JOURNAL OF PHARMACEUTICAL SCIENCE AND BIOSCIENTIFIC RESEARCH (JPSBR)

(An International Peer Reviewed Pharmaceutical Journal that Encourages Innovation and Creativities)

Formulation, Evaluation and Optimization of Carboxymethyl Tamarind Powder Based Baclofen Floating Matrix Tablet Using 3^2 Full Factorial Designs

Bhatt Bhargav[1], Patel Anuradha[2] and Dr.Sachine Narkhede[2]

1. Student of M.pharm, Department of Pharmaceutics, Smt. B.N.B Swaminarayan Pharmacy College, Salvav, Vapi-396191, India.

2. Assistant professor, Department of Pharmaceutics, Smt. B.N.B Swaminarayan Pharmacy College, Salvav, Vapi-396191, India.

ABSTRACT:

The present study was undertaken to assess the potential of Carboxymethylated Tamarind powder (CM-TP) as a matrix forming agent in floating matrix tablet of Baclofen. Baclofen is a centrally acting muscle relaxant. Half life of baclofen is 3-4 hours and absorption window is in upper gastrointestinal tract and intestine. This characteristic of drug shows that it is preferable to formulate a floating dosage form. The drug and excipients were found to be compatible as confirmed by IR spectral studies. Floating matrix tablet of Baclofen were prepared by wet granulation method using carboxymethyl tamarind as matrix former. A 32 full factorial design had been applied in which two independent variables and two dependent variables were employed to optimize drug release profile and are evaluated. Concentration of Carboxymethylated Tamarind (X1) and concentration of Sodium bicarbonate (X2) were taken as independent variables. The dependent variables selected were % drug release (Y1) and Total floating time (Y2). The optimized formulation showed a slow and complete drug release of 98.86±0.44 % over a period of 12 hr with 'R2' value 0.987 indicating that the release mechanism was Non-fickian release. The R2 value is highest in Higuchi model so the drug release mechanism mainly follow Higuchi model. The polymer carboxymethyl tamarind had significant effect on drug release which was seen in the study.

KEY WORDS: Carboxymethyl-tamarind, Baclofen, Floating matrix tablet, Sodium bicarbonate.

Article history:

Received 01 April 2016
Revised 14 April 2016
Accepted 16April 2016
Available online 20 April 2016

Citation:

Bhatt B, Patel A and Narkhede S. B. Formulation, Evaluation and Optimization of Carboxymethyl Tamarind Powder Based Baclofen Floating Matrix Tablet Using 3^2 Full Factorial Designs **J Pharm SciBioscientific Res**. 2016, 6(3): *221-230*

For Correspondence:
Bhatt Bhargav

Student of M.pharm, Department of Pharmaceutics, Smt. B.N.B Swaminarayan Pharmacy College, Salvav, Vapi-396191, India.

INTRODUCTION:

Novel oral sustained release dosage form which retained in the stomach for prolong and predictable period of time is of major interest among academic and industrial research groups. The real challenge in the development of oral sustained release dosage forms is not just to prolong the delivery of drugs for more than 12 hours, but also to prolong the presence of the dosage forms in the stomach or upper gastrointestinal tract until all the drug is released within desire period of time. One of the most feasible approaches for achieving prolong and predictable drug delivery profile in the GI tract is to control gastric residence time (GRT). There are several approaches have been reported for prolonging the residence time of drug delivery system in a particular region of the gastrointestinal tract, such as floating drug delivery systems, swelling and expending systems, polymeric bioadhesive systems, swelling and expanding systems, modified shape systems, high density systems and other delayed gastric emptying devices.

Floating drug delivery system is one of the approaches to increase the gastric residence time of the drug. Placement of the drug delivery system in a

specific region of the gastrointestinal tract offers numerous advantages, especially to the drugs having narrow absorption window in gastrointestinal tract, primaryabsorption in the stomach, stability problem in intestine, poor solubility at alkaline pH, local activity in stomach and property to degrade in colon.[1,2,3,4]

Floating system is also a low density system that have sufficient buoyancy to float over the gastric contents and remain in the stomach without affecting the gastric emptying rate for a prolong period of time. The system float on the gastric fluid only when it has density less than that of gastric fluids, i.e. <1g/cm^3. The drug is released slowly at the desired rate, which results in increased gastric retentive time and reduces fluctuation in plasma drug concentration. This technology has generated enormous attention over the last few decades owing to its potential application to improve the oral delivery of some important drugs for which prolonged retention in the upper gastrointestinal tract can greatly improve their therapeutic outcome. From the formulation and technological point of view, the floating drug delivery system is considerably easy and logical approach in the development of gastro retentive dosage forms. The excellent floating system is effective only in the presence of sufficient fluid in the stomach; otherwise, buoyancy of the tablet may be hindered. [1,4,5,]

