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DEVELOPMENT AND CHARACTERIZATION OF BILAYER TABLET DOSAGE FORM FOR TREATMENT OF BACTERIAL DISEASE

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Abstract:

Controlled-release buoyant bilayer tablets reduce dosage system improve patient compliance with enhanced therapeutic action. It is a single dosage system have, two different tablets layers of clarithromycin and lansoprazole, respectively, are given for the treatment of bacterial infection and it might be worth incorporating both in a single tablet. The main objective of the present research work was emphasized on development and characterizes a bilayer tablet of Clarithromycin and Lansoprazole with separate layers to avoid incompatibility. The bilayered tablet gives biphasic drug release through loading dose; prepared using croscarmellose sodium as a superdisintegrant for immediate release of lansoprazole and HPMC K 15 polymer used for maintenance dose of clarithromycin using several viscosity grades of hydrophilic polymers. Bilayered tablet were evaluated for hardness, thickness, friability, drug content uniformity and in vitro drug dissolution.

Keywords: *Controlled release, buoyant bilayer tablets, Clarithromycin and Lansoprazole*

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INTRODUCTION:

Tablet is intact dosage form and offers the best capabilities of all oral dosage forms for accuracy in size and content of the lowest variability and it was prepared with the lowest cost of manufacture (if it is calculated per dose) [1]. Tablets is an oral dosage form of the lightest, most compact, easiest and most inexpensive way to packed and shipped. The compressed tablets most popular dosage form in use today. A tablet s a mixture of active substance and excipients usually in powder form pressed or compacted into a solid. Tablet is intact dosage form and offers the best capabilities of all oral dosage forms for accuracy in size and content of the lowest variability. Tablet can be used as a product of specific release profiles, such as the release in the intestine or slow release products [2]. Bilayer tablet is new era for successful development of controlled release formulation along with various features to provide successful drug delivery system. Bilayer tablets can be a primary option to avoid chemical incompatibilities between API by physical separation, and to enable the development of different drug release profiles. Bilayer tablet is suitable for sequential release of two drugs in combination, separate two incompatible substances and also for sustained release tablet in which one layer is immediate release as loading dose and second layer is maintenance dose. In case of bilayered tablets drug release can be rendered almost unidirectional if drug can be incorporated in the upper non adhesive layer its delivery occurs into the whole oral cavity [3]. A bi-layer tablet should have elegant product identity while free of defects like chips, cracks, discoloration and contamination. The objectives of bilayer tablet solid dosage forms are to control the delivery rate of either single or two different active pharmaceutical ingredient and provide separate incompatible active pharmaceutical ingredient (APIs) from each other. The dosage forms also help to control the release of API from one layer by utilizing the functional property of the other layer (such as, osmotic property [4-5]. The proposed work emphasized on development and characterize a bilayer tablet of Clarithromycin and Lansoprazole. Where each of the proposed bi-layer tablets is composed of an immediate-release layer and a sustained- release layer, rapid drug release that starts in the stomach to rapidly alleviate the symptoms and continues in the intestine to maintain protracted effect. Clarithromycin is an 6-O-methyl erythromycin derivative, comes under the category of Macrolide antibiotic. It is used for the treatment of a various bacterial infections. The bacteriostatic or bactericidal character of drug is totally depends on the type of organism and drug concentration. Lansoprazole, an acid proton-pump inhibitor similar to omeprazole, is used as an untiulcer drug in the treatment and maintenance of healing of duodenal or gastric ulcers, erosive and reflux esophagitis, NSAID-induced ulcer, Zollinger-Ellison syndrome, and Barrett's esophagus. Lansoprozole is active against Helicobacter pylori. The plasma elimination half-life of lansoprazole does not reflect its duration of suppression of gastric acid secretion. Thus, the plasma elimination half-life is less than two hours, while the acid inhibitory effect lasts more than 24 hours.

MATERIAL AND METHODS:

Preformulation studies: Preformulation study is the first step in the rational development of dosage form of a drug substance. Preformulation studies include studies of identification of physiochemical properties of drug, and an assessment of their relevance to the final formulation [6].

