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Formulation and *in vitro* evaluation of bilayer floating tablet of Aceclofenac and esomeprazole by using natural and synthetic polymer

Rajia Sultana Nijhu, Ambia Khatun and Md. Abdul Mannan

Abstract
The goal of this study was to create bilayer floating tablets containing Aceclofenac and Esomeprazole. OTC analgesics, such as NSAIDs, are widely used, but they are commonly misused and possibly harmful, and users are often uninformed of the potential for negative side effects. It is made up of a floating Esomeprazole instant release layer and a sustained release Aceclofenac layer created utilizing the direct compression approach. Sodium starch glycolate super disintegrants were used to create six floating instant release layer formulations containing Esomeprazole (F1–F6). Natural and synthetic release retarding polymers (Xanthangum, HPMC E15, HPMC K100M, HPMC E5) at three different doses, as well as additional additives, were used to make six formulations of sustained release layer containing Aceclofenac (F1–F6). The floating instant release layer recipe was designed to release the largest amount of Esomeprazole possible. The sustained release formulation (F3) released 98 percent of the Aceclofenac in 6 hours, had a 48-second buoyancy lag, and was floatable throughout the experiments. The amount of medication released was inversely related to the amount of polymer present. An FTIR analysis found no chemical interactions between the medication and the polymers utilized. Gastric ulcers affect 10-20% of people who take nonsteroidal anti-inflammatory drugs (NSAIDs). This Aceclofenac and Esomeprazole bilayer floating tablet is suitable for treating pain and inflammation, as well as controlling NSAID-induced ulcers.

Keywords: Aceclofenac, esomeprazole, bilayer floating tablet, sustained release

Introduction
The development of controlled release formulations with a bilayer tablet is a revolutionary technology. Bilayer tablets are created by combining two or more active medicinal components in a single dose form. The use of bilayer tablets has risen in recent years. The progressive release of two active components in combination is better achieved with a bilayer tablet. Bilayer tablet technology separates two incompatible compounds, with one layer providing quick release as a loading dosage and the other providing controlled/sustained release as a maintenance dose. By adding an inert intermediary layer, two incompatible medications can be synthesized into a bilayer tablet. These are created in order to produce a drug's customized release. In the case of traditional dose forms, there would be a large range of medication concentration changes, resulting in undesired toxicity and low efficacy [1, 2].

Ideal Characteristics
- It should be beautiful and free of flaws such as chipping, cracking, discoloration, and contamination [3].
- It should be of sufficient quality to withstand mechanical shock throughout the tablet manufacturing process [4].

Challenges
When the two components of a tablet do not completely bind, the tablet splits into fragments. When compacted into a bilayer tablet, the two granulations should adhere well [5].
- Cross-contamination occurs when the granulation of the primary layer combines with the granulation of the second layer or vice versa.
- Expensive as compared to single-layer dosage forms or traditional dosage forms.
- The tablet press, which is used to make bilayer tablets, is expensive [6, 7, 8].
- It is necessary to develop two compatible granulations, which necessitates more time spent on formulation, analysis, and validation [9].

- Although the oral route is the most preferred method of medication delivery, it does have certain disadvantages, such as a sluggish start of effect and poor absorption. This difficulty can be solved by employing different dose forms or administering the medicine through different methods. When choosing a dosage form or method for medication administration, various factors should be addressed, such as the formulation's stability and bioavailability, as well as the active pharmaceutical components [10]. Effervescent floating tablets can be used as an alternate dose form to help alleviate some of the issues that come with traditional dosage forms. Effervescent floating tablets can also be utilized to promote medication bioavailability by reducing drug concentration changes [11]. Effervescence is defined as the release of CO_2 gas as a result of the reaction of acids and bicarbonates in the presence of H_2O. Citric, malic, tartaric, adipic, and fumaric acids are some of the major acids utilized in this process. Bicarbonates employed in the effervescent reaction include sodium bicarbonate, potassium bicarbonate, sodium carbonate, and potassium carbonate. The acid-base reaction between sodium bicarbonate and citric acid is the most common reaction used in pharmaceuticals.

$3NaHCO_3\,(aq) + H_3C_6H_5O_7\,(aq) = 3Na_3C_6H_5O_7\,(aq) + 3H_2O + 3CO_2$

Even with a modest quantity of catalytic agent, this reaction happens in the presence of water, which speeds up the process. Because water acts as a catalyst in the process, all moisture-sensitive or effervescent items must be stored in a dry environment [12]. The density of effervescent floating drug delivery systems is lowered when gas forms, and the dosage form remains buoyant in the stomach for a longer period of time, allowing the medicine to be given slowly and at the appropriate pace. Using effervescent floating drug delivery devices or a hydrodynamically balanced system, it is feasible to extend the medication's stomach residence period [13]. Effervescent floating medication delivery methods require matrices made of swellable polymers like Chitosan and effervescent components like sodium bicarbonate and citric or tartaric acid, or matrices having liquid chambers that gasify at body temperature [14]. Tablets containing effervescent floating medications that irritate the gastrointestinal mucosa are made by compressing the active components with a solution of sodium bicarbonate and organic acids like citric and tartaric acid [15]. The fundamental benefit of effervescent floating tablets is that they produce a solution quickly. As a result, it is easier to absorb [16]. Floating drug delivery systems (FDDS), on the other hand, are engineered to have a lower bulk density than gastric fluids, allowing them to float in the stomach for longer periods of time (about 3-4 hours) without influencing the gastric emptying rate [17, 18]. The basic idea is to make the dose form less thick than the gastric juices, allowing it to float on top of them. The medicine is slowly withdrawn from the system at the desired rate, and the remaining system is evacuated from the stomach once the drug has been discharged. As a result, stomach residence duration is extended, and plasma drug concentration variations can be better regulated [19].

