 3400 -1 corresponding to the presence of surface hydroxyl groups and the presence of Si -O -Si at 1100 -1. O-H broad band (3400 cm -1) and aromatic C=C (approximately 1600 cm -1) are important phenolic and flavonoid groups of licorice, making it the correct compound to include as a bioactivity component.

The functional groups of the drug, excipients and bilayer floating tablet that was formulated were analysed using FTIR spectroscopy. The peaks seen in the FTIR spectrum are the vibrations of certain molecular bonds such as stretching and bending as well as information about the chemical integrity and compatibility of formulation components:

- -3420-3300 cm -3 OH stretching vibrations, generally attributed to hydroxyl groups in excipients such as HPMC or other polymers, and OH carboxylic acid functionalities of amoxicillin; the presence of broad OH peaks is indicative of intra- or intermolecular hydrogen bonding.
- 3350 3250 cm -NH stretching, which is a characteristic of the N-H, primary and secondary amines in the 3-ring of the amoxicillin core and, therefore,, confirms that the core structure of the drug was preserved.
- ~29402850 cm - sharp peaks, which are C-H stretching vibrations, especially of the aliphatic -CH 2 and -CH 3 groups; these are due to the amoxicillin backbone, and most common tablet excipients (HPMC or microcrystalline cellulose).
- C=O stretching of the β-lactam ring in amoxicillin -17701740 cm -1: a sharp and high peak indicative of the integrity of the drug structure; the lack of peak shift in the end product indicates that the 2-lactam ring had not been degraded chemically.
- -16501600 cm -1: peaks are associated with amide carbonyl (C=O) or C=C stretching in aromatic rings, in amoxicillin, this confirms the presence of peptidic amide bonds and aromatic nuclei in the thiazolidine ring.
- -14501380 cm -1: peaks which represent C-H-bending vibrations, especially, deformation vibrations of CH 2 and CH 3 groups, which are characteristic of amoxicillin, as well as the polymeric excipients.
- C-N stretch - C-O stretch 1270-1000 cm -1: C-N stretch - C-O stretch: this is visible both in amoxicillin (C-N of the amine / amide groups) and in polymers or sugars (C-O).
- 980 600 cm -1: area in which C-H out-of-plane bending vibrations are commonly observed, and which can refer to aromatic ring structures, also cover fingerprint areas of heterocyclic structures, including the thiazolidine ring of amoxicillin.

The final formulation retained all the major functional groups of amoxicillin, 1 of which is 2 -lactam C=O, another 1 amine NH, and the last carboxyl C=O. There were no notable changes, loss, or exposure of new peaks in comparison with the spectra of individual components, indicating no interaction between the chemical, or degradation of drugs in formulation. O-H, C-H, and C-O characteristic values ensured the presence of excipients (e.g., HPMC, DGL, or NaHCO 3), which are in line with previously known spectral fingerprints.

Hardness was measured as 4.326 kg/cm 2 in batch T5 and 6.589 kg/cm 2 in batch F2 (see Table 12 and Figure 21). Such findings indicate that all the tablets have sufficient mechanical strength to endure handling and packaging.

Thickness

Tablet thickness was observed at 5 batches and ranged between 7.11 mm in batch F5 to 7.28 mm in batch F2 (see Table 10 and Figure 22)