Physiochemical properties of clarithromycin and lansoprazole: The evaluation by sensory characters-taste, appearance, odor, feel of the drug, etc. The solubility of the drug was determined by taking some quantity of drug (about 1-2 mg) in the test tube separately and added the 5 ml of the solvent (water, ethanol, methanol, 0.1N HCL, 0.1N NaOH, Chloroform and acetone). The drugs were determine for melting pointdetermination. The drugs were also tested for drug excipients incompatibility test by FTIR Spectroscopy. Infra- red spectrum is an important record which gives sufficient information about the structure of a compound. This technique provides a spectrum containing a large number of absorption band from which a wealth of information can be derived about the structure of an organic compound. The region from 0.8 µ to 2.5 µ is called Near Infra-red and that from 15 µ to 200 µ is called Far infra-red region. Identification of Clarithromycin and Lansoprazole was done by FTIR Spectroscopy with respect to marker compound. Clarithromycin and Lansoprazole was obtained as White or almost white crystalline powder. It was identified from the result of IR spectrum as per specification. The wave number in cm-1 Functional groups Pure drug Clarithromycin 700-900 C-H Bending 891.60 cm-1, C-O Stretching 1049.30 cm-1, -C-H Bending 1373.95 cm-1, C=O Stretching 1691.72 cm-1, O-H Stretching 2978.17 cm-1. FTIR spectra of pure drug lansoprazole, and its physical mixture were obtained by using KBr pellets methods. About 2% (w/w) of samples was mixed with potassium bromide (KBr) disc. Each disc was scanned at a resolution of 4 cm-1 over a wave number region of 400–4000 cm-1 by a FTIR spectrometer [7].

Determination of λ_{max} of drug samples: The λ_{max} of Clarithromycin and Lansoprazole was determined by running the spectrum of drug solution in double beam ultraviolet spectrophotometer seperately. The spectrum of this solution was run in 200-400 nm range in U.V. spectrophotometer (Labindia-3000+).

Preparation of Instant Layer of Lansoprazole: Fast dissolving tablets of Lansoprazole were prepared by direct compression method after incorporating different superdisintegrants such as, crosscarmellose sodium (Ac-Di-Sol), in different concentrations. Magnesium stearate as lubricant and talc as glidant were added in a final step and mixed, this blend was subjected to analysis of pre-compression parameters. All the ingredients given in Table 1 were weighed and mixed in geometric progression in a dry and clean mortar. Then the ingredients were passed through mesh #60. The Blend was compressed on 8 mm (diameter) fat punches on a single station compression machine. Various formulations of Lansoprazole granules were prepared and each formulation contained one of the three disintegrate in different concentration [8]. Each tablets weighing 120 mg, were obtained. Composition of tablets is mentioned in **Table 1**.

Preparation of SR layer of Clarithromycin: Direct compression was followed to manufacture the gas generating floating tablets of Clarithromycin. Six different formulations (CSR1, CSR2, CSR3) were prepared by direct compression. All the polymers selected, drug and excipients were passed through sieve no.# 40 before using into formulation. The amount and ratio of drug and polymers were weighed as per given in **Table 2** and all the formulation were used for further evaluations parameters [8].

Formulation of bilayer tablet: After optimized of various formulations of instant release and sustained release layer by various parameters i.e. flow properties of granules, shape and color of tabletst, thickness test (height and diameter), weight variation test, hardness test, friability test, uniformity of drug content, in-vitro release characterstics. The formulation LIR1 of Instant release layer (Lansoprazole) and formulation of CSR2 (Clarithromycin) for control release were selected and used for formulation of Bi-layer tablet [9].

Evaluation of tablets:
All the tablets were evaluated for following different parameters which includes;

General Appearance: Five tablets from different batches were randomly selected and organoleptic properties such as color, odor, taste, shape, were evaluated. Appearance was judged visually. Very good (+++), good (++), fair (+) poor (-), very poor (--).

Thickness and diameter: Thickness and diameter of tablets were determined using Vernier caliper. Five tablets from each batch were used, and an average value was calculated.

Hardness: For each formulation, the hardness of five tablets was determined using the Monsanto hardness tester (Cadmach).

Friability: The friability of a sample of 10 tablets was measured using a Friability tester (Electro Lab). Ten tablets were weighed, rotated at 25 rpm for 4 minutes. Tablets were reweighed after removal of fines (dedusted) and the percentage of weight loss was calculated.

Uniformity of weight: Twenty tablets were randomly selected from each batch individually weighed, the average weight and standard deviation of 20 tablets was calculated.

Drug content: Twenty tablets were taken and amount of drug present in each tablet was determined. The tablets were crushed in a mortar and the powder equivalent to 25 mg of clarithromycin was transferred to 100ml standard flask. The powder was dissolved in 25 ml of 0.1 N HCL and made up to volume with 0.1 N HCL. The sample was mixed thoroughly and filtered through a 0.45µ membrane filter. The filtered solution was further diluted 0.1 ml to 10 ml suitably (10 ppm of clarithromycin) and prepares individually 10 ppm solution of Lansoprazole determine the Conc. of both drugs using 293 nm and 271 nm separately respectively.