The floating drug delivery system delivers local administration to particular regions such as the stomach and proximal small intestine, as well as increased bioavailability, therapeutic action, and significant patient advantages [20]. Esomeprazole has been shown to be equally effective as diclofenac, indometacin, piroxicam, aceclofenac, phenylbutazone, naproxen, and flurbiprofen in the treatment of rheumatoid arthritis. In NSAID recipients, esomeprazole prophylaxis is beneficial for preventing gastroduodenal ulcers, maintaining remission, and alleviating dyspeptic symptoms. Esomeprazole is well tolerated, and the most common side effects are gastrointestinal [21]. Bioequivalence of the fixed-dose combination esomeprazole to the individual monotherapies has been proven. The combination was observed to have a reduced frequency of digestive issues and the requirement for dosage reduction than its components. The first fixed-dose NSAID/PPI composition to be authorized is esomeprazole modified-release tablets. Because the PPI is co-administered with the NSAID, this formulation promotes compliance with the gastroprotective prophylaxis. Furthermore, the once-daily formulation has the potential to increase anti-inflammatory drug adherence [22].

Novelty of the work

For rheumatic conditions such osteoarthritis (OA), rheumatoid arthritis (RA), and ankylosing spondylitis, non-steroidal anti-inflammatory medicines (NSAIDs) are among the most regularly recommended medications (AS). Despite the documented link between NSAID usage and gastropathy, only around one-third of patients at risk of NSAID-induced gastrointestinal toxicity obtain effective gastroprotection, with up to 44% of these patients not adhering to their treatment regimen. We examine the use of proton pump inhibitors (PPIs) in combination with nonsteroidal anti-inflammatory drugs (NSAIDs) to prevent NSAID-induced gastropathy, with a focus on the first fixed-dose NSAID/PPI formulation: Esomeprazole and Aceclofenac in modified release dosage form. The esomeprazole fixed-dose combination is available as a once/twice-daily treatment in dosages of 40 mg /20 mg. When used to treat OA, esomeprazole monotherapy has been demonstrated to be generally equal to other NSAIDs. In RA, esomeprazole has demonstrated equivalent efficacy to diclofenac, indometacin, piroxicam, aceclofenac, phenylbutazone, naproxen and flurbiprofen. In NSAID recipients, esomeprazole prophylaxis is beneficial for preventing gastroduodenal ulcers, maintaining remission, and alleviating dyspeptic symptoms. Esomeprazole is well tolerated, and the most common side effects are gastrointestinal. Bioequivalence of the fixed-dose combination eomeprazole to the individual monotherapies has been proven. The combination was observed to have a reduced frequency of digestive issues and the requirement for dosage reduction than its components. The first fixed-dose NSAID/PPI composition to be authorized is esomeprazole modified-release tablets. Because the PPI is co-administered with the NSAID, this formulation promotes compliance with the gastroprotective prophylaxis. Furthermore, the once-daily formulation has the potential to increase anti-inflammatory drug adherence.

Drug profile

Aceclofenac

Aceclofenac is an anti-inflammatory and analgesic non-steroidal anti-inflammatory medication (NSAID). In double-

blind investigations, it was found to have a stronger anti-inflammatory impact or at least equal effects to conventional NSAIDs [23, 24, 25]. Aceclofenac inhibits the cyclo-oxygenase enzyme (COX), which is involved in the production of prostaglandins, inflammatory mediators that induce pain, swelling, inflammation, and fever. It's taken orally to treat osteoarthritis, rheumatoid arthritis, and ankylosing spondylitis pain and inflammation. Aceclofenac is classified as a BCS Class II drug because of its low water solubility [26]. It has a high permeability to permeate synovial joints, where the loss of articular cartilage produces joint discomfort, soreness, stiffness, crepitus, and local inflammation in individuals with osteoarthritis and associated diseases [27]. Aceclofenac has also been shown to help with other painful illnesses like dental and gynecological issues. Aceclofenac was created in 1991 as a chemically modified version of the regularly prescribed NSAID Diclofenac in order to improve the drug's gastrointestinal tolerance. In Europe, it is a more regularly given medication.

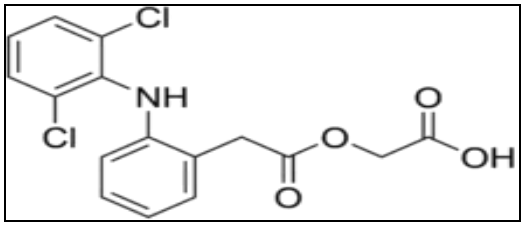

Fig 1: Aceclofenac

Chemical Name: [[2-[(2', 6'-Dichlorophenyl) amino] phenyl] acetyloxy] acetic acid

Molecular formula: $C_{16}H_{13}Cl_2NO_4$

Description: White to almost white crystalline powder.

Molecular weight: 354.2

Solubility: Practically insoluble in water, freely soluble in acetone and alcohol.

Category: Anti-inflammatory agent.