Hydrophilic matrices are an interesting option while developing an oral sustained-release formulation. They can be used for controlling release of both water-soluble as well as water insoluble drugs. Polysaccharides are one of the choice of material for sustain release drug delivery system. Tamarind seed polysaccharide is a natural polysaccharide isolated from seed kernel of *Tamarindusindica,* family Leguminoseae. It has been significantly evaluated for use in hydrophilic drug delivery system. Its application is as release retardant polymer and binder in pharmaceutical industry. In addition to these other important properties of tamarind have been identified recently, which include non-carcinogenicity, mucoadhesivity, biocompatibility, high drug holding capacity, high thermal stability, availability and biocompatibility. It also became a material of choice for various types of chemical modification.

Carboxymethyl Tamarind powder (CM-TP) is a derivative of Tamarind kernel powder (TKP). The viscosity of CM-TP in solutions is higher compared to native gum. Derivatization of TKP i.e. CM-TP disrupts the organization and exposes the polysaccharide network for hydration which results in higher viscosity due to which it's swelling index is also higher as compared to TKP. The presence of carboxymethyl groups makes the molecule resistant toward enzymatic attack. This led to its application as excipient in hydrophilic drug delivery system.Since carboxymethyl tamarind is having improved properties which are required for the retardation of release. [6,7,8]

Baclofen, a centrally acting skeletal muscle relaxant, which acts as a gammaaminobutyric acid (GABA)-B receptor agonist. It is indicated in long-term treatment of spasticity resulting from multiple sclerosis and spinal cord injuries. Baclofen is rapidly and extensively absorbed and eliminated from the body. The half-life of the drug is 2.5 to 4 hours in plasma. Oral bioavailability of baclofen is about 40%. It is stable and well absorbed within pH range 1-4. Currently, baclofen is administered as the immediate release (IR) tablet 5-25 mg three times a day. Also the frequent administration of baclofen tablets leads to fluctuations in plasma concentration, producing peaks and throughs. High solubility, chemical and enzymatic stability and absorption profile of baclofen in acidic pH values, points to the potential of gastro retentive dosage form. Therefore, this work aims at modifying oral baclofen release, to minimize dose fluctuation and improve therapeutic response for patients suffering from spasticity and chronic musculoskeletal condition. [9,10,11]

2. MATERIALS AND METHODS

Materials

Baclofen was obtained as gift sample from Sun Pharma. Ltd, Vapi, India.Carboxymethyl tamarind powder was procured in college laboratory. Sodium bicarbonate, HPMC K100M, Microcrystalline cellulose, Talc, Magnesium stearate, PVPK 30, Isopropyl alcohol was purchased from Vishal Chemicals, Vapi, India.

Methods

Calculation of Loading and Maintenance dose [11,12,13]

Theoretical Sustained-release profile needed for Baclofen was evaluated based on its

pharmacokinetic parameters. The formulation involves the calculation of loading dose (Di), desired release rate (Ks), maintenance dose (Dm) and total dose needed for

Baclofen floating matrix tablets for twice daily administration as follows:

- Oral dose: 25 mg
- Dosing Interval (τ): 8 hours
- Elimination Half-life (t1/2): 4 h
- Time of peak concentration (tp): 1.9 hours
- Elimination rate constant (Ke): 0.693/ t1/2 = 0.693/4 =0.1732
- Initial dose (Di): Css.Vd / F

  But, Css = F.Xo/ Ke.Vd.τ

  Thus, Di = F.Xo / Ke.Vd.τ * Vd / F

  = Xo / Ke. T = 25 / 0.1732*8 =13.01mg
- Desired rate of drug release (Ks): Di * Ke = 13.01* 0.1732 =2.25mg/hr
- Maintenance dose (Dm): Ks * τ = 2.25 * 11 =24.75mg
- Corrected initial dose (Di*): Di – (Ks * tp) = 13.01 – (2.25 * 1.9) =8.73mg
- Total dose (Dt): Dm + Di* = 24.75 + 8.73 = 33.48 mg ≈34mg