Table 10: Thickness

Formulation Code	Thickness
F1	7.24
F2	7.28
F3	7.25
F4	7.24
F5	7.11

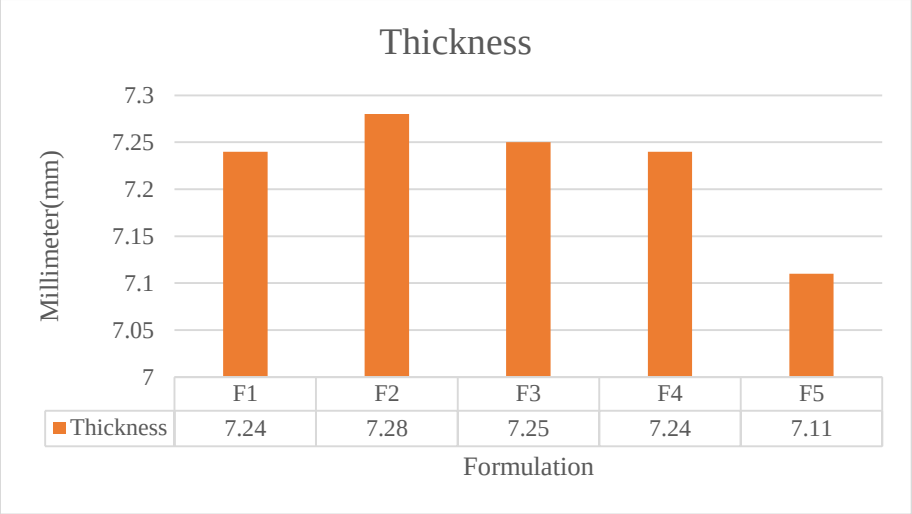

Figure 22: Thickness

Friability

The slight difference in thickness shows a steady compression of the tablet through formulation. The weight of the tablets was also homogeneous with the range of 981.77 mg (F5) up to 1002.67 mg (F1) and thus met the pharmacopeial requirements of weight variation (see Table 14 and Figure 16). Friability was maintained at acceptable levels being below 1%. It also varied between 0.543 0.871 percent in F2 and F5, respectively, which were good mechanical strength and crumbling resistant (see Table 15 and Figure 23).

Table 11: Friability

Formulation Code	Friability
F1	0.83%
F2	0.54%
F3	0.63%
F4	0.75%
F5	0.87%

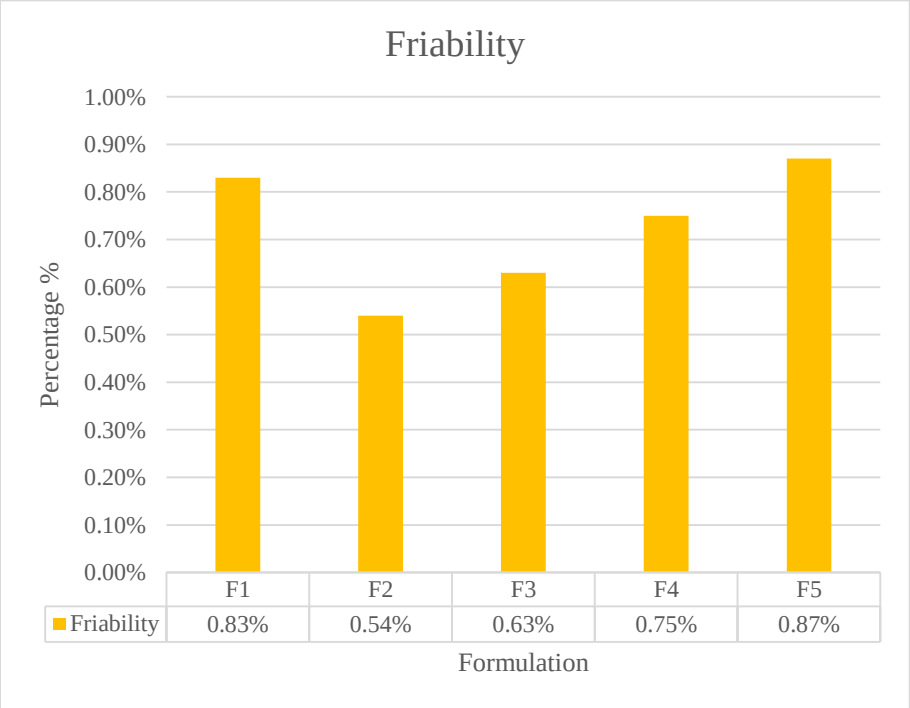

Figure 23: Friability

Equilibrium Moisture Contents

Equilibrium moisture determinations of batches F1 to F5 were done. Equilibrium moisture content values were found to be 4.93% in F1, 4.54% in F2, 4.73% in F3, 4.91% in F4, and 3.89% in F5 (see Table16 and Figure 24).