Dose: 100 mg two times a day.

Mode of action: Aceclofenac alleviates pain and inflammation through a number of methods, as well as stimulating cartilage matrix formation.

Anti-inflammatory effects

Aceclofenac's anti-inflammatory properties have been demonstrated in both acute and chronic inflammation. It suppresses a variety of pain and inflammatory mediators, including:

1. It inhibits COX-2 and COX-1 activity, which directly prevents PGE2 synthesis at the site of inflammation.
2. It prevents the inflammatory cytokines interleukin 1 (1L-1) and tumor necrosis factor from causing the COX-1 enzyme to be produced.

Pharmacokinetic properties

The following are the pharmacokinetics of aceclofenac:

i. Oral accessibility: 100%.
ii. Bound in plasma: 99%
iii. Urinary excretion: 70% to 80%
iv. Distribution volume: 25-30 L/kg
v. 3-4 hour half-life [28].

Esomeprazole

Esomeprazole is a proton-pump inhibitor that lowers stomach acid production. Dyspepsia, peptic ulcer disease, gastroesophageal reflux disease, and Zollinger-Ellison syndrome are all treated with it. It inhibits the H+/K+-ATPase in the parietal cells of the stomach, lowering acid output. The medication reduces stomach acid production by blocking the action of this transporter. The (S)-()-enantiomer of omeprazole is esomeprazole. Esomeprazole is now available without a prescription in the United States, the United Kingdom, Australia, and Canada [29].

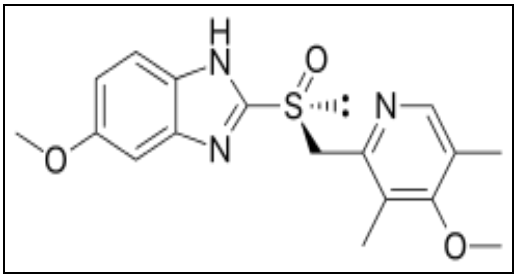

Fig 2: Esomeprazole

Pharmacokinetic data:

i. Oral availability: 50-90%
ii. Metabolism: Liver
iii. Elimination half-life: 1-1.5hour
iv. Excreation: 80% Kidney, 20% Facial

Adverse Effects:

1. Headache, diarrhea, nausea, flatulence, reduced appetite, constipation, dry mouth, and stomach discomfort are all common adverse effects. Severe allergic responses, chest discomfort, dark urine, rapid heartbeat, fever, paresthesia, persistent sore throat, severe stomach pain, unusual bruising or bleeding, unusual weariness, and yellowing of the eyes or skin are among the most serious adverse effects [29].
2. Proton pump inhibitors have been linked to an increased incidence of hip fractures [30] as well as Clostridium difficile-related diarrhea. Patients in critical care are routinely given the medications as a preventative strategy against ulcers, but their usage has been linked to a 30% increase in the prevalence of pneumonia [31]. In patients treated with *Helicobactor pylori*, long-term usage of PPIs has been demonstrated to significantly increase the incidence of stomach cancer [32].

Materials and methods

Aceclofenac is an anti-inflammatory and analgesic non-steroidal anti-inflammatory medication (NSAID). In double-blind tests, it was found to have a stronger anti-inflammatory impact or at least equivalent effects to traditional NSAIDs.

Esomeprazole, on the other hand, is a proton-pump inhibitor that decreases stomach acid and is offered under the brand names Nexium and others. Dyspepsia, peptic ulcer disease, gastroesophageal reflux disease, and Zollinger-Ellison syndrome are all treated with it [29].

Table 1: List of ingredients used in the experiment

Name of Ingredients	Source	Origin
First Layer		
Aceclofenac	Techno pharmachemical	Bangladesh
HPMC E15 HPMC K100M HPMC E5	Colorcon Asia Pvt Ltd	Verna
Xanthan Gum	Colorcon Asia Pvt Ltd	Verna
Poly-venyl pyrolodine	-	-
Sprayed-dried Lactose	-	-
Mg-stearate	Wilfrid Smith Ltd	UK
Second Layer	-	-
Esomeprazole	-	Bangladesh
$NaHCO_3$	Wilfrid Smith Ltd	U K
Citric Acid	Merck	Germany
Sodium Starch Glycolate	-	Bangladesh
Talc	-	-
Aerosil	-	-
Mg-stearate	-	-

Table 2: List of reagents and solvents used in the experiment

Serial No.	Name	Source	Origin
1	Hydrochloric Acid (37%)	Merck	Germany
2	Distilled Water	Laboratory	Bangladesh

Table 3: Equipments used in the experiment

Name	Model	Origin
Electric balance	DENVER Instrument Model-M 310	Switzerland
KBR Press	-	India
Manual Hardness Tester	Monsanto Type Model-MHT 20	India
Tapped Density Tester	PHARMA TEST Model-TD 200	Germany
Vernier Caliper	Tricle Brand	Shanghai,China
Single Drum Friability Tester	PHARMA TEST Model-F10E/ER	Germnay
pH Meter	LIDA Instrument Model-PHS 25	Shanghai,China
Disintegration Tester	PHARMA TEST	Germany
Dissolution Tester	PHARMA TEST Model-DT 70	Germany
UV-Visible Spectrophotometer	HACH Spectrophotometer Model-DR/4000u	USA
Single Die Punch	-	India

Preparation of bilayer floating tablets

Formulation of immediate release layer

The instant release (Esomeprazole) granules were made by sieving all of the excipients (NaHCO3, Citric Acid, Sodium starch glycolate, Talc, Aerosil, and Mg-Stearate) and then combining the drug with other excipients. The granules were employed to create a medication release layer in bilayer floating tablets with an instant release layer.