Preparation of floating matrix tablet

Each tablet containing 34 mg of Baclofen were prepared. Different tablet formulations were prepared by wet granulation technique. All the powders were passed through a sieve of 80 mesh size. Required quantities of drug, polymer, and diluents were mixed thoroughly and a sufficient volume of granulating agent (isopropyl alcohol solution of PVP K-30) was added slowly. After enough cohesiveness was obtained, the mass was sieved through 10 mesh. The granules were dried at room temperature. Once dry, the granules were passed through 40 mesh. Talc and magnesium stearate were finally added as glidant and lubricant, respectively. The tablets were compressed (8.25 mm diameter, concave punches) using a tablet compression machine, Mini press-2,Karnavati. Each tablet contained 34 mg of Baclofen and other pharmaceutical ingredients. Prior to the compression, the granules were evaluated for several tests.

Optimization using 3^2 full factorial design[10]

A 3^2 randomized full factorial design was used in development of the dosage form. In this design, 2 factors were evaluated each at 3 levels and experimental trials were performed using all possible 9 combinations. In the present study, the amount of sodium bicarbonate (X1) and amount of carboxymethyl tamarind (X2) were selected as independent variables. The total floating time (TFT) and % drug release at 12 hours were selected as dependent variables. The actual 9 formulations designed according to experimental design are shown in Table no.1.

Drug Excipients Compatibility Study by FTIR

Compatibility studies for Baclofen were carried out with those excipients which were likely to be incorporated into the final formulation to determine possibility of any drug-excipient interaction/incompatibility. Drug was mixed separately with individual excipients in 1:1 ratio. These samples were subjected to compatibility studies for 30 days at elevated temperature and humidity conditions of 40±2^{o}C/75±5% RH. Samples were checked for physical changes and FT-IR spectra of these stored samples were then obtained after 30 days.

Evaluation of granules

Bulk density and tapped density

Both poured (or fluff) bulk (Do) and tapped bulk densities (DF) were determined, according to the method reported, where by a quantity (10 g) of granules from each formula, previously lightly shaken to break any agglomerates formed, was introduced into a 50 ml measuring cylinder. After the initial volume was observed, the cylinder allowed to fall under its own weight onto a hard surface from the height of 2.5 cm at 2 sec intervals. The tapping was continued until no further change in the volume was noted. The value of bulk density and tapped density were calculated by using equation:

LBD = Wt of Powder / Vol. of Powder

TBD = Wt of Powder / Tapped Vol. of Powder

Compressibility Index

Carr's Compressibility Index for the prepared granules was determined by the equation,

Carr's Index (%) = TBD – LBD/TBD x 100

Hausner's ratio

Hausner's ratio is an indirect index of ease of measuring the powder flow. It is calculated by the following formula,

Hausner's ratio = Tapped density / Bulk density

Angle of repose

Angle of repose for prepared granules was determined by fixed funnel method. A funnel was fixed with its tip at a given height (h), above a flat horizontal surface to which a graph paper was placed. The granules were carefully poured through a funnel till the apex of the conical pile just touches the tip of the funnel. The angle of repose was then calculated using the formula,

$$\theta = \tan^{-1}(h/r)$$

Where, 'θ' is the angle of repose,
'h' is height of pile,
'r' is radius of base of the pile.

Evaluation of floating matrix tablet

Prepared tablet were evaluated for quality control tests like weight variation test, hardness test, friability test, content uniformity study, and *in vitro* release study.

Weight variation test

To study weight variation, 20 tablets from each formulation were selected at random and average weight was determined using an electronic balance. Then individual tablets were weighed and the individual weight was compared with an average weight. Weight values were reported in mg. Mean and SD were calculated.

Hardness test

For each formulation, the hardness of six tablets was determined using a hardness tester (Pfizer). Hardness values were reported in kg/cm^2. Mean and SD were calculated.

Friability test

For each formulation, six tablets were weighed. The tablets were placed in a Roche friabilator (Roche) and subjected to 100 rotations in 4 min. The tablets were then dedusted and reweighed. The friability was calculated as the percent weight loss. Mean and SD were calculated.

%F = (1 - W/W0) x 100

Where, W0 = weight of tablet before test,
W = weight of tablet after test

Drug content uniformity study

Five tablets were weighed individually, then placed in a mortar and powdered with a pestle. An amount equivalent to 100 mg drug was extracted with 100 ml of 0.1N HCl (pH 1.2), stirred for 15 min. The solution was filtered through a filter (0.22 µm pore size), properly diluted with 0.1N hydrochloric acid and the drug content was measured using UV-VIS spectrophotometer at 266 nm. Mean and SD were calculated.