Table 12: Equilibrium Moisture Content

Formulation Code	Equilibrium Moisture Content
F1	4.93%
F2	4.54%
F3	4.73%
F4	4.91%
F5	3.89%

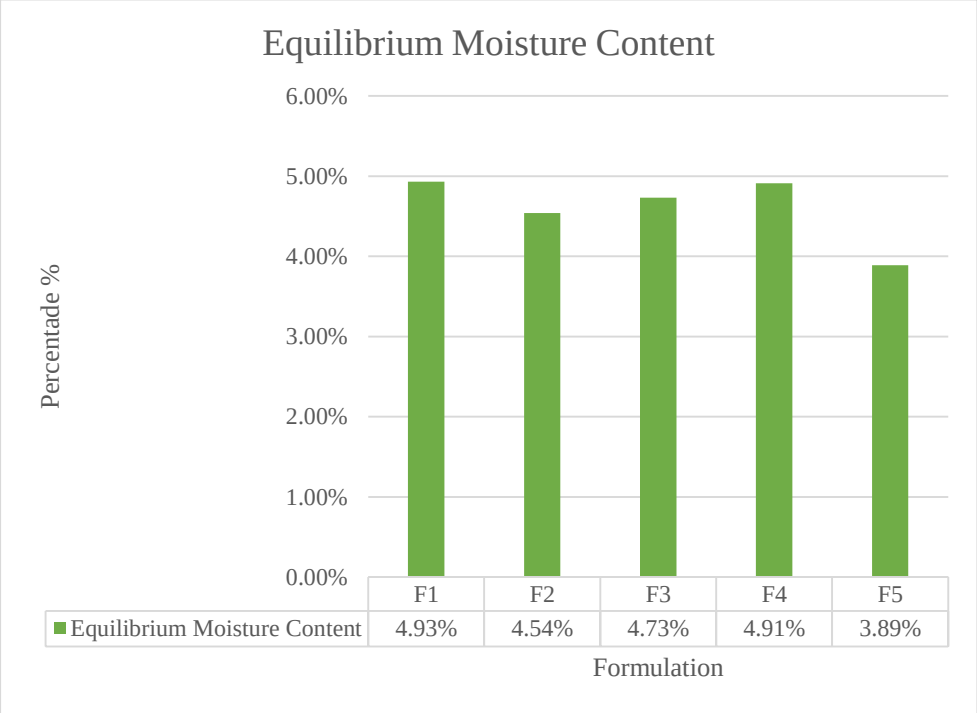

Figure 24: Equilibrium Moisture Content of Amoxicillin

The results indicate that there were minor differences in moisture levels in the batches. The retention of carbon dioxide in the batches was also similar with a slight variation, with batches F1, F3, and F4 recording 230 mg, F2 with 223 mg and F5 with a slight higher figure of 231mg. These results indicate that there was homogenous gas retention in the tablets. The lag time of all the five formulations was found to be between 23 and 25 seconds and this shows rapid buoyancy of the tablet when it comes in contact with the medium. All formulations had a total floating time longer than 8 hours and batch F2 had a longest time of more than 10 hours and hence confirmed prolonged gastric retention.

Carbon Dioxide Content

Table 13: Carbon dioxide content

Formulation Code	Carbon dioxide Content
F1	230 mg
F2	223 mg
F3	230 mg
F4	230 mg
F5	231 mg