Formulation of sustained release layer

Drug quantity required, as well as polymers (for synthetic, HPMC E15 25%, HPMC E5 30%, and HPMC K100M 40%). Xanthan Gum 25 percent, 30 percent, and 40 percent for Natural). Other excipients (Magnesium stearate, lactose, PVP) were weighed, and the active component aceclofenac was sieved via sieve no. 16. After that, the drug combination blend was manually fed into the die and compacted directly. To achieve prolonged drug release, six formulation batches were created using various polymers at varied concentrations.

Formulation of bilayer floating tablets

The bilayer floating tablets were made utilizing a single punch direct compression machine and the direct compression method. The granules of the sustained release layer were first poured into the die cavity and squeezed. Following compression, the top punch was raised, and the floating immediate release grains of medicine were poured into the die, which contained a compressed sustained release layer and was compacted to form a bilayer.

Preparation of standard calibration curve in 0.1N HCl solution

In 0.1 N HCl solution, a stock solution of standard aceclofenac and esomeprazole at a concentration of 100 g/ml was produced. The stock solution was then used to make five different concentrations of standard working solution: 10, 15, 20, 25, and 30 g/ml, respectively. Using HCl solution as a blank, the absorbance of each sample solution was measured at max 275nm and 301nm.

Evaluation of tablet properties

Determination of precompression parameters

The powder was subjected to preformulation tests that included bulk density, tapped density, hausner's ratio, and angle of repose [33].

Bulk density

The Digital Automatic Tap Density Test Apparatus was used to determine the loose bulk density (LBD) and the tapped bulk density (TBD). In a 10 ml measuring cylinder, 3g of powder from each recipe (previously softly shaken to break any agglomerates produced) were placed. The apparatus was turned on once the starting volume was determined, and the cylinder was permitted to fall onto a hard surface under its own weight. The tapping reading was kept up until there was no more change in loudness. LBD and TBD were estimated using the following equation:

LBD = Weight of the powder / volume of the packing.

TBD = Weight of the powder / Tapping volume of the packing.

Compressibility index

The compressibility index of the granules was determined by Carr's compressibility index:

Carr's index (%) = {(TBD – LBD) X 100}/TBD

Angle of repose

The angle of repose of granules was measured using the funnel technique. A funnel was used to collect the precisely weighed grains. The height of the funnel was adjusted such that the tip of the funnel just touched the top of the granules mound. The granules were allowed to freely flow out of the funnel onto the surface. The powder cone's diameter was measured, and the angle of repose was computed using the equation:

Angle of repose $\theta = \tan^{-1} h/r$

Where,

h = Height of the powder cone.

r = Radius of the powder cone [34].

Determination of post compression parameters consider the following

Hardness

The capacity of a tablet to tolerate mechanical shocks while being handled is measured by its hardness. A monsanto hardness tester was used to determine the tablets' hardness. It's measured in kilograms per square meter. Six pills were chosen at random and their hardness was assessed [35].

Friability test

The roche friabilator was used to determine the friability of the tablets. It's measured in percentages (%). Initially, ten tablets were weighed and placed in the friabilator. The friabilator was spun at 25 revolutions per minute for 4 minutes or up to 100 revolutions per minute. The tablets were once again weighed. Percentage of Friability was then used to compute the percent friability. Tablets with a friability of less than 1% are regarded acceptable [35].

Weight Variation

Twenty tablets were chosen at random from the batch and weighed separately to see whether there was any weight difference [36].

Tablet density

The density of floating tablets is an essential factor to consider. When the density of the tablet is less than that of stomach fluid (1.004 g/cc), it will float. The density was calculated using the formula below.

$v = r^2h$

d = m/v = volume of tablet (cc)

r = radius of tablet (cm)

h = crown thickness of tablet (mm)

m = mass of tablet

Buoyancy / Floating test

The tablets were put in a beaker with a capacity of 250 mL and 200 mL of 0.1 N HCl. [37]. The time between the administration of the dosage form and its buoyancy on the simulated stomach fluid, as well as the duration the dosage form remained buoyant, were both measured. The time it takes for the dose form to emerge on the medium's surface is known as Floating Lag Time (FLT) or Buoyancy Lag Time (BLT), and the entire amount of time it takes for the dosage form to stay buoyant is known as Total Floating Time (TFT).

Drug content (Assay)

Five tablets were coarsely pulverized, and 50 mg of Aceclofenac and esomeprazole were carefully weighed and placed to a 100 mL volumetric flask. The flask was filled with 0.1N HCl solution (pH 1.2 buffers) and properly stirred. The solution was filtered after it was produced up to a volume of 100 mL. Using 0.1N HCl, dilute 1 mL of the resultant solution to 100 mL. Using a Shimadzu UV visible spectrophotometer, the absorbance of the resultant solution was measured at 275 nm and 301 nm [38].

Assay

Instrument

UV- visible spectrophotometer

Standard solution

A total of 50 mg of standard aceclofenac and esomeprazole were precisely weighed and placed into two separate 100 mL volumetric flasks. Then, using dissolving medium (0.1 N HCl), dilute to volume up to 100 mL. Then 5ml was taken and dilute with dissolving media till it reached 25mL.