Buoyancy study

The *in vitro* buoyancy was determined by floating lag time. The tablets were placed in a 100 ml beaker containing 0.1 N HCl. The time required for the tablet to rise to the surface for floating was determined as Floating Lag Time (FLT) and the time period up to which the tablet remained buoyant is determined as Total Floating Time. Mean and SD were calculated.

***In vitro* drug release study**

The *In vitro* drug release study was performed using USP 24 type II apparatus (Electrolab) at 50 rpm in 900 ml of 0.1N HCl (pH 1.2) maintained at 37±0.5°C. The samples were withdrawn at predetermined time intervals for period of 12 hr and replaced with the fresh medium. The samples were filtered through 0.45 µm membrane filter, suitably diluted and analyzed at 266nm using double beam UV-VIS spectrophotometer (Lab india). The content of drug was calculated using equation generated from calibration curve. The test was performed in triplicate and the mean value was used to construct the release profile. Mean and SD were calculated.

Kinetic modelling and mechanism of drug release [4]

Various models were tested for explaining the kinetics model of drug release. To analyzed the mechanism of

drug release from the dosage form, the obtained data of optimized batch were fitted into various models like Zero order, First order, Higuchi model, Hixson-Crowell kinetics, Korsmeyer-Peppas release model.

4. RESULT AND DISCUSSION

Baclofen floating matrix tablets were prepared by using carboxymethyl tamarind powder as a retardant material and sodium bicarbonate as a gas forming agent to float the tablets in stomach. Carbon dioxide which is formed by sodium bicarbonate is entrapped by the polymer and decreases the density of tablet below the density of gastric fluid which results in floating of the tablet.

The FTIR Spectra study for all Drug + excipients mixtures is shown in figure no.1. The peaks 1018cm^{-1}, 1529cm^{-1}, 1627cm^{-1}, 1095cm^{-1}, 3424cm^{-1}, 735cm^{-1}, responsible for C-C stretching, C=C aromatic ring, C=O stretching, C-N stretching (aliphatic amine), N-H stretching, C-Cl stretching respectively remained unaltered. Thus it shows that Baclofen does not interact with any of the excipients chosen for the formulation.

A 3^2 factorial design had been applied and different batches of tablet had been prepared which is coded as F1 to F9 respectively. After entering all the results in design which is obtained by evaluating all the coded batches. Figure no.2 and 3 showed 3D surface plot of both factor X1 and X2, Figure no.4 shows flag of checkpoint batch. A checkpoint batch is obtain which is coded as F10 (optimized batch) which shows desired results. Further this formulation is also evaluated and all the results are shown in respective tables and figures.

The ingredient to be used for tablet preparation with its quantity in mg is enclosed in table no.1. Ingredient and concentration of all coded batch had been shown it (F1 to F10).

The granules of baclofen were prepared by wet granulation were evaluated by angle of repose, bulk density, tapped density, Hausner's ratio, and %compressibility. The micromeritic parameters of different formulation batches (F1 to F10) are shown in Table no.2. The bulk density and tapped density of prepared granules of all batches (F1 to F9) were found to be in the range from 0.35±0.009 to 0.41±0.012 gm/cm^3 and 0.38±0.010 to 0.46±0.015 gm/cm^3. The bulk density and tapped density of optimized batch (F10) was found to be 0.353±0.009 and 0.387±0.010 respectively. Angle of repose for all formulations (F1 to F9) were found to be in the range from 25.27 ±0.16 to 26.89 ±0.18 and for optimized batch (F10) was 20.93±0.205 which indicates a good flow property of all batches of granules. The % compressibility and Hausner's ratio of prepared granules of all batches (F1 to F9) were found to be in the range from 9.68 ±0.274 to 11.54 ±0.377% and 1.09 ±0.007 to 1.11 ±0.003, optimized batch (F10) was found to be 9.68±0.274 and 1.09±0.002 respectively. The result of % compressibility and Hausner's ratio further support the good flow property of granules.