***In vitro* buoyancy studies:** In vitro buoyancy was determined by floating lag time by the tablets were placed separately in a 100 ml glass beaker containing simulated gastric fluid (SGF), pH 1.2 as per USP. The time required for the tablet to rise to the surface and float was determined as floating lag time.

Dissolution rate studies: *In vitro* drug release was performed according to the USP dissolution apparatus II at 50 rpm and 37±0.5ºC temperature over a 12 hrs periods for bilayer tablets, using an automated paddle dissolution system (Labindia). A minimum of 6 tablets per batch were tested. The media used was 0.1N HCl at a pH 1.2 and a volume of 900 ml was maintained at 37±0.5◦C. Test sample (1ml) was withdrawn at particular time interval and replaced with fresh dissolution media maintained at the same temperature and the concentration of

dissolved drug was determined using U.V. (Ultraviolet Labindia 3000+) spectrophotometer at λmax 293 nm and 271 nm separately [10-11].

RESULTS AND DISCUSSION:

The preformulation studies of drug samples selected for the proposed study was clarithromycin and lansoprazole. Both drugs was used for the preparation of bilayer tablet for better effect of GRDDS disease with immediate effect of lansoprazole and sustainable release of clarithromycin in single solid dosage form as tablet. The both dosage forms was physicallly evaluated by sensory characters-taste, appearance, odor, feel of the drug, etc. The Solubility of the drug was determined by in various solvents water, ethanol, methanol, 0.1N HCL, 0.1N NaOH, Chloroform and acetone at room temperature. The melting point of both drug samples was identified and showed 118-119°C for clarihromycin & for lansoprazole Both drug samples were identified by FTIR Spectroscopy with respect to marker compound. The IR spectrum of sample drug shows the peak values which are characteristics of the drug and the graph were shown in **Figure 1** and wave number in cm-1 Functional groups Pure drug Clarithromycin 700-900 C-H Bending 891.60 cm-1, C-O Stretching 1049.30 cm-1, -C-H Bending 1373.95 cm-1, C=O Stretching 1691.72 cm-1, O-H Stretching 2978.17 cm-1. The FTIR spectra of pure drug lansoprazole **(Figure 2)**, and its physical mixture were obtained by using KBr pellets methods. About 2% (w/w) of samples was mixed with potassium bromide (KBr) disc. Each disc was scanned at a resolution of 4 cm-1 over a wave number region of 400–4000 cm-1 by a FTIR spectrometer. The Calibration curve of Lansoprazole at λ_{max} 293 nm & Clarithromycin at λ_{max} 271 nm was observed **Figure 3 – 4)**. The prepared bilayer tablets formulation was prepared with combination of **LIR1** of Instant release layer (Lansoprazole) and optimized formulation of **CSR2** (Clarithromycin) for control release in a single solid dosage form tablet. The formulation was evaluated with various parameters as given previous section. The general appearance of different batches was randomly selected and organoleptic properties such as color, odor, taste, shape, were evaluated. Appearance was judged visually. Thickness and diameter of tablets were determined using Vernier caliper. The hardness of five tablets was determined using the Monsanto hardness tester (Cadmach).The friability of a sample of 10 tablets was measured using a Friability tester (Electro Lab). Twenty tablets were randomly selected from each batch individually weighed, the average weight and standard deviation of 20 tablets was calculated. The formulation was crushed and amount of drug present was determined as conc. of both drugs using 293 nm and 271 nm separately respectively by double beam UV spectrophotometrically. In vitro buoyancy was determined by floating lag time i.e. time required for the tablet to rise to the surface and float was determined as floating lag time. *In vitro* drug release was performed according to the USP dissolution apparatus II for 12 hrs periods for bilayer tablets, using an automated paddle dissolution system (Labindia) **(Figure 5-6)**. The results of dissolution rate studies of bilayer tablets as percent cumulative drug release was determined and instant layer of Lansoprazole release Approx 89.98 percent drug within 15 minutes and control floating layer Clarithromycin shows release up to 12 Hours Approx 99.56±0.47 percent.