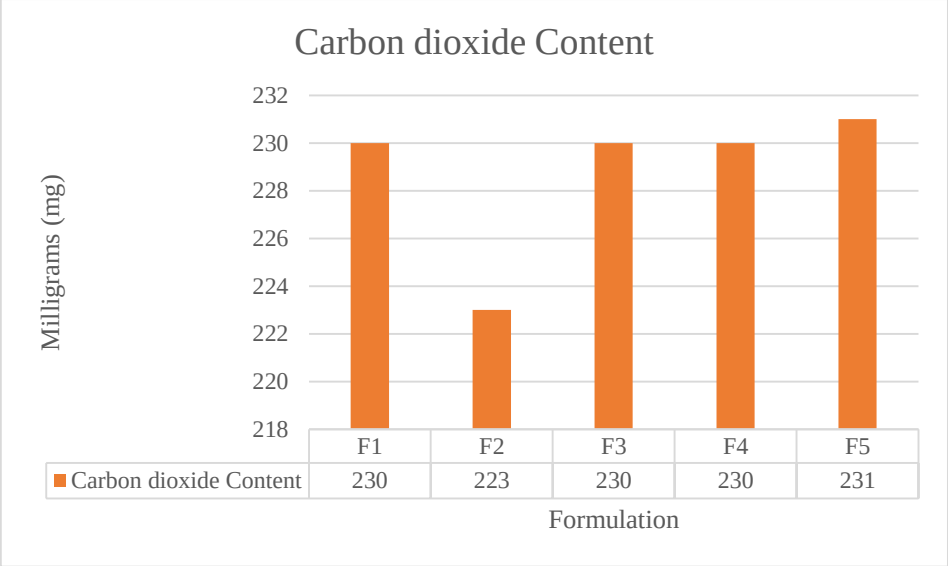

Figure 25: Carbon dioxide content

Floating Lag Time

Table 14: Floating Lag Time

Formulation Code	Floating Lag Time
F1	25 sec
F2	23 sec
F3	25 sec
F4	25 sec
F5	25 sec