The appearance of tablet was found to be cream color, smooth, convex with no visible cracks. All data of physical parameter of baclofen floating matrix tablet were tested and results was shown in table no.3 with standard deviation of each batches. Physical parameter includes Hardness, Weight Variation, Friability, % Drug content. Hardness of all batches (F1 to F10) was measured by Monsanto hardness tester and results were found in between 5.16 ±0.28 to 6.33 ±0.28 kg/cm^2indicating satisfactory mechanical strength. The weight variation of all batches (F1 to F10) was measured and results were found in the range of 198.56±2.4 to 201.92±2.8 mg which is in the range ±7.5% complying with pharmacopoeia specifications. The %friability data results shows below 1% for all the formulations, which was measured by Roche friabilator and indicates good mechanical resistance of the tablets. The % drug content uniformity of all formulation (F1 to F10) showed values in the range of 95.74±0.1% to 99.56±0.1%, which reflects good uniformity in % drug content among all formulations. All the formulations showed values within the prescribed limits for tests like hardness, friability, % content uniformity and weight variation which indicate that the prepared tablets are of standard quality.

The tablet formulations were prepared by floating approach. Total floating time is considered as one of the factor for optimization. Sodium bicarbonate was used as a gas-generating agent. Sodium bicarbonate get reacted and carbon dioxide is generated in presence of 0.1M hydrochloric acid (stomach fluid). It was observed that formulation F1 to F9 content different amount of sodium bicarbonate (12.5%, 15%, 17.5%) and other polymer; which holds the carbon dioxide within the tablet matrix as a result they are able to float. The formulations F1 to F9 shows appreciable floating lag time 48.0±2 to 152.3±1.5 min. as the sodium bicarbonate concentration increases the increase in total floating time of tablet. The

desired floating time that is 12 hours is obtained in F7 to F9 formulation. The desired results were obtained by changing the concentration of sodium bicarbonate 25.04mg for optimized batch (F10) obtained after applying factorial design showed floating lag time 46.33±2.08 sec and desired total floating time for 12 hours.

% swelling index study results showed gradual increase in swelling index with respect to time and concentration of carboxymethyl tamarind. As the tablet comes in contact with 0.1 M hydrochloric acid it showed burst release due to improper swelling. To overcome this effect addition of HPMC K100M in small quantity is done. The result obtained from the study was enclosed in table no.4. The results showed that formulation F1 to F3 swells 91.8±0.7% to 92.8±1.1% after 12 hours. This is due to the lowest concentration 60mg of polymer used. Formulation F4 to F6 contain middle concentration 70mg of polymer and swelling was seen in range of 94.0±1.7% to 96.1±0.7%. Formulation F7 to F9 contains highest concentration 80mg of polymer which showed swelling range from 95.5±0.5% to 98.1±1.0%. Optimized batch F10 shows swelling index 98.16±0.28 within 12 hours. Graphical representation had been done in figure no.5 for F1 to F9 and figure no.6 is represented of optimized batch. Overall study represent that as the concentration of carboxymethyl tamarind increases the % swelling index also increases gradually.

The dissolution study has been performed and the results were obtained is enclosed in table no.5. Formulation code F1 to F3 showed 77.5±1.4% to 80.1±1.4% of drug release in 7 to 8 hours. The concentration of polymer was lowest in the formulation so it could not float for 12 hour and get settled down before desired time interval. Formulation F4 to F6 contain medium amount of polymer concentration and results showed 90.3±2.4% to 97.6±0.9% of drug release in 9 to 11 hours and which also does not floated for desired interval of time. Formulation F7 to F9 contain highest amount of polymer concentration which is able to float for 12 hours and showed drug release from 95.2±0.5% to 97.7±0.4%. The optimized batch that is F10 obtained by applying factorial design showed 98.86±0.44% of drug release and remain in floating for 12 hours which was desired condition. The amount of polymer required for obtaining desired drug release and total floating time is mentioned in table no.1. The graphical representation figure no.7 for formulation F1 to F9 and figure no.8 for optimized had be done were % cumulative drug release verses time interval had been done for all the formulation.

Dissolution profile of optimized batch were fitted to various model and release data were analyzed on the basis of Korsmeyer-Peppas equation, first order, hixson-crowell kinetics, Zero order and Higuchi kinetics. The result shows Higuchi model, the dissolution exponent is 0.987 which is highest in all models. From the results, it is seen that formulations showed Non-Fickian release. Coefficients of correlation (R^2) were used to evaluate the accuracy of the fit. Drug release mechanisms follow Higuchi order rather than First order. The R^2 value is highest in Higuchi model so the drug release mechanism mainly follow Higuchi model.