Table 1: Composition of Lansoprazole Fast Dissolving Tablets

Ingredients(mg)	Formulation code		
	LIR1	LIR2	LIR3
Lansoprazole	15	15	15
Croscarmellose sodium	10	15	20
Microcrystalline cellulose	75	70	65
Talc	10	10	10
Magnesium stearate	10	10	10
Total weight	120	120	120

Table 2: Various formulations of Clarithromycin

Ingredients (mg)	Formulation code		
	CSR1	CSR2	CSR3
Clarithromycin	250	250	250
HPMC K 15	50	60	70
Lactose	25	15	5
PVP K30	15	15	15
Magnesium stearate	5	5	5
Talc	5	5	5
Total Weight	350	350	350

Table 3: Post-Compressional Parameters of Optimized Formulation

Formulation code	Hardness test (kg/cm^2)	Friability (%)	Weight variation	Thickness (mm)	Drug content
Bilayer tablets	4.56 ± 0.32	0.589± 0.45	Passes	4.58±0.15	99.89

Table 4: Post-Compressional Parameters of Optimized Formulation

Formulation code	In vitro Disintegration Time (sec.) (n=3) Mean ± SD	Floating lag times (sec)	Total Floating Time (h)
Bilayer tablets	4.56 ± 0.32	18	>12

Table 5: Results of Dissolution rate studies of bilayer tablets

Time	Percent Cumulative Drug Release
(h)	BLCT1
0	0
1	36.56±0.35
2	44.48±0.42
3	49.65±0.65
4	59.78±0.12
5	73.45±0.25
6	79.58±0.47
7	88.56±0.74
8	94.98±0.65
12	99.56±0.54

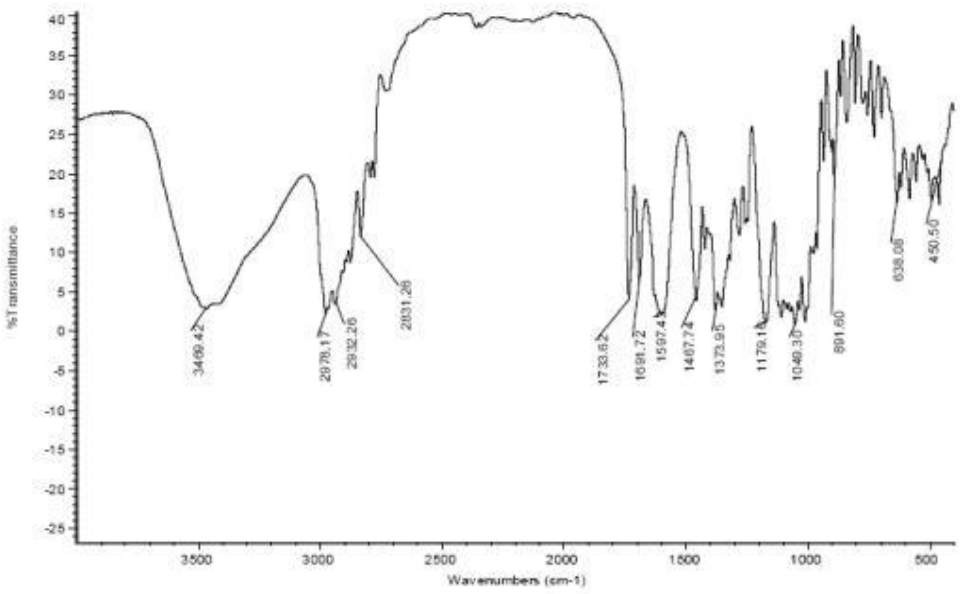

Figure 1: FT-IR Spectrum of Pure Drug (Clarithromycin)

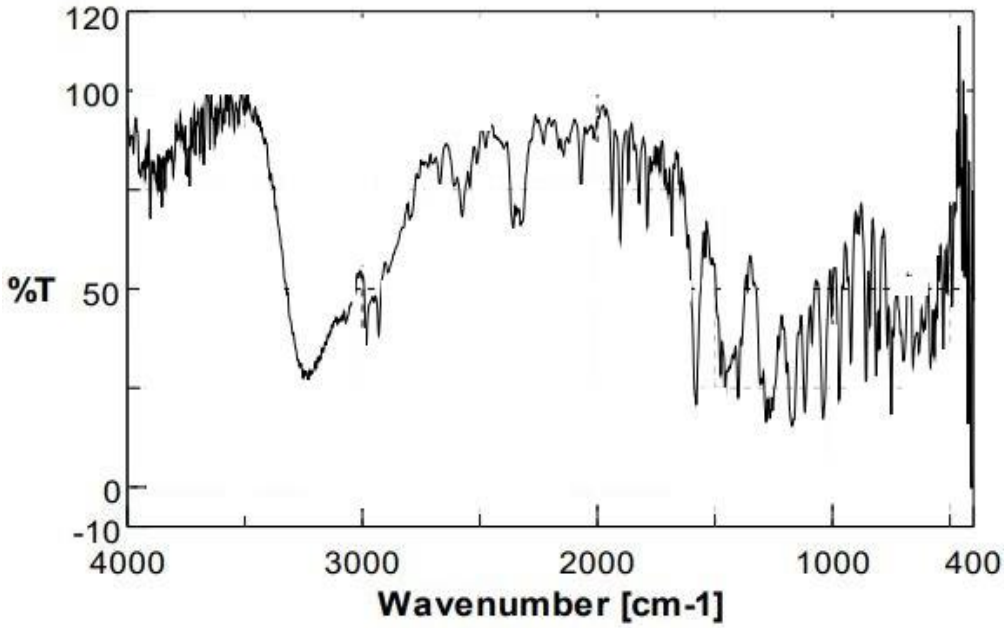

Figure 2: FT-IR Spectrum of Pure Drug (Lansoprazole)