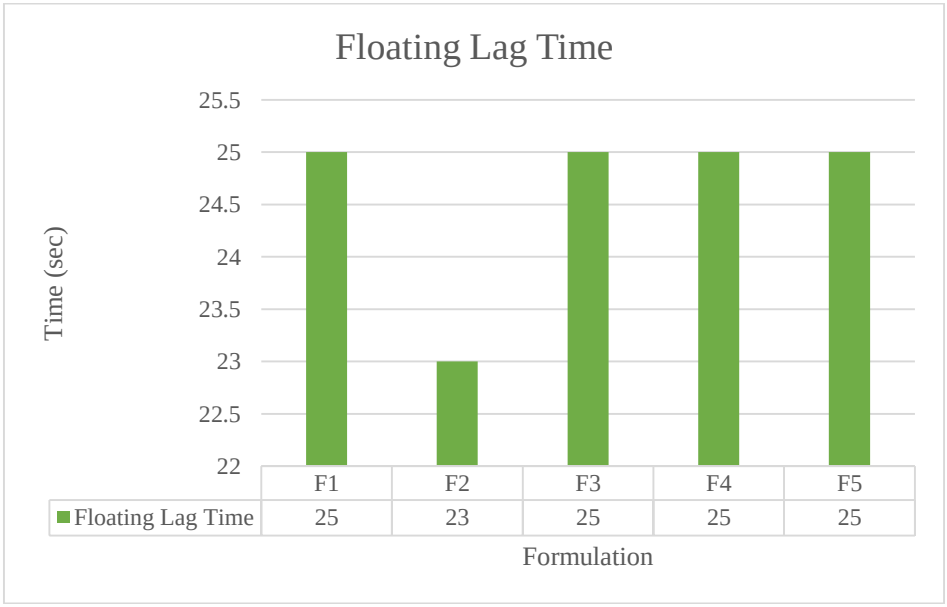

Figure 26: Floating Lag Time of Amoxicillin

Total Floating Time

Table 15: Total Floating Time

Formulation Code	Total Floating Time
F1	9.3
F2	10.2
F3	9.5
F4	9.1

F5	8.3

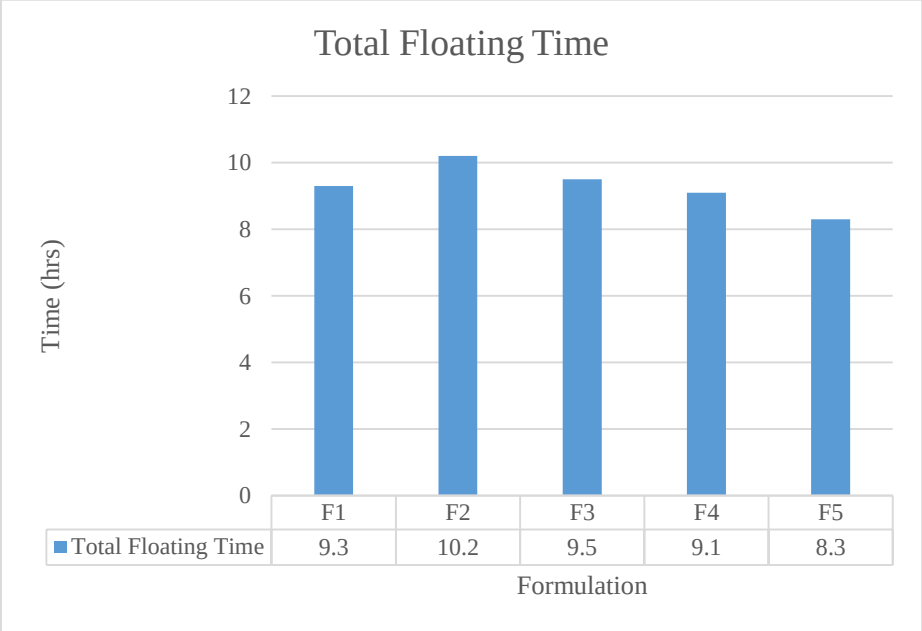

Figure 27: Total Floating Time of Amoxicillin

Swelling Index

Formulations showed consistent swelling index values of between 12.7 14.4 10, which exhibited a uniform swelling behaviour, which was suitable to gastro-retentive delivery (see Table 20 and Figure 28).

Table 16: Swelling Index

Formulation Code	Swelling Index
F1	13.10%
F2	12.70%
F3	13.30%
F4	14.40%
F5	13.70%

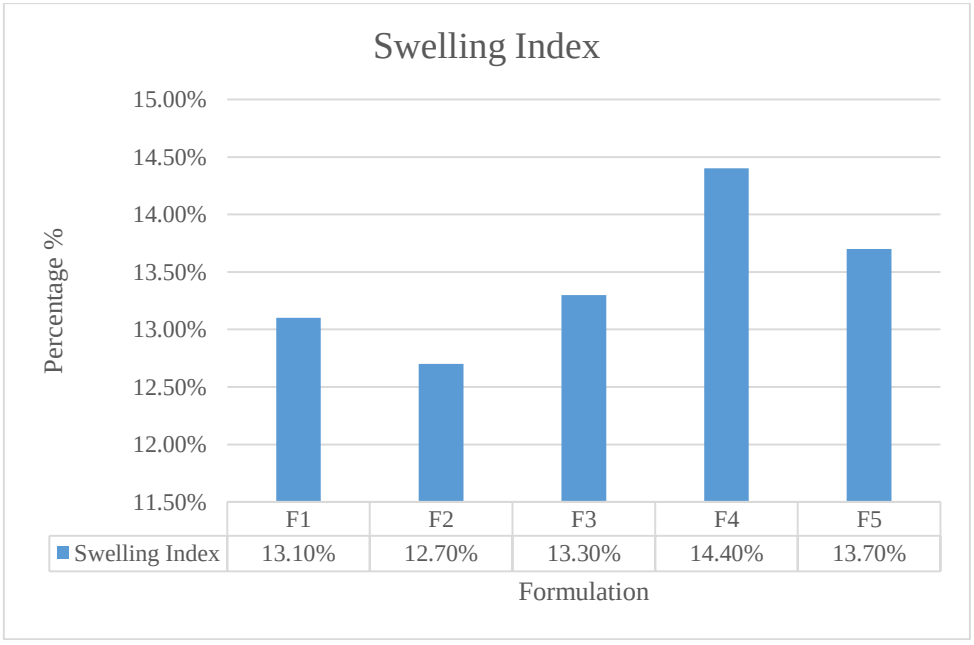

Figure 28: Swelling Index

Uniformity of Weight

Table 17: Uniformity of Weight

Formulation Code	Uniformity Of Weight
F1	1002.67
F2	1001.52
F3	1000.24
F4	1001.44
F5	981.77

The content uniformity of batches was different with the maximum of 96.73 in F5 and the minimum of 86.99 in F2. Although this is a range, all the values were acceptable, which means that there was good distribution of drugs in the tablets. To determine dissolution profiles, the release of drugs was studied on five batches (F1-F5) in a 10-hour period. The maximum rate of drug release was seen in the batch F3 (100 percent dissolution), F5 (99.73 percent), F4 (98.12 percent), F2 (98.45 percent), and F1 (97.65 percent) at the end of the study. There were considerable differences in release rates in the early hours.