Test solution

From each natural and synthetic polymer mixture, 5 tablets were weighed and crushed into fine powder. A total of 250 mg of powder, corresponding to 50 mg of Aceclofenac, was precisely weighed and placed into a 100 mL volumetric flask. A total of 30 mL of dissolving media was added and shaken mechanically. The solution was then diluted to volume with 0.1 N HCl. Whatsman filter paper #1 was used to combine the solution and filter it. The filtrate was then diluted to 100 mL with 0.1 N HCl for the first 10 mL.

Blank solution: 0.1 N HCl

Procedure: The absorbance of the resulting Standard and Test Solutions was measured in 1 cm cell at 275 nm against the Blank Solution.

Calculation
Content of Aceclofenac/ esomeprazole per tablet

$$= \frac{AT \times WS \times 5 \times 250 \times 100 \times P \times W}{AS \times 250 \times 100 \times WT \times 5 \times 100}$$

= mg of Aceclofenac/ Esomeprazole

Where,
AT = Absorbance of the Aceclofenac in the sample preparation.
AS = Absorbance of the Aceclofenac in the standard Solution.
WS= Weight of the working standard sample in mg.
WT= Weight of the test sample in mg.
P = Potency of standard expressed in % on as is basis.
W = Average weight of 20 tablets in mg.

***In vitro* drug release study**
The USP XXIII paddle dissolving test device was used to conduct *in vitro* release experiments. In a dissolving vessel, 900 mL of simulated stomach fluid (pH 1.2) was added, and the medium temperature was maintained at 370°C 0.50°C. The rotational speed was 50 rpm. For 6 hours, 10 mL of sample was taken at 1 hour intervals and replaced with the same volume of new medium. Using a UV-Spectrophotometer, the samples were evaluated for drug concentration against 0.1N HCl as a blank at max 275 nm and 301 nm.

Conditions
Apparatus: USP 2 (paddle)
Medium: 0.1N HCl
Volume: 900 mL
Speed: 50 rpm
Time: 1hr-6 hr

The equation is as follows:

$$= \frac{AT(sample) \times WS \times 5 \times 900 \times 100 \times P \times 100}{AS(std) \times 100 \times 25 \times WS \times L \times 10 \times 100}$$

Where,
AT (sample) =Absorbance of the sample
AS (std) =Absorbance of the standard
WS= Weight of the standard
L= Label claim of Aceclofenac bilayer
P= Potency

Result
Micromeritic studies
Bulk density, tapped density, compressibility index, hausner's ratio, and angle of repose of the granules were all determined. In a precompression examination, the flow properties of the formulation were determined to be satisfactory.

Physical parameters
The physical features of compressed tablets were determined. The degree of brittleness was maintained to a minimum. The hardness of the formulation varied from 5.1 to 6 kg/cm^2, which was sufficient to prevent chipping and breaking during transit.

Floating characteristics
With a floating lag period of up to 2 minutes 15 seconds, more than three of the six formulations floated for more than 20 minutes. During the floating process, formulas maintain the matrix intact. The optimal sodium bicarbonate concentration for producing the shortest floating lag time and longest flotation period. The number of polymers in a formulation has been demonstrated to influence the floating duration and lag time. The floating time of synthetic polymer formulations is longer than that of natural polymer formulations.

Table 4: Layer 1(immediate release) Esomeprazole

Ingredients (mg)	F1	F2	F3	F4	F5	F6
Esomeprazole	40	40	40	40	40	40
$NaHCO_3$	60	60	60	60	60	60
Citric acid	45	45	45	45	45	45
Na-Starch glycolate	3	3	3	3	3	3
Talc	0.75	0.75	0.75	0.75	0.75	0.75
Aerosil	0.50	0.50	0.50	0.50	0.50	0.50
Mg-stearate	0.75	0.75	0.75	0.75	0.75	0.75
Total tablet weight	150	150	150	150	150	150

Table 5: Layer 2(Sustain Release) Aceclofenac.

Ingredients (mg)	F1	F2	F3	F4	F5	F6
Aceclofenac	100	100	100	100	100	100
HPMC E15	87.5	-	-	-	-	-
HPMC E5	-	105	-	-	-	-
HPMC K100M	-	-	140	-	-	-
Xanthan Gum	-	-	-	87.5	105	140
PVP	98	98	98	98	98	98
Lactose	63.75	46.25	11.25	63.75	46.25	11.25
Mg-stearate	0.75	0.75	0.75	0.75	0.75	0.75
Total amount	350	350	350	350	350	350

Table 6: Recompression study of Esomeprazole

Formulation Number	Bulk Density (gm/ml)	Tapped Density (gm/ml)	Carr's index (%)	Hausner ratio	Angle of repose
F1	0.55	0.62	12.72	1.12	19.28
F2	0.48	0.58	20.83	1.20	22.23
F3	0.50	0.55	10.00	1.1	24.5
F4	0.52	0.57	9.61	1.09	18.4
F5	0.53	0.64	20.75	1.20	27.51
F6	0.49	0.59	20.40	1.20	32.33

Table 7: Precompression study of Aceclofenac

Formulation	Bulk Density (gm/ml)	Tapped Density (gm/ml)	Carr's index (%)	Hausner ratio	Angle of repose
F1	0.621	0.682	9.82	1.09	19.07
F2	0.597	0.645	8.04	1.08	22.29
F3	0.631	0.697	10.45	1.10	20.55
F4	0.582	0.635	9.10	1.09	28.59
F5	0.599	0.653	9.01	1.09	34.69
F6	0.610	0.698	14.42	1.14	29.35

Table 8: Post compression study of bilayer tablet.