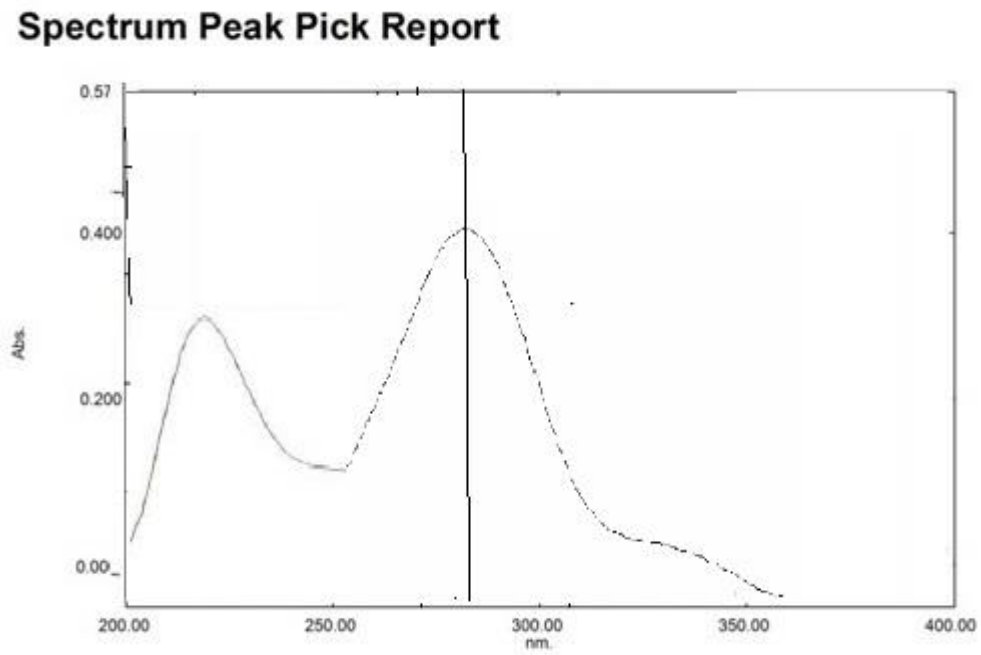

Figure 3: Determination of λ max of Lansoprazole

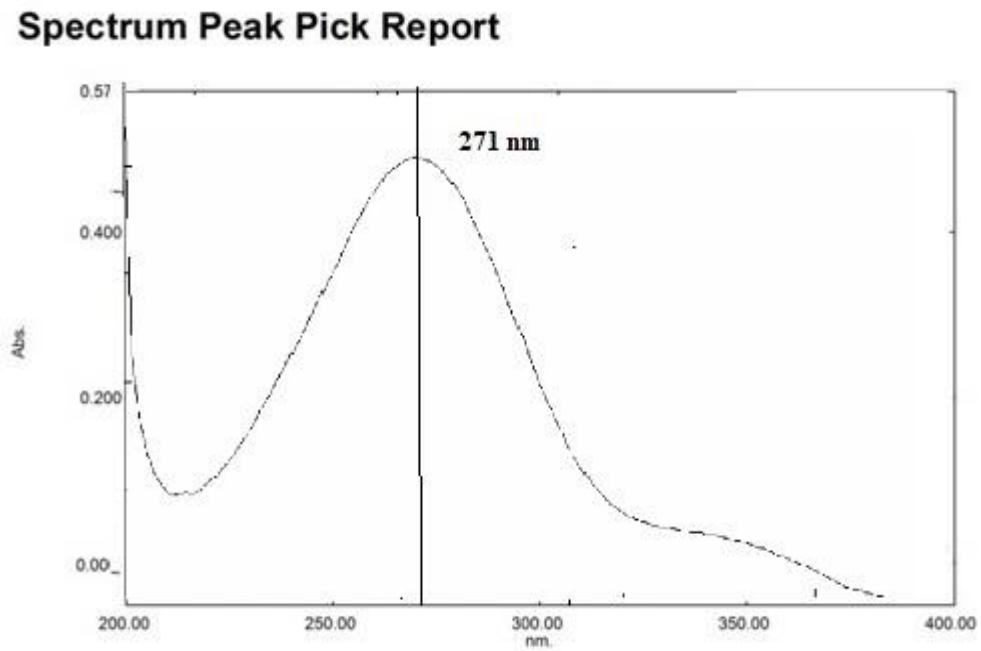