DISCUSSION

This study focuses on the formulation and evaluation of a bilayer-floating tablet of amoxicillin combined with deglycyrrhizinated licorice powder for treating peptic ulcers. The bilayer tablet aims to provide a synergistic antiulcer effect by prolonging the drug's gastric retention and enhancing its bioavailability. The tablet uses both effervescent and non-effervescent preparations to obtain prolonged drug delivery. The effervescent system also produces carbon dioxide hence increasing the buoyancy in addition to the long residence time in the gastrointestinal tract, whilst the non-effervescent system makes use of colloidal hydroxypropyl methylcellulose (HPMC) gel barriers in combination with microporous compartments to facilitate the diffusion of drugs. In the study, the importance of sodium bicarbonate, citric acid and HPMC in enhancing the floating ability and the controlled release kinetics are highlighted.

The relatively elevated solubility of amoxicillin, a hydrophilic antimicrobial, supports the appropriateness of drug-centered systems and promotes the role of matrix development in guaranteeing anticipated pharmacokinetic characteristics. To check the solubility of amoxicillin, it is dissolved in different solvents like ethanol, methanol, and water. After the test, it is proven that amoxicillin is a hydrophilic drug because it is more soluble in water than in other solvents. Different tests are performed on the bilayer floating tablet of amoxicillin with deglycyrrhizinated licorice, like melting point and to check the density of powder, hardness, thickness, etc. Compared the ATR-FTIR of amoxicillin trihydrate to the previous article, it lies in the frequency region 4000-400/cm, while in this article, it shows observed peaks in the FTIR spectrum that correspond to specific molecular bond vibrations, such as stretching and bending, and offer insight into the chemical integrity and compatibility of the formulation components ~3420–3300 cm^{-1} [20].

In pre-formulation studies, the first test performed is ATR-FTIR spectroscopy on different samples, such as pure amoxicillin trihydrate, deglycyrrhizinated licorice, and different excipients, to optimize bilayer floating tablet formulation. The chemicals used for the FTIR spectroscopy show the chemical integrity and compatibility of amoxicillin and excipients in the bilayer floating tablet. The peak characteristics indicate the retention of the drug's chemical structure and functional groups, suggesting no significant chemical degradation or interaction [21]. Then, the melting test is performed on the amoxicillin powder, which is 195°C, determined by the capillary fusion method.

After that, pre-compression parameters were conducted for the analysis of samples by passing them through sieves of different sizes to determine the granular size. In the pre-compression evaluation, different densities were assessed for powder samples to determine their flow properties and compressibility. Tap density was determined by performing the test to ensure accuracy and consistency. The recorded average values were 0.7323 g/cm^3, 0.7142 g/cm^3, 0.7322 g/cm^3, 0.7043 g/cm^3, and 0.7121 g/cm^3. The results showed minor variations, indicating good repeatability and reliable tap density, which reflects the powder's uniform packing behaviour under mechanical tapping. The compressibility test was calculated by Carr's Index, which was between 20.47 and 26.22,

and tauser's ratio is between 1.25 and 1.36, indicating good properties of the powder. The angle of repose is 35.19° to 38.36° to confirm the acceptable behaviour of the powder. The evaluation of the floating tablet was performed to assess floating lag time, total floating time, and swelling index. Each tablet is floating within 8 hours 25 seconds of soaking, indicating rapid buoyancy. This is advantageous in improving stomach drug retention time.