4. CONCLUSION

The present investigation deals with formulation and evaluation of floating matrix tablet of Baclofen by using carboxymethyl tamarind as matrix forming polymer. Optimization was done using 3^2 full factorial design. From the polynomial equation and contour plots generated, both independent factors showed significant effect on dependent variables. The sustained release of Baclofen was observed and good fit to Higuchi model was demonstrated. The optimized batch shows all criteria within specification.

Acknowledgement

I convey my deep sense of gratefulness and sincere thanks to my respected guide, Patel Anuradha Smt. B.N.B Swaminarayan Pharmacy College, Salvav, Vapi, who has been a stable source of inspiration to me with her scholastic guidance and valuable suggestions at all stages of my work. It was one of the golden opportunities to work under him.

Reference

1) JagtapLeena S, Swami Seema P, Mali Prabha R, TripathiPallavi S, DeshmukhKishor R, “Formulation and evalution of floating matrix tablets of fomatidine using natural polymer”, *Int. Res. J. of Pharm.*, 2011;2(6):110-115.
2) Mohammed AsifHussain, Mahender B, MaimunaAnjum, “Formulation and evaluation of effervescent floating matrix tablets of ofloxacin”, *Int. J. of Drug Dev. and Res.*, 2014;6(1):188-198.

3) Sanjay Dey, SnigdhaDutta, BhaskarMazumder, "Formulation and evaluation of floating matrix tablet of atenolol for gastro-retentive drug delivery", *Int. J. of Pharm. and Pharm. Sci.,* 2013;4:433-437.
4) DevarajanKrishnarajan, Rangasamy, ChandrothNidhin, NatesanSenthilkumar, "Design and charecterisation of floating tablets of ranolazine", *Int. Res. J. of Pharm.*, 2012;3(4):268-272.
5) Ramji Anil Kumar Arza, Chandra SekharaRaoGonugunta, Prabhakar Reddy Veerareddy, "Formulation and evaluation of swellable and floating gastroretentive ciprofloxacin hydrochloride tablets", *AAPS PharmSciTech.*, 2009;10(1):220-226.
6) Ashwini R. Madgulkar, Mangesh R. Bhalekar, Rahul R. Padalkar, Mohseen Y. Shaikh, "Optimization of carboxymethyl-xyloglucan-based tramadol matrix tablets using simlex centroid mixture design", *J. of Pharm.*, 2013;1-11.
7) RashmiManchanda, BirendraShrivastava, S. C. Arora, Rajesh Manchanda, "Optimization of carboxymethyl tamarind seed polysaccharide based glipizide matrix tablets using 32 full factorial design and response surface methodology", *Sch. Res. Lib.*,2015;7(2):297-309.
8) C. MallikarjunaSetty, Anand S. Deshmukh, Aravind M. Badiger, "Hydrolysed polyacrylamide grafted carboxymethylxyloglucan based microbeads for pH responsive drug delivery", *Int. J. of Bio. Macr.*,2014:67;28-36.
9) AshanVeerakumar, Jennifer J. Cheng, Abraham Sunshine, Xiaobu Ye, Richard D. Zorowitz, William S. Anderson, " Baclofen dosage after traumatic spinal cord injury: A multi-decade retrospective analysis", *Clin. Neur. and Neurosur.*, 2015;129:50-56.
10) Ranpise N.S, Kolhe S.R, Ranade A.N, "Development and evaluation of bilayer gastroretentive floating drug delivery system for baclofen", *Ind. J. of Phar. Edu. and Res.,* 2013;47(1):41-46.
11) Sagar L. Vekariya, Parul K. Patel, Shreya T. Solanki, NiravVasava, Dr. RisadJivani, "Influence of hydrophilic polymer on release profile of baclofen from bilayer tablet", *Int.J. of Pharm. and Pharm. Sci.,* 2012;4(3):454-458.
12) E.W. Wuis, M.J.M. Dirks, T.B. Vree, E. Van der Kleijn, "Pharmacokinetics of baclofen in spastic patients receiving multiple oral doses", *Pharm. Wee. Sci. edi.*, 1990;12(2):71-74.
13) M. Soumya, M. Saritha, "Preparation and optimization of valsartan bilayered release matrix tablets", *Int. J. of Phar. And Bio. Arc.,*2011:2(3);914-920.

TABLES AND FIGURES

Table No. 1: Formula for floating matrix tablet preparation

Ingredient	Formulation (mg)									
	F1	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**	**F10**
Baclofen	34	34	34	34	34	34	34	34	34	34
Carboxymