Journal of Neonatal Surgery
ISSN(Online): 2226-0439
Vol. 14, Issue 32s (2025)
https://www.jneonatalsurg.com

OPEN ACCESS

Formulation, Evaluation Of Combination Of Rabeprazole And Baclofen Bilayer Tablet For The Treatment Of Gastroesophageal Reflux Disease (Gerd)

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Cite this paper as: Muddassir Shamim, Rajkumari Thagele, Mahesh Kumar Gupta, Ajay Singh, (2025) Formulation, Evaluation Of Combination Of Rabeprazole And Baclofen Bilayer Tablet For The Treatment Of Gastroesophageal Reflux Disease (Gerd). *Journal of Neonatal Surgery*, 14 (32s), 2062-2080.

ABSTRACT

Gastroesophageal Reflux Disease (GERD) is a chronic condition characterized by the reflux of gastric contents into the esophagus, often requiring both acid suppression and control of lower esophageal sphincter relaxation. The present study focuses on the formulation and evaluation of a bilayer tablet containing Rabeprazole in the immediate-release layer and Baclofen in the sustained-release layer to provide dual-phase therapeutic action. Rabeprazole offers rapid proton pump inhibition, while Baclofen, a GABA-B agonist, reduces reflux episodes by decreasing transient lower esophageal sphincter relaxations.

The bilayer tablets were formulated using appropriate polymers and excipients, optimized through preformulation studies, and evaluated for weight variation, hardness, friability, drug content, disintegration time, and in-vitro drug release. Results showed satisfactory physicochemical properties, effective separation of release profiles, and promising sustained action. The bilayer design significantly enhances patient compliance by combining two therapeutic approaches into a single dosage form, offering potential for improved clinical outcomes in GERD management.

Keywords: *GERD, Rabeprazole Sodium, Baclofen, Bilayer Tablet, Immediate and sustained release layer, In-vitro evaluation and Controlled release formulation*

1. INTRODUCTION

Gastroesophageal reflux disease (GERD) refers to a condition where stomach acid and other contents move backward into the esophagus, leading to discomfort and potential health issues (1). It is also defined by the American College of Gastroenterology as “Persistent symptoms or injury to the esophageal lining result from the unusual backward flow of stomach contents into the esophagus” (2). Heartburn is a frequent symptom associated with GERD, and studies suggest that approximately 20% to 40% of individuals experiencing heartburn are diagnosed with the condition (3). GERD may also present with symptoms such as the sensation of food coming back into the throat, a feeling of a lump in the throat (globus), throat irritation, persistent coughing, discomfort in the chest, and difficulty swallowing. Gastroesophageal reflux disease (GERD) encompasses not only nonerosive reflux disease but also its associated complications, such as esophagitis, esophageal ulcers or strictures, Barrett’s esophagus, and esophageal adenocarcinoma (4).

Rabeprazole sodium is a proton pump inhibitor (PPI) which is most effective gastric acid suppressant that block the proton pump, H^+, K^+, -ATPase, by acting on the last pathway of stomach acid secretion (5). A common treatment for GERD is proton pump inhibitors (6).

Baclofen is a skeletal muscle relaxant that is derived from gamma-amino-butyric acid (GABA). Because Baclofen activates GABA-B receptors, muscular spasms occur less frequently and with less amplitude. It is particularly helpful in treating spinal cord injury-related muscular stiffness. It seems to mainly function at the level of the spinal cord by blocking spinal

polysynaptic afferent pathways and, to a lesser degree, monosynaptic afferent pathways (7). To address these issues, controlled-release and sustained-release drug administration methods have been thoroughly investigated; they provide lower dosage frequency and more stable drug plasma levels. Bi-layer tablet technology has drawn the most interest among these. An immediate-release (IR) layer for quick therapeutic effect and a sustained-release (SR) layer to sustain medication levels over time are the two major components of a bi-layer tablet (8). Drugs like Baclofen and Rabeprazole sodium, which need both immediate onset and sustained activity, benefit greatly from this dual-layer strategy. Bi-layer formulations have been shown in studies to increase pharmacokinetic stability, reduce gastrointestinal adverse effects, and improve bioavailability (9,10)

The aim of present work involves ‘ Formulation, evaluation of combination of rabepreazole and baclofen bilayer tablet for the treatment of Gastroesophageal Reflux Disease (GERD)’, using Rabeprazole sodium (Proton Pump Inhibitor) for immediate release to reduce acid secretion and Baclofen (GABA- B agonist) for sustained release to reduce transient lower esophageal sphincter relaxation (TLESR) along with different concentrations of excipients. It is prepared by wet granulation method.

1.2 Background:

In order to treat gastrointestinal and musculoskeletal disorders, a rabeprazole and baclofen bilayer tablet combines the advantages of a proton pump inhibitor (rabeprazole) for acid reduction with the muscle relaxant qualities of baclofen. The purpose of this formulation is to enhance overall therapy results, efficacy, and patient compliance. Research on baclofen and rabeprazole bilayer tablets frequently focuses on, enhancing both medications' release characteristics, assessing the tablet formulation's stability, examining how the medications and excipients work together, and Evaluating the combined medication's safety and clinical effectiveness (11,12).

1.3 Rationale of study:

The necessity to overcome the drawbacks of the current single-layer dosage forms served as the justification for creating a bi-layer tablet formulation of baclofen and rabeprazole sodium. Formulations with immediate release frequently cause quick absorption and excretion, necessitating frequent dosage adjustments and possible variations in plasma concentrations. Even while sustained-release formulations lower the frequency of doses, they could not have the desired initial therapeutic effect.

Gastroesophageal reflux disease (GERD) is a chronic and relapsing condition characterized by the backward flow of gastric contents into the esophagus, often leading to symptoms like heartburn and regurgitation and mucosal injury (13). Conventional therapies for GERD typically involve the use of proton pump inhibitors (PPIs), such as Rabeprazole, which reduce gastric acid secretion. However, acid suppression alone may not effectively address all aspects of GERD—especially the reflux of non-acidic gastric contents and poor esophageal motility (14).

To overcome this limitation, combination therapy involving a PPI and a prokinetic agent like Baclofen—a GABA_B agonist that reduces transient lower esophageal sphincter relaxations—offers a more holistic therapeutic approach. However, administering both drugs in separate dosage forms often leads to poor patient compliance and inconsistent therapeutic outcomes. Therefore, the development of a bilayer tablet formulation presents an innovative strategy: One layer provides immediate release of Rabeprazole for rapid acid suppression. The second layer ensures sustained release of Baclofen to maintain prokinetic action over an extended period. This bilayer design enhances therapeutic effectiveness, reduces dosing frequency, and improves patient compliance. The study is further justified by the lack of commercially available bilayer tablets combining Rabeprazole and Baclofen, making this formulation potentially valuable for clinical translation and market potential (15).

1.4 Formulation strategy for Bilayer Tablet:

The formulation of a bilayer tablet comprising Rabeprazole sodium and Baclofen was strategically designed to address the multifactorial pathophysiology of gastroesophageal reflux disease (GERD). Rabeprazole sodium, a proton pump inhibitor (PPI), is intended for immediate release to achieve rapid acid suppression. Since it is acid-labile, sodium bicarbonate was included as an alkalinizing agent to stabilize the drug and create a local pH conducive to its activity. Crospovidone, a superdisintegrant, was added to enhance the disintegration rate, while microcrystalline cellulose (MCC) improved compressibility and flow properties. This layer was formulated using the direct compression method to minimize exposure to heat and moisture (16).

The Baclofen layer was designed for sustained release to maintain prolonged muscle relaxation of the lower esophageal sphincter. To achieve extended drug release, hydrophilic polymer HPMC and hydrophobic ethyl cellulose were incorporated as release-retardant agents. PVP K30 served as a binder, while MCC again provided good compressibility. Talc and magnesium stearate acted as glidant and lubricant, respectively. The two layers were compressed sequentially using a bilayer tablet press to ensure structural integrity and prevent delamination. This dual-release system improves therapeutic effectiveness and enhances patient compliance by reducing dosing frequency and addressing both acid secretion and motility components of GERD (17).

1.5 Biopharmaceutical and Clinical relevance:

The bilayer tablet formulation of Rabeprazole and Baclofen is designed to target the multifactorial nature of GERD. Rabeprazole, a proton pump inhibitor, requires rapid release and protection from stomach acid due to its acid-labile nature. An immediate-release layer with sodium bicarbonate ensures stability and fast action (16). Baclofen, a GABA-B agonist, reduces transient lower esophageal sphincter relaxations but has a short half-life; hence, its sustained-release formulation maintains therapeutic levels for extended reflux control (17). The combination improves bioavailability, reduces dosing frequency, enhances patient compliance, and provides dual-phase relief—immediate acid suppression and prolonged reflux prevention—making it clinically valuable in GERD management (18).

1.6 Scope of study:

This study aims to develop and evaluate a bilayer tablet combining Rabeprazole (immediate release) and Baclofen (sustained release) for improved GERD management. The formulation focuses on enhancing patient compliance by delivering rapid acid suppression and prolonged reflux control. The scope includes preformulation analysis, bilayer tablet design using appropriate excipients, optimization of manufacturing processes, evaluation of physical parameters (weight variation, hardness, friability, thickness, disintegration), drug content uniformity, in-vitro dissolution studies, and release kinetics modeling to establish therapeutic efficacy and performance reliability.

2. MATERIAL AND METHODS:

2.1 Material used:

Rabeprazole sodium USP (Astitva Chemicals), Baclofen USP(Jigs Chemicals Limited), Sodium bicarbonate (Jigs Chemicals Limited), Cross povidone (Bhavi chemicals, Mumbai), Microcrystalline Cellulose (Shree Ashtak Private Limited), Talc powder (APS Minerals amd Additives Private Limited), Magnesium stearate (SBF Pharma Private Limited), HPMC (Algol Chemicals India Private Limited), Ethyl Cellulose (SD Fine Chmicals, Mumbai), PVP K30 (Alpha Genic Healthcare) were procured from IndiaMart of analytical grade.

2.2 Preformulation studies:

To assess the drug's and excipients' physicochemical and flow characteristics, preformulation studies were carried out. Carr's index, Hausner ratio, bulk density, tapped density, and angle of repose were evaluated to guarantee that the granules utilized in the immediate-release (IR) and sustained-release (SR) layers had the proper flowability and compressibility.

Pre- Compression studies:

- **Angle of repose:**

The angle of repose of the granules was determined using the funnel method. Granules that had been precisely weighed were collected using a funnel. The funnel's height was set so that its tip just touched the top of the granule heap. As the granules travelled through the funnel, they were free to flow onto the surface. The powder cone's diameter was measured, and an equation was used to determine the angle of repose (19).