Figure 4: Determination of λ max of Clarithromycin

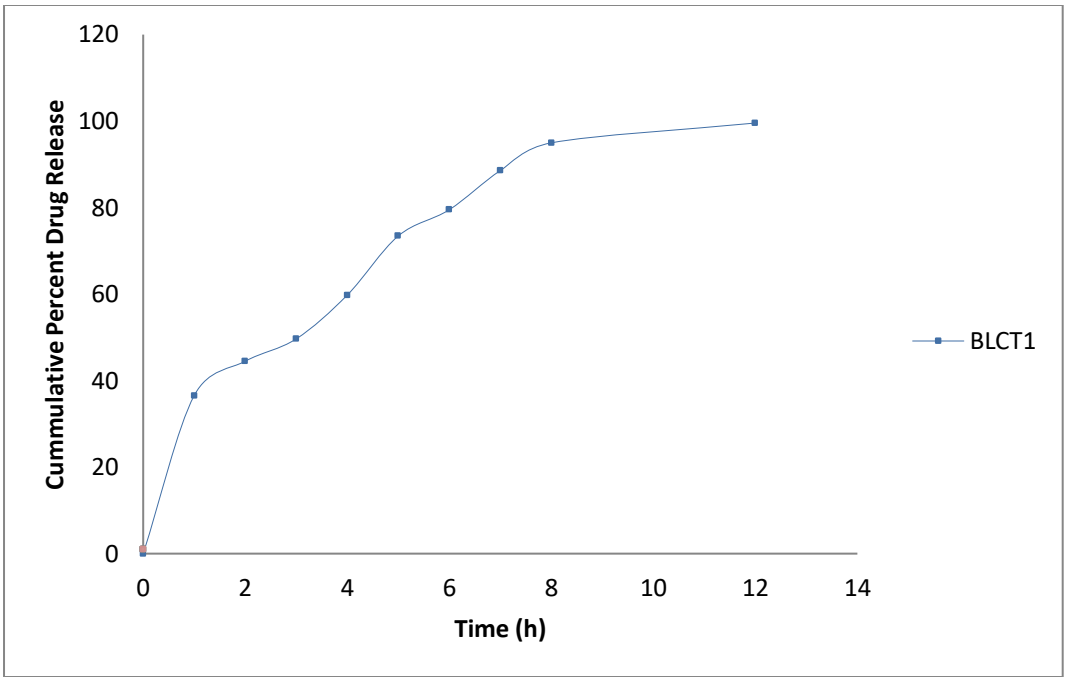

Figure 5: Zero-order kinetic in-vitro drug release kinetic study of bilayer tablets

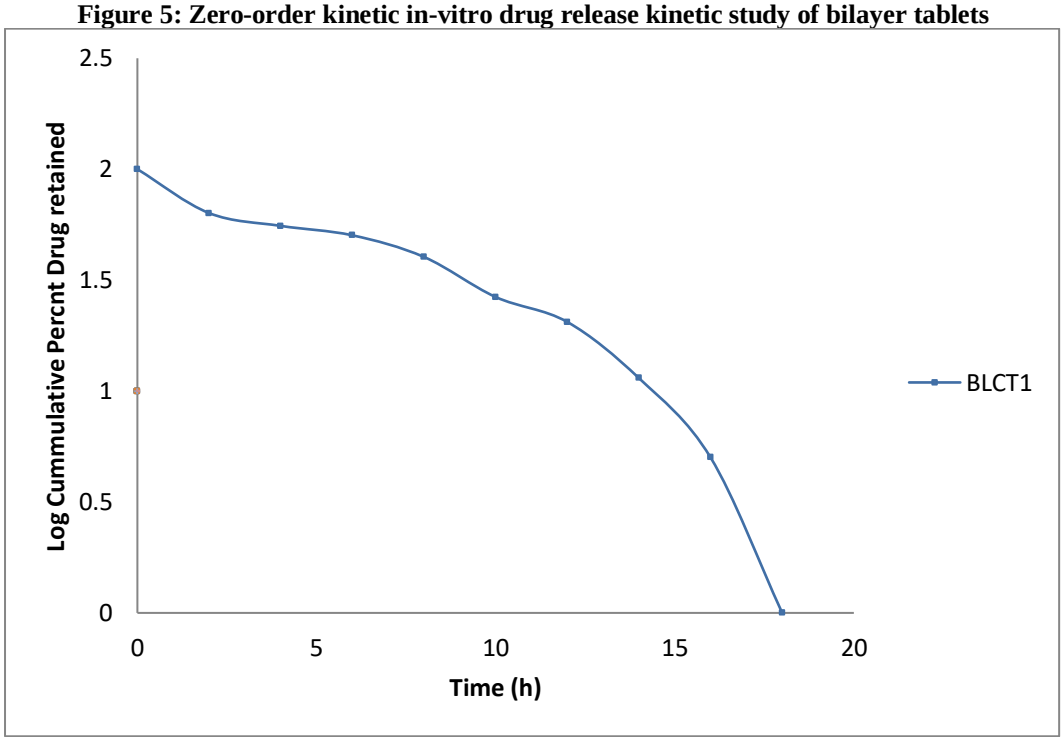

Figure 6: First-order kinetic in-vitro drug release kinetic study of bilayer tablets

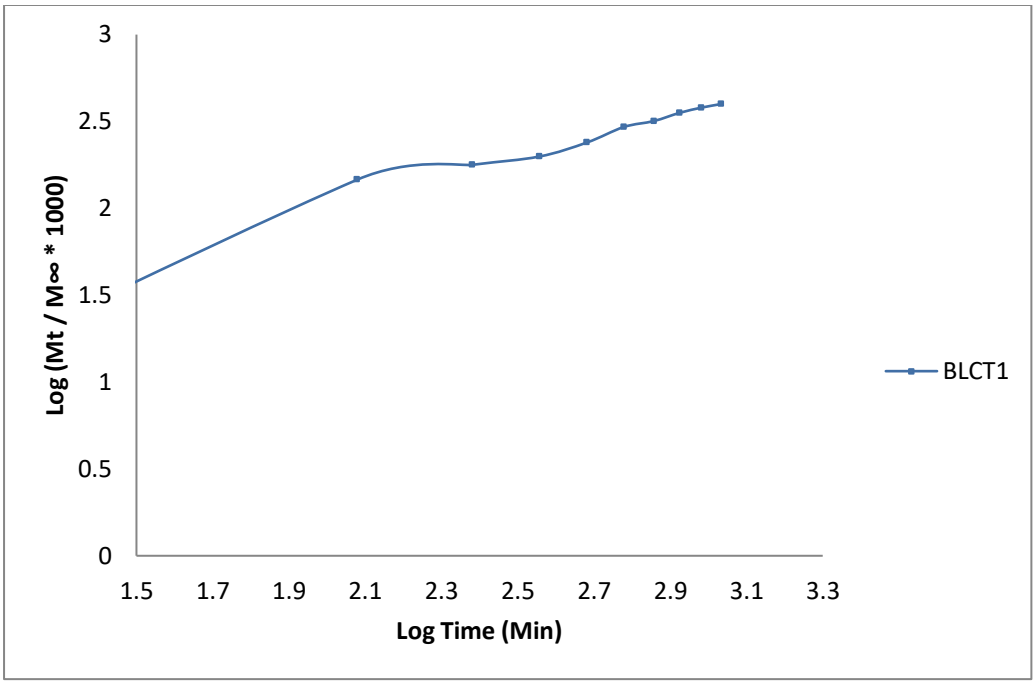

Figure 7: Korsmeyer-peppas kinetic in-vitro drug release kinetic study of bilayer tablets