Formulation	Weight Variation	Thickness (mm)	Diameter (mm)	Hardness (Kg/cm^2)	Friability	Lag time (sec)	% Drug content
F1	498.5	2.36	13.17	3.3	0.17	30	89%
F2	502	2.27	13.17	3.2	0.13	39	87%
F3	501.5	2.28	13.18	3.0	0.12	48	88%
F4	499.5	2.25	13.16	3.3	0.09	80	87%
F5	500.7	2.25	13.18	3.2	0.15	103	86%
F6	503.2	2.29	13.17	3.2	0.08	Not satisfactory	88%

Standard calibration curve

A UV visible spectrophotometer was used to create and scan the spectra of aceclofenac and esomeprazole in a 20 mcg/ml solution. The absorbance of the solution peaks at 275 nm and 301 nm. For different doses of Aceclofenac/ esomeprazole, the calibration curve was plotted versus absorbance. Figures 1 and 2 above illustrated this. The correlation coefficient of aceclofenac in HCl solution was determined to be 0.992. It demonstrated a strong correlation between concentration and absorbance in that range.

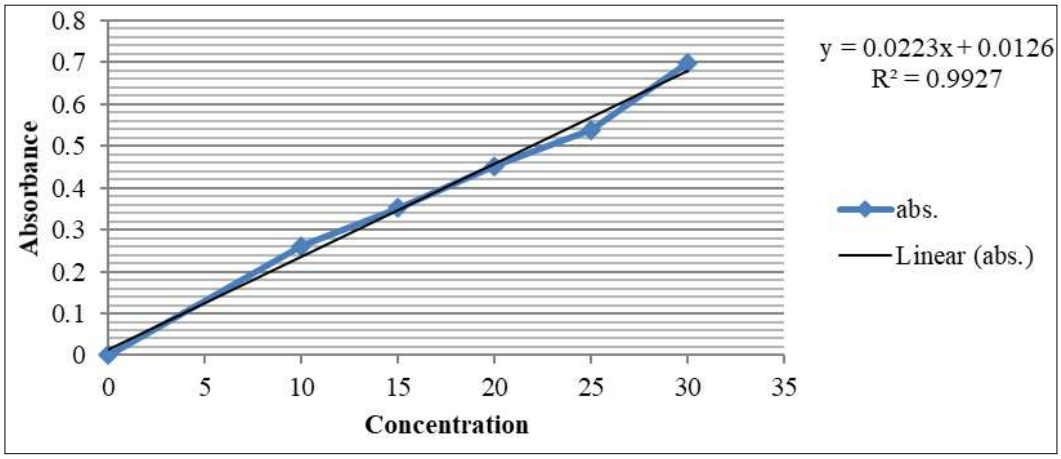

Fig 1: Standard calibration curve of Aceclofenac

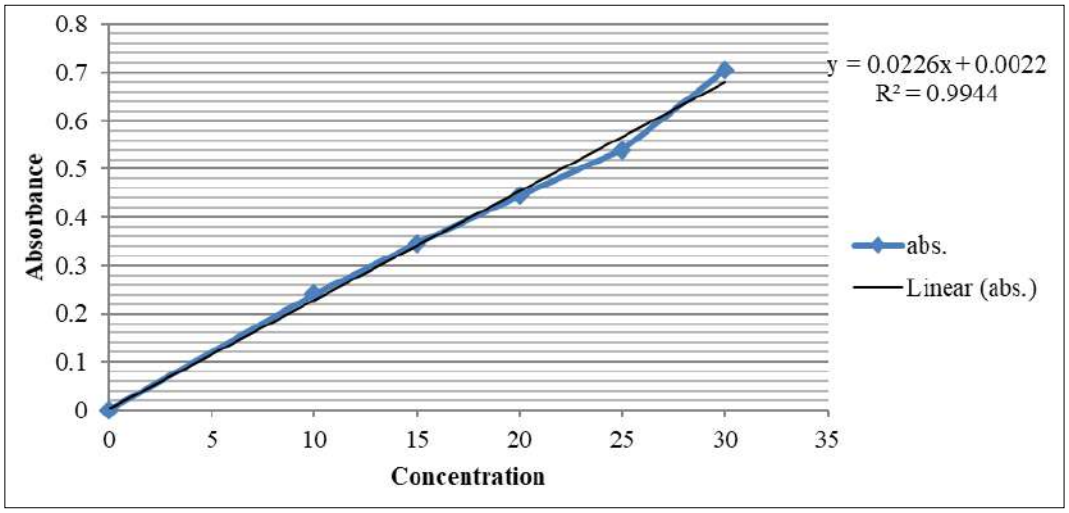

Fig 2: Standard calibration curve of Esomeprazole

Table 9: Drug release (%) of different formulation of Aceclofenac

Time	Formula- 1	Formula- 2	Formula- 3	Formula- 4	Formula- 5	Formula-6
After 1st hr	23	30	35	12	13	08
After 2nd hr	44	41	48	34	26	15
After 3rd hr	58	56	61	39	37	27
After 4th hr	78	75	79	48	45	36
After 5th hr	89	87	88	62	52	42
After 6th hr	97	93	98	79	59	48

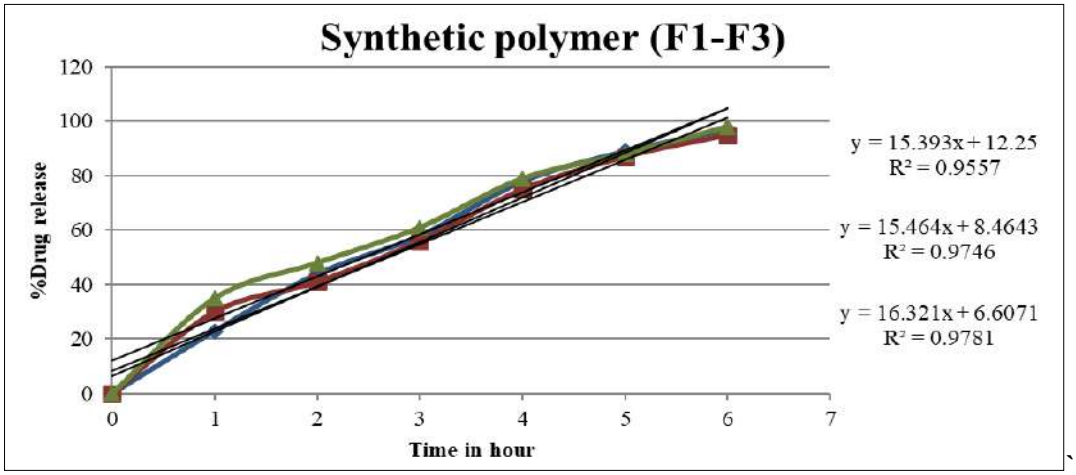

Fig 3: Drug release in % vs Time

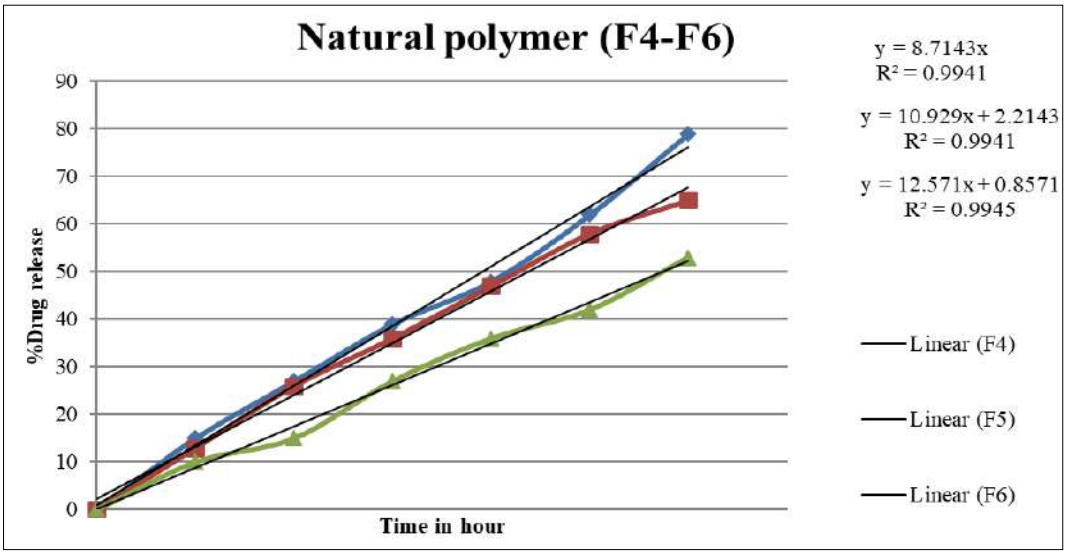

Fig 4: Drug release in % vs Time

Table 10: Drug release (%) of different formulation of Esomeprazole

Time	Formula- 1	Formula- 2	Formula- 3	Formula- 4	Formula- 5	Formula-6
After 10min	25	27	26	28	25	24
After 20min	36	39	40	39	35	36
After 30min	49	47	52	48	48	51
After 40min	68	62	67	65	69	68
After 50min	79	77	82	81	81	83
After 60min	98	89	91	92	92	92

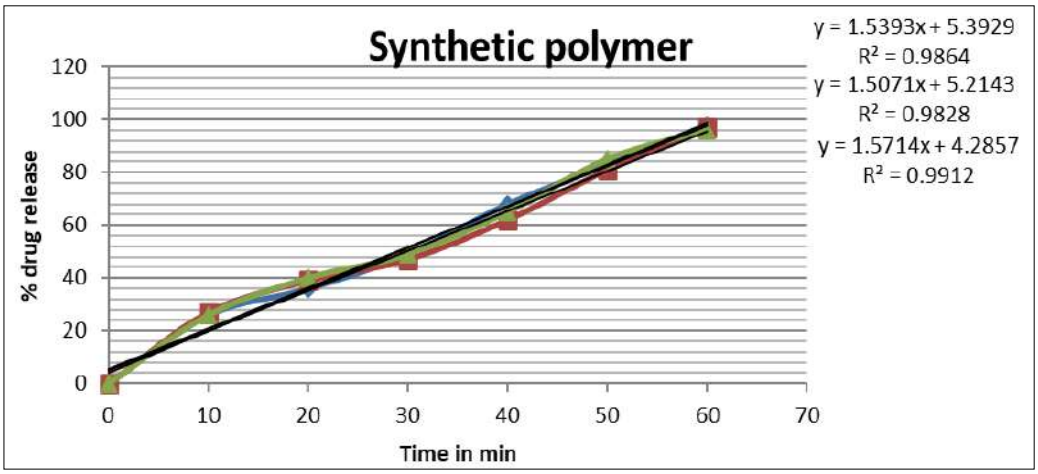

Fig 5: Drug release in % vs Time

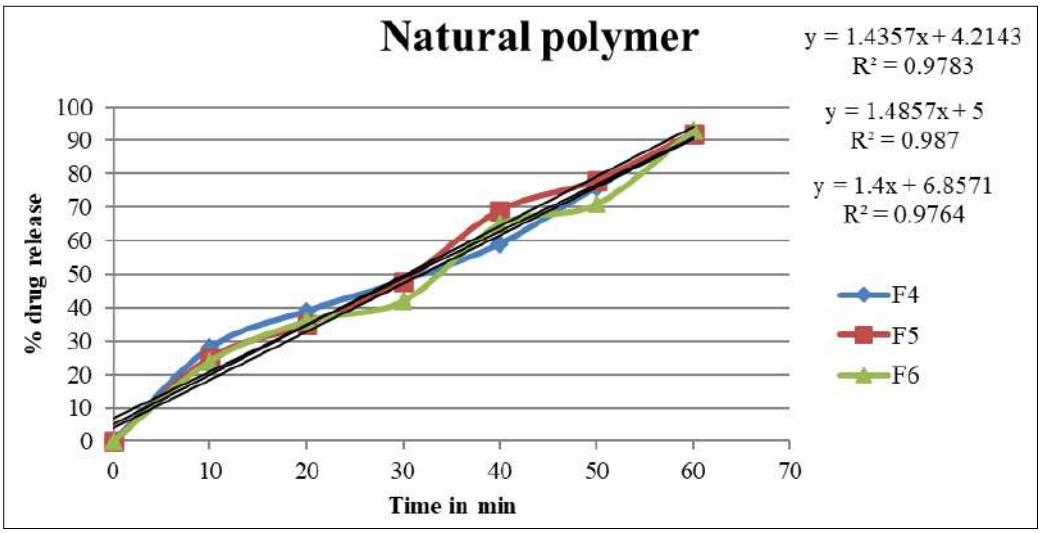

Fig 6: Drug release in % vs Time

Discussion

Angle of repose, compressibility index, Hausner's ratio, and other parameters are studied prior to compression of powder. The purpose of a powder pre-compression research is to assess the flow parameters of the powder. For these calculations, there are certain ranges. These calculations were completed for each and every formulation. According to the findings of a pre-compression research of powder comprising synthetic and natural polymer in the case of angle of repose, all of the formulas had good to probable flow qualities owing to a range of 18-32, which is according to the angle of repose range. It denotes that the powder has good flow characteristics. According to the findings of a pre-compression research of powders including synthetic and natural polymers, all of the formulas had excellent to fair flow qualities owing to the range of 9-21, which according to the Compressibility index range signifies excellent fair flow properties. In the instance of Hausner's ratio, all of the formulas had good flow qualities owing to the range of 1.25, which signifies good powder flow properties according to Hausner's ratio range.

Hardness, thickness, friability, drug content, and dissolving tests are all part of the post-compression investigation of Aceclofenac bilayer floating tablets. The average hardness of Aceclofenac bilayer floating tablets including natural and synthetic polymer was determined to be about 3.00-3.30 Kg/cm^2 during hardness testing. Friability testing of Aceclofenac bilayer floating tablets using natural and synthetic polymer revealed that the results were less than 1% of the weight of the tablets and that the formulation having natural polymer had greater friability than the synthetic polymer containing formulation. Drug content tests on compressed Aceclofenac bilayer floating tablets yielded average findings of up to 89%. The majority of the prepared pills floated well. Buoyancy Lag is the outcome of this. The duration was around 1 minute 43 seconds, and the total floating period was over 6 hours, however one formulation did not float; instead, it expanded and disintegrated in the HCl solution after 6 hours, with no buoyancy lag time, and it included natural polymer. The quantity of pharmacological substances that dissolve per unit time under specified conditions of liquid or solid interface, temperature, and solvent composition is known as dissolution. For a prolonged release preparation, the dissolution test is critical. Because sustained release dosage promises to release the drug at a specified rate in order to maintain a constant drug concentration for a certain amount of time, drug release is a critical component to consider, and drug release may be anticipated using a dissolution test. Different types of release retarding polymers can be used to regulate medication release. To investigate the release pattern of Aceclofenac, different percentages of natural and synthetic polymer were utilized in this experiment.

Conclusion

Acelofenac and Esomeprazole were effectively synthesized and analyzed as a bilayer floating tablet. Aceclofenac F1, F2, F3 had good results in the quick release formulation and floating matrix tablet. The study found that the manufactured bilayer floating tablet of Aceclofenac and Esomeprazole may effectively treat chronic inflammatory disorders such as arthritis while also being devoid of stomach side effects.

Competing interests

The authors report no conflicts of interest.

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