$\tan(\theta) = h/r$

Acceptance range: ≤ 30° (Good Flow);

>40° (Poor Flow)

- **Carr's Index:**

A powder's compressibility was gauged by its compressibility index (CI). Consequently, it served as a gauge for the relative significance of inter particulate interactions. Such interactions were less important in a free-flowing powder, because the values of the tapped and bulk densities were close to one another. It was calculated by following equation (20).

$CI = (T.D - B.D) / T.D \times 100$

Acceptance range: < 15% (Good Flow);

> 25% (Poor Flow)

- **Hausner ratio:**

Hausner's ratio was calculated as the ratio of tapped density to bulk density (20).

$HR = T.D / B.D$

Acceptance range: < 1.25 (Good Flow);

> 1.5 (Poor Flow)

- **Melting point:**

Melting point of drug samples was identified by using melting point apparatus as per I.P.

- **Solubility profile:**

The solubility of drug at room temperature was determined in different solvents like Water, Ethanol, Ether and DCM as per U.S.P.

- **UV absorption:**

Preparation of standard stock solution of Rabeprazole sodium:

After precisely weighing 10 mg of rabeprazole sodium, it was transferred to a 100 ml volumetric flask. After dissolving it in 25 milliliters of 0.05N NaOH and sonicating it for ten to fifteen minutes, 0.05N NaOH (100 µg/ml) was used to make it up to volume.

Calibration Curve of Rabeprazole Sodium:

Fresh aliquots of the standard stock solution were pipetted out and appropriately diluted with 0.05N NaOH to achieve a final concentration between 2 and 18 µg/ml. A sharp peak was found at 292 nm after the solutions were scanned in spectrum mode for the 200–400 nm wavelength range (Fig. 1). Plotting a calibration curve with the absorbance on the Y-axis and the standard solution concentration on the X-axis was done (Fig-2) (21).

Preparation of standard stock solution of Baclofen:

The primary standard stock solution was made by dissolving 10 mg of baclofen in 10 ml of water to achieve a concentration of 1 mg/ml (1000µg/ml). Throughout the investigation, the solution was kept at room temperature. Daily preparation of the secondary stock solution involved diluting 1 ml of the primary stock solution with 10 ml of water to achieve a concentration of 0.1 mg/ml (100µg/ml) (22).

2.3 Formulation design of Bilayer Tablet:

The formulation consist of two functional layers. The IR layer (immediate release layer) with different formulation code was designed for onset action using superdisintegrants and the SR layer (sustained release layer) with different formulation code used hydrophilic matrix polymers to extend the duration of release. Granules were prepared by Wet granulation technique and were compressed using a double compression technique.

2.4 Post compression evaluation:

• Weight variation:

Twenty tablets of each formulation were weighed using an electronic balance in order to evaluate weight variation, and the test was conducted using the standard procedure (20).

•Hardness:

A Monsanto hardness tester was used to measure the hardness of each formulation of Tablets (20).

- **Thickness:**

The thickness was measured with Vernier Calipers. It was determined by taking measurements of the thickness of ten distinct tablet formulations (20).

• Friability:

Before being put in a Roche friabilator and spun for 100 revolutions at 25 rpm, the weight of ten tablets was determined. After being taken out of the friabilator, the tablets are dusted and weighed once more, with the weight being noted (20).

Disintegration test for Rabeprazole immediate release layer:

Placed one tablet in each tube of disintegration test apparatus. Operated the apparatus (up/ down motion) at 29-32 cycle per minute. Observed at what time the Rabeprazole sodium layer completely breaks down (without living any residue except insoluble excipients like HPMC from baclofen layer) (23).

- **In- vitro Dissolution studies:**

Used U.S.P. type II apparatus (paddle type) for the dissolution studies. 0.1N HCl was used for Rabeprazole sodium initially first 2 hours. Used pH 6.8 phosphate buffer solution for Baclofen next 6- 12 hours. Samples were taken a time interval of 5

minutes and analysed by the UV spectroscopy at 284 nm and 267 nm respectively (24).

Table.1 Melting point of Rabeprazole Sodium and Baclofen

Sr. no.	**Drugs**	**Melting point**			
		MP1	**MP2**	**MP3**	**Average**
1	Rabeprazole Sodium	203	202	204	203°C
2	Baclofen	133	136	136	135°C

Table.2 Solubility profile of drugs

Sr. no.	Drugs	Solubility of drugs in different solvent system			
		Water	Ethanol	Ether	DCM
1	Rabeprazole sodium	Soluble	Soluble	Insoluble	Soluble
2	Baclofen	Soluble	Soluble	Insoluble	Soluble

Table.3 Calibration value of Rabeprazole Sodium

Sr. no.	Concentration (µg/ml)	Absorbance (nm)
1	0	0
2	2	0.086
3	4	0.18
4	6	0.260
5	8	0.343
6	10	0.429
7	12	0.520
8	14	0.597
9	16	0.690
10	18	0.769
11	20	0.873