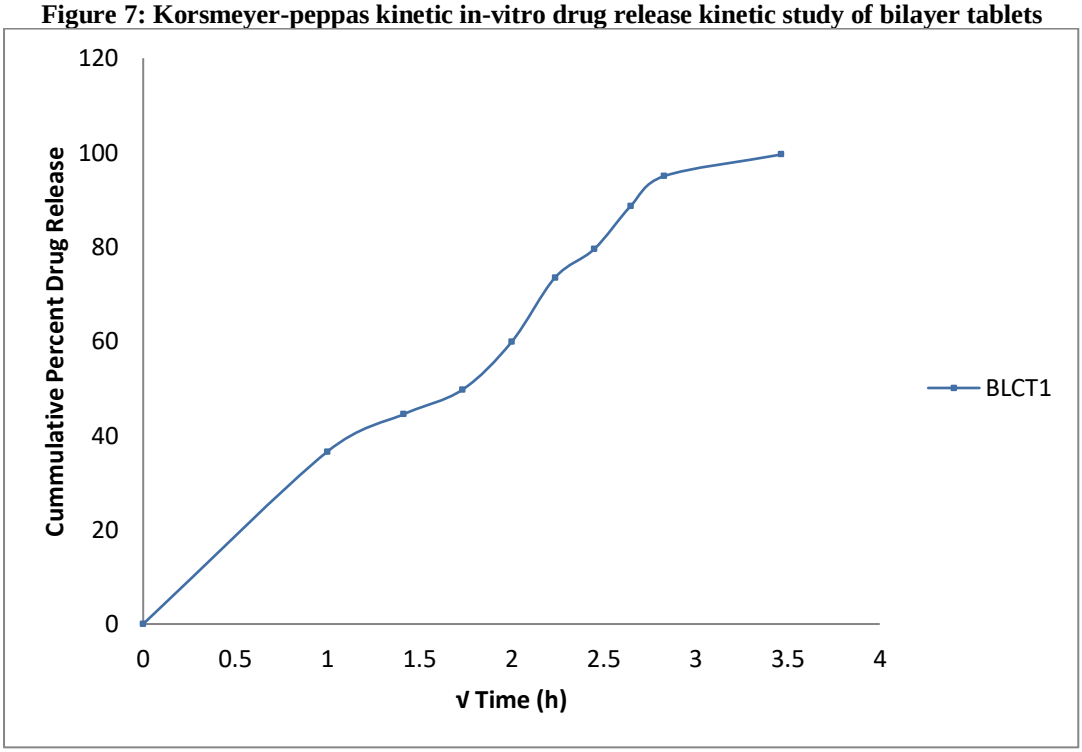

Figure 8: Higuchi kinetic in-vitro drug release kinetic study of bilayer tablets

SUMMARY AND CONCLUSION:

The proposed dosage form relates to formulation and development of oral pharmaceutical bilayer tablet of lansoprazole and clarithromycin for administration of therapeutically and prophylactically. The present investigation aimed to develop a bilayer tablet of Clarithromycin and Lansoprazole. Experiment conclude that Bi-layer tablet is suitable for delivering drugs with different release pattern like one layer of drug as immediate release to get quick relief and second drug as sustained release of drug which gives effect of drug for sufficient long time and reduce frequency of dose.

REFERENCES:

1. Talukder R, Fassihi R. Gastroretentive Delivery Systems: A Mini Review. Drug Dev Ind Pharm.2004; 30(10): 1019-28.
2. Garg R, Gupta GD. Progress in Controlled Gastroretentive Delivery Systems. Trop J Pharm Res. 2008 Sep; 7(3): 1055-66.
3. Patil JM, Hirlekar RS, Gide PS, Kadam VJ. Trends in floating drug delivery systems. J Sci Ind Res. 2006 Jan; 65: 11-21.
4. Shaha SH, Patel JK, Pundarikakshudu K, Patel NV. An overview of a gastro- retentive floating drug delivery system. Asian Journal of Pharmaceutical Sciences. 2009 Jan; 4(1): 65-80.
5. Jain N.K. Progress in controlled and Novel Drug Delivery Systems. 1sted Delhi: CBS Publishers and Distributors; 2004. P.76-95.
6. Avinash B. Darekar, Sonali N. Jadhav, R.B. Saudager. Bilayer tablet technology: An overview. International Journal of ChemTech Research.2017; 10(5): 595-603.
7. Metkar V, Kumar A, Pant P, Pal D, Sahu, Shurngarpure M, Dutta M. Formulation development and evaluation of Bilayer tablets of Lornoxicam. International Journal of Drug Development & Research.2012; 4 (2): 173- 179.
8. Gupta B, Bebnath R, Ghosh S, Chakraborty M, Biswas A. Formulation development studies of bilayer tablet glipizide: a novel and evolutionary approach in the treatment of diabetes. Asian J Pharm Clin Res.2013; 6(4):131-137.
9. Abbas J, Bashir S, Samie M, Laghari S, Nargis A, Habib U, Nazir I. Formulation and evaluation of a bilayer tablet comprising of diclofenac potassium as orodispersible layer and diclofenac sodium as sustained release core. Marmara Pharmaceutical Journal.2017; 21(3):707-716.
10. Kumar PD, Rathnam G, Prakash CR, Saravanan G, Karthick V, Panneer S. Formulation and Characterizatioin of Bilayer Floating Tablets Of Ranitidine.Rasayan J.Chem.2010; 3(2) 368-374.
11. Prabhakar S. Formulation and Evaluation of Bilayer Tablets of Diclofrenac Sodium with Ranitidine HCL for Sustained and Immediate Release. Journal of Applied Pharmaceutical Science.2012; 02(05):136-141.