The floating lag time is between 23 seconds and 25 seconds. The swelling index is between 12.7% to 13.3% reflecting optimal hydration and swelling of the matrix. This behaviour is important to ensure that the tablet is alive and in contact with the stomach environment to facilitate a longer release of the drug. The batch F5 showed the lowest hardness, which is 4.326kg/cm², but this hardness is still within the acceptable range. The variation in weight and uniformity of most batches was within ranges. However, the batch F2 exhibits a slightly lower hardness, which is 86.99% indicating the need to improve the mixing and powder equivalence. The moisture content is between 4.93% and 4.54%, while the CO2 content remains constant [22]. This implies good environmental and formulation control at the time of production and storage. Batch F3 had a 100 % release rate with Batch F5 having an initial release profile of 44.33⁻ 1 after 15 minutes, which could be encouraged to diffuse faster because of reduced hardness. The addition of new polymers, such as natural excipients and stimulants, may further enhance the control of release of active-ingredients and gastric retention time.

The following polymers used in this formulation are HPMCK100M and HPMCK4M, etc. To compare the drug release with the previous article, it was released within 8 hours, but in this article, dissolution studies demonstrated that all phrasings released nearly the entire medicine Cargo within 10 hours. Specifically, batch F3 achieved 100 releases, while F5 showed a more [23]. Rapid-fire original release (44.33 at 15 twinkles), probably due to its lower. Hardness, which may have eased rapid matrix hydration and medicine diffusion. In relation to antibiotic resistance, such formulations for sustainable release may improve treatment outcomes by maintaining drug plasma concentrations over a long period of time at minimal inhibitory concentrations (MICs).

The advantage of the bilayer floating tablet of amoxicillin with deglycyrhhyzinated licorice for the treatment of peptic ulcers over the other conventional preparations of oral solid dosage forms include used in the combination therapy, as it consist of two active ingredients in a bilayer form. It helps to enhance the bioavailability of the drugs that have a decreased half-life. It reduces the dosage frequency and helps to deliver two incompatible drugs. It increases patient compliance. It has a more effective action as its plasma drug concentration remains constant throughout.

The current research has significant strengths. It used a rational design of a bilayer floating drug delivery system, which is a combination of a classical antibiotic and a natural gastroprotectant. It allows sustaining antimicrobial effects and protecting the mucous membrane with a single dosage. This formulation methodology is more solid through thorough preformulation and post-compression testing, such as physicochemical characterization, floating behavior, swelling index, content uniformity, and in vitro drug release testing, which contribute to the strength and reproducibility of the developed system. This research contributes to the literature because it shows that the process of preparation of a gastro-retentive bilayer pill (including deglycyrrhizinated licorice) can be used to increase local gastric therapy, without affecting amoxicillin kinetics. The developed formulation has extended gastric retention time and prolonged release of the drug. It is unlike the traditional immediate-release formulations, which could enhance the effectiveness of the eradication of Helicobacter pylori and patient adherence. This method can potentially lower the dosing schedule, minimize plasma drug fluctuations, and also assist the process of ulcer healing. Future research should focus on the validity of therapeutic benefits and safety in patients with peptic ulcer disease. It should be achieved with regard to in vivo pharmacokinetic and pharmacodynamic studies, and tests of anti-H. Pylori efficacy, testing of long-term stability via controlled clinical trials.

CONCLUSION

The development and evaluation of Bilayer Floating Tablets of amoxicillin with deglycyrrhizinated licorice for the treatment of gastric ulcers successfully demonstrated that they provide a synergistic effect of two antiulcer drugs. The retention time of amoxicillin was effectively prolonged by developing a floating drug delivery system utilizing optimized levels of hydroxypropyl methylcellulose (HPMC),

sodium bicarbonate ($NaHCO_3$), and citric acid. The formulated tablets exhibited excellent buoyancy, optimal swelling index, and sustained drug release over 10 hours, facilitating targeted delivery in the stomach and thereby enhancing the healing and soothing characteristics. It also demonstrates the acceptable physicochemical properties like moisture content, weight variation, etc. The main purpose of this formulation was to enhance treatment outcomes by improving gastric retention time, along with improving patient compliance by reducing dosage frequency. This study confirms that a bilayer floating tablet with optimal flow properties and controlled release characteristics can be successfully developed by fine-tuning the concentrations of key excipients.

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