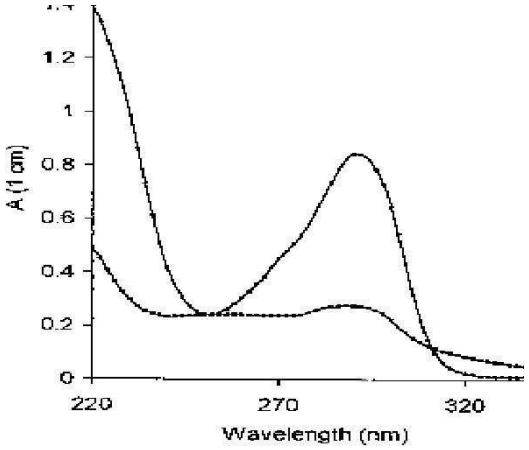

Fig.1 Spectrum of Rabeprazole sodium in 0.5M NaOH

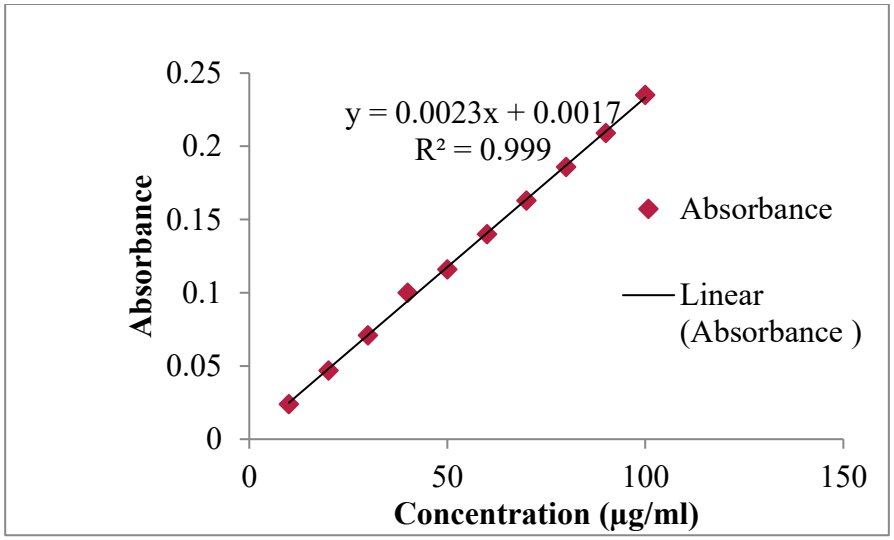

Fig.2 Calibration curve of Rabeprazole Sodium

Table.4 Calibration value of Baclofen

Sr. no.	Concentration (µg/ml)	Absorbance at 220 nm
1	10	0.024
2	20	0.047
3	30	0.071
4	40	0.100
5	50	0.116
6	60	0.140
7	70	0.163
8	80	0.186
9	90	0.209
10	100	0.235

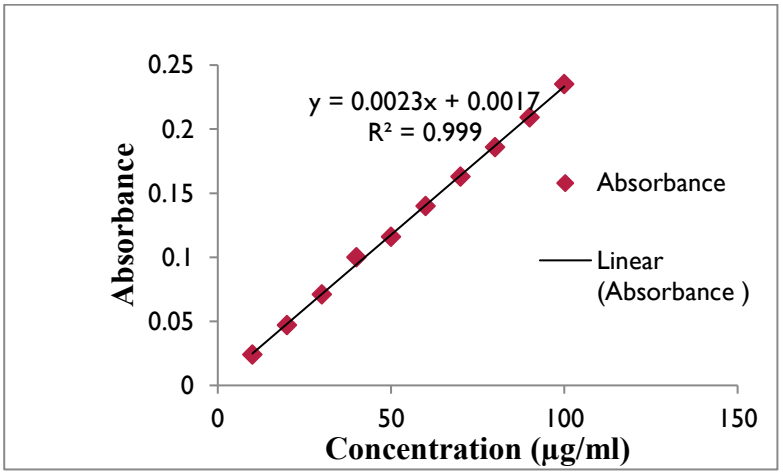

Figure.3 Calibration curve of Baclofen at 220 nm

Table.5 Formula of Rabeprazole immediate release for hundred Tablets

Ingredients (mg)	FR1	FR2	FR3
Rabeprazole sodium	2000	2000	2000
Sodium Bicarbonate	1000	1000	1000
Cross povidone	800	600	400
MCC	5500	5500	5500
Talc	200	200	200
Magnesium stearate	100	100	100

Table.6 Formula of Baclofen sustained release layer for hundred tablet

Ingredients (mg)	FB1	FB2	FB3
Baclofen	1000	1000	1000
HPMC	3000	3000	3000
Ethyl Cellulose	1000	500	250
MCC	5000	5000	5000
PVP k30	100	100	100
Talc	200	200	200
Magnesium stearate	100	100	100

Table.7 Angle of repose of Rabeprazole immediate release layer

Formulation code	1st reading	2nd reading	3rd reading	average
FR1	28^0	29.7^0	24.3^0	27.3^0
FR2	25.1^0	28.8^0	29.7^0	27.8^0
FR3	28.3^0	26.6^0	25.4^0	26.76

Table.8 Angle of repose of Baclofen sustained release layer

Formulation code	1st reading	2nd reading	3rd reading	average
FB1	26.6^0	27.3^0	24.8^0	26.2^0
FB2	26.6^0	27.3^0	25.5^0	26.4^0
FB3	26.6^0	25.8^0	27.0^0	26.5^0

Table.9 Carr's Index of Rabeprazole sodium immediate release layer

Formulation code	1st reading	2nd reading	3rd reading	average
FR1	13.46%	13.21%	12.00 %	12.89%
FR2	11.76%	12.00%	11.54%	11.76%
FR3	13.43%	14.06%	15.00%	14.16%

Table.10 Carr;s Index of Baclofen sustained release layer:

Formulation code	1st reading	2nd reading	3rd reading	average
FB1	11.54%	11.76%	13.72 %	12.34%
FB2	11.76%	12.00%	13.21%	12.32%
FB3	11.54%	12.00%	13.46%	12.33%

Table. 11 Hausner Ratio of Rabeprazole immediate release layer

Formulation code	1st reading	2nd reading	3rd reading	average
FR1	1.16	1.16	1.15	1.16
FR2	1.16	1.16	1.16	1.16
FR3	1.15	1.16	1.16	1.16

Table.12 Hausner Ratio of Baclofen sustained release layer

Formulation code	1st reading	2nd reading	3rd reading	average
FB1	1.16	1.16	1.15	1.16
FB2	1.18	1.18	1.19	1.18
FB3	1.17	1.18	1.18	1.18

Table.13 Weight variation test of bilayer tablet prepared from formula FR1 and FB1

Tablet no.	Weight (mg)	Average weight (mg)	Deviation %
1	189.5	190.0	-0.26%
2	190.2		+0.11%
3	189.8		-0.11
4	190.5		++0.26
5	190.0		0.00%
6	189.6		-0.21%
7	190.3		+0.16%
8	189.9		-0.05%
9	190.1		+0.05%
10	189.7		-0.16%
11	190.4		+0.21%
12	190.0		0.00%
13	190.2		+0.11%
14	189.8		-0.11%
15	189.5		-0.26%
16	190.5		+0.26%
17	190.3		+0.16%

18	189.6		-0.21%
19	190.1		+0.05%
20	189.7		-0.16%

Table.14 Weight variation test of bilayer tablet prepared from formula FR2 and FB2

Tablet no.	Weight (mg)	Average weight (mg)	Deviation %
1	192.5	193.0	-0.26%
2	193.3		+0.16%
3	192.8		-0.10%
4	193.5		+0.26%
5	193.5		0.00%
6	192.6		-0.21%
7	193.2		+0.10%
8	192.9		-0.05%
9	193.2		+0.05%
10	192.7		-0.16%
11	193.4		+0.21%
12	193.0		0.00%
13	193.3		+0.16%
14	192.8		-0.10%
15	192.5		-0.26%
16	193.5		+0.26%
17	193.2		+0.10%
18	192.6		-0.21%
19	193.1		+0.05%
20	192.7		-0.16%

Table.15 Weight variation test of bilayer tablet prepared from formula FR3 and FB3

Tablet no.	Weight (mg)	Average weight (mg)	Deviation %
1	188.2	188.5	-0.16%
2	188.7		+0.11%
3	188.6		+0.05%
4	188.4		-0.05%
5	188.9		+0.21%
6	188.1		-0.21%
7	189.0		+0.26%

8	188.3		-0.11%
9	188.5		0.00%
10	188.6		+0.05%
11	188.4		-0.05%
12	188.2		-0.16%
13	188.7		+0.11%
14	188.5		0.00%
15	188.3		-0.11%
16	188.9		+0.21%
17	188.1		-0.21%
18	189.0		+0.26%
19	188.4		-0.05%
20	188.5		0.00%

Table.16 Hardness test of bilayer tablet prepared from formula FR1 and FB1

Tablet no.	**Hardness kg/ cm^2**	**Range**	**Average Hardness**
1	**6.5**	**6.2- 6.7 kg/cm2**	**6.46 kg/cm^2**
2	**6.3**		
3	**6.6**		
4	**6.4**		
5	**6.5**		
6	**6.2**		
7	**6.7**		
8	**6.3**		
9	**6.6**		
10	**6.5**		

Table.17 Hardness test of bilayer tablet prepared from formula FR2 and FB2

Tablet no.	**Hardness kg/ cm^2**	**Range**	**Average Hardness**
1	6.4	6.3- 6.7 kg/cm^2	6.48 kg/cm^2
2	6.6		
3	6.5		
4	6.3		
5	6.7		
6	6.4		
7	6.5		

8	6.6		
9	6.3		
10	6.5		

Table.18 Hardness test of bilayer tablet prepared from formula FR3 and FB3

Tablet no.	Hardness kg/ cm^2	Range	Average Hardness
1	6.4	6.2- 6.6 kg/cm^2	6.48 kg/cm^2
2	6.2		
3	6.5		
4	6.3		
5	6.6		
6	6.4		
7	6.3		
8	6.5		
9	6.4		
10	6.6		

Table.19 Thickness of bilayer tablet prepared from formula FR1 and FB1

Tablet no.	Thickness (mm)	Range	Average Thickness
1	3.48	3.47- 3.52 mm	3.50 mm
2	3.50		
3	3.52		
4	3.47		
5	3.49		
6	3.51		
7	3.50		
8	3.48		
9	3.51		
10	3.49		

Table.20 Thickness of bilayer tablet prepared from formula FR2 and FB2

Tablet no.	Thickness (mm)	Range	Average Thickness
1	3.43	3.43- 3.47 mm	3.45 mm
2	3.46		
3	3.45		
4	3.44		
5	3.47		

6	3.45		
7	3.43		
8	3.46		
9	3.44		
10	3.45		

Table.21 Thickness of bilayer tablet prepared from formula FR2 and FB2

Tablet no.	Thickness (mm)	Range	Average Thickness
1	3.38	3.37- 3.42 mm	3.40 mm
2	3.42		
3	3.40		
4	3.39		
5	3.41		
6	3.40		
7	3.37		
8	3.41		
9	3.38		
10	3.40		

Table.22 Friability test of bilayer tablet prepared from formula FR1 and FB1

Initial weight of 20 tablet	Final weight 20 tablet after de-dusting	% Friability
4.000 gm	3.964 gm	0.90

Table.23 Friability test of bilayer tablet prepared from formula FR2 and FB2

Initial weight of 20 tablet	Final weight 20 tablet after de-dusting	% Friability
3.860 gm	3.827 gm	0.85

Table.24 Friability test of bilayer tablet prepared from formula FR3 and FB3

Initial weight of 20 tablet	Final weight 20 tablet after de-dusting	% Friability
3.770 gm	3.738 gm	0.85

Table.25 Disintegration test of Bilayer tablet prepared from FR1 and FB1 for FR1 layer

Tablet no.	Disintegration time (min: sec)	Average disintegration time
1	2:45	2 minutes and 44 second
2	2:52	
3	2:38	
4	2:49	
5	2:43	
6	2:41	

Table.26 Disintegration test of Bilayer tablet prepared from FR2 and FB2 for FR2 layer

Tablet no.	Disintegration time (min: sec)	Average disintegration time
1	3:21	3 minutes and 15 second
2	3:17	
3	3:10	
4	3:14	
5	3:16	
6	3:11	

Table.27 Disintegration test of Bilayer tablet prepared from FR3 and FB3 for FR3 layer

Tablet no.	Disintegration time (min: sec)	Average disintegration time
1	4:12	4 minutes and 13 second
2	4:18	
3	4:09	
4	4:14	
5	4:11	
6	4:16	

Table.28 In-vitro dissolution studies of bilayer Tablet prepared from FR1 and FB1 for FR1

Time (min)	% Drug Release
0	0
5	55.3%
10	83.7%
15	96.4%
30	98.9%
45	99.1%
60	99.3%

Table.29 In-vitro dissolution studies of bilayer Tablet prepared from FR1 and FB1 for FB1

Time (Hrs)	% Drug Release
0	0
1	12.1%
2	25.6%
4	44.8%
6	63.2%
8	79.9%
10	92.3%
12	98.1%

Table.30 In-vitro dissolution studies of bilayer Tablet prepared from FR2 and FB2 for FR2

Time (min)	% Drug Release
0	0
5	21.3%
10	34.5%
15	49.1%
30	61.8%
45	69.7%
60	73.2%

Table.31 In-vitro dissolution studies of bilayer Tablet prepared from FR2 and FB2 for FB2

Time (Hrs)	**% Drug Release**
0	0
1	8.4%
2	16.2%
4	27.8%
6	39.6%
8	52.9%
10	65.4%
12	71.1%

Table.32 In-vitro dissolution studies of bilayer Tablet prepared from FR3 and FB3 for FR3

Time (min)	% Drug Release
0	0
5	12.2%
10	24.8%
15	35.5%
30	47.1%
45	54.6%
60	59.8%

Table.33 In-vitro dissolution studies of bilayer Tablet prepared from FR3 and FB3 for FB3

Time (Hrs)	**% Drug Release**
0	0.0%
1	4.9%
2	11.3%

4	19.8%
6	30.5%
8	40.2%
10	49.7%
12	55.0%

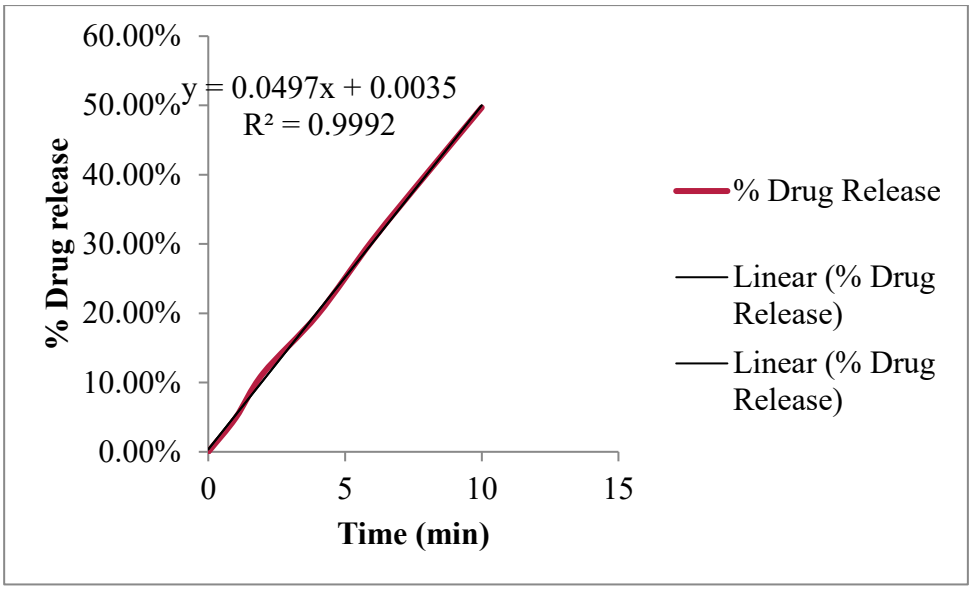

Fig.4 Graph of In-vitro dissolution studies of bilayer Tablet prepared from FR1 and FB1 for FR1

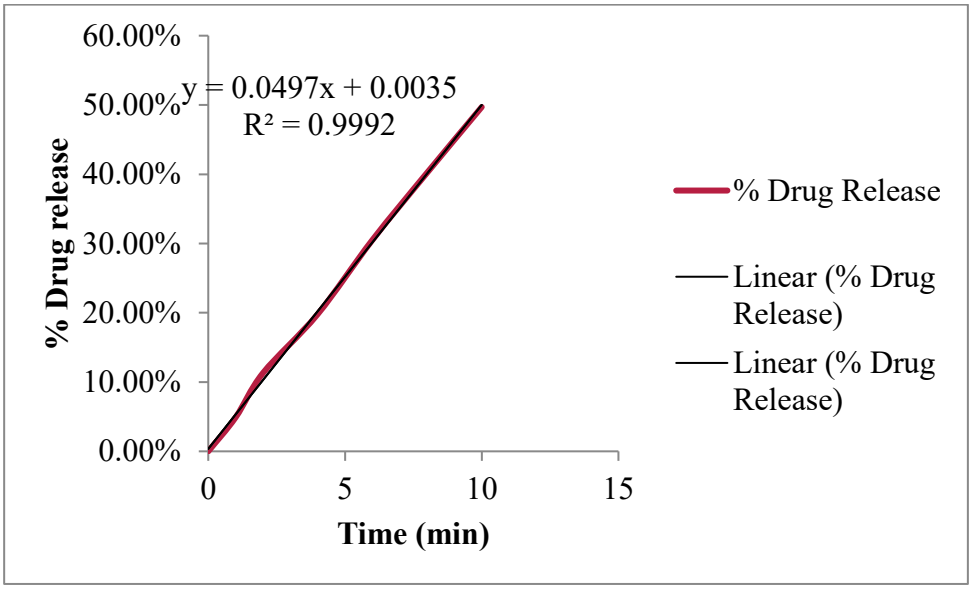

Fig.5 Graph of In-vitro dissolution studies of bilayer Tablet prepared from FR2 and FB2 for FR2

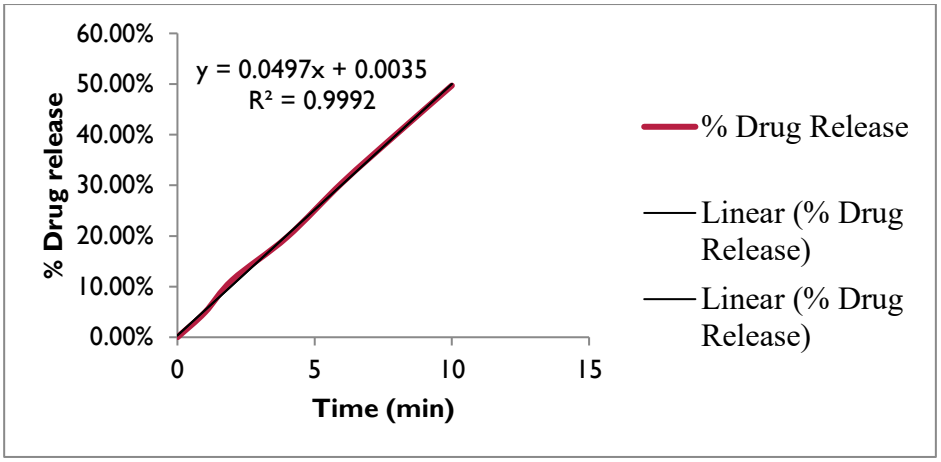

Fig.6 Graph of In-vitro dissolution studies of bilayer Tablet prepared from FR3 and FB3 for FR3

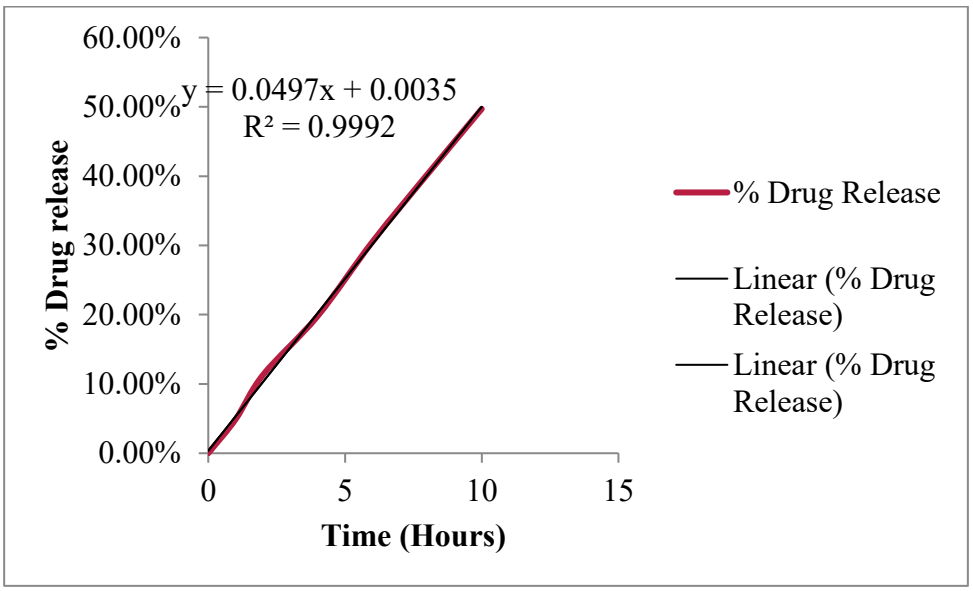

Fig.7 Graph of In-vitro dissolution studies of bilayer Tablet prepared from FR1 and FB1 for FB1

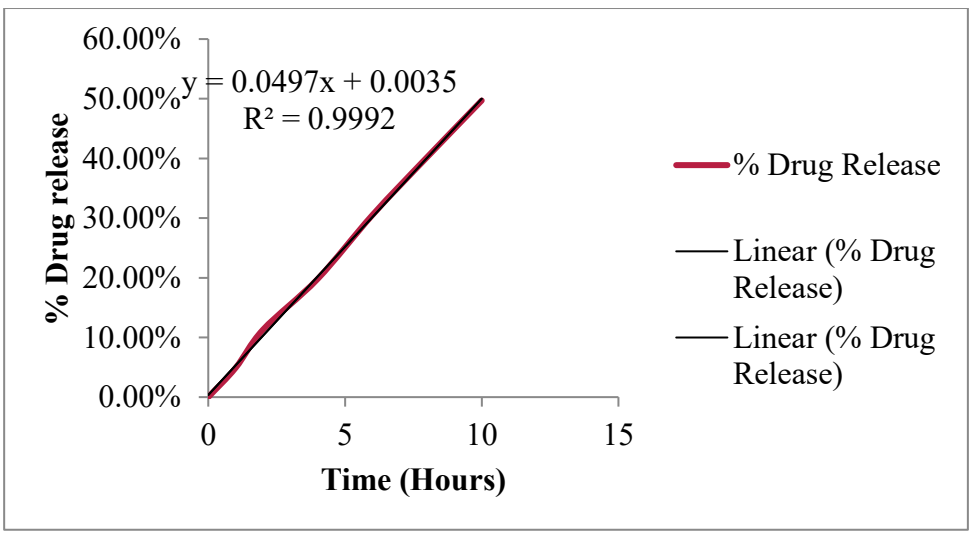

Fig.8 Graph of In-vitro dissolution studies of bilayer Tablet prepared from FR2 and FB2 for FB2

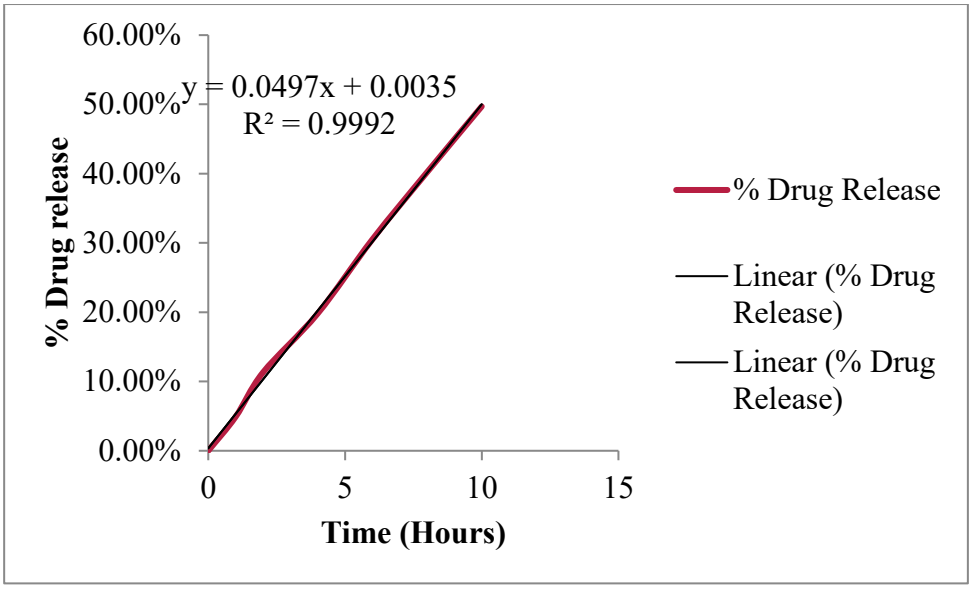

Fig.9 Graph of In-vitro dissolution studies of bilayer Tablet prepared from FR3 and FB3 for FB3

3. RESULT AND DISCUSSION:

The melting point of the drug was found to be 203ºC and 135 ºC, that were reported respectively in Table no.1.

The powder drugs were studied for solubility in various solvents. It was found to be soluble in water, ethanol and insoluble in ether and DCM, Table no.2.

The drug sample was scan in spectrophotometer in the range λmax 200-400 nm. .The absorption maxima for Rabeprazole sodium was found at 292 nm and for Baclofen at 220 nm which is fully compiled with pharmacopoeia specification. The drug sample was almost 99% pure as analysed by official method that was reported in figure no.2 and Fig. 3.

Angle of repose:

All batches showed good flow (<30^0), with FR1- FB1 having better due to higher disintegrant and polymer level.

Carr's Index%:

All data found within the acceptable limits (≤15%). FR1- FB1 again shows better compressibility.

Hausner Ratio:

Values<1.25 confirmed good powder flow. Slight increase in FR3-FB3 due to lower binder and disintegrants.

Weight variation:

All data found within the range as per I.P. limits.

Hardness:

All data founds within the acceptable limits. FR3- FB3 has lowest due to reduced binder/polymer.

Thickness:

Uniform thickness across batches indicates good die-filling and compaction.

Friability:

All data <1%. FR3-FB3 approaches the limit due to low binder content.

Disintegration:

FR1 shows the fastest disintegration, FR3 the slowest due to reduced disintegrants.

In-vitro dissolution studies of rabeprazole layer:

FR1 demonstrated the most effective burst release, owing to optimal concentration of cross povidone. FR3 with the least disintegrants, failed to reach adequate release in one hour.

For Baclofen layer:

FB1 formulation maintained a control and complete release profile up to 12 hours. FB3 lacked sufficient matrix forming agent resulting in poor sustainment.

4. CONCLUSION

FR1- FB1 showed the best overall results in terms of flow, compressibility, hardness, disintegration, and drug release, making it the ideal formulation.

FR2- FB2 showed moderate results but acceptable performance overall.

FR3- FB3 displayed poorest dissolution and tablet strength indicating under optimization due to low level of critical excipients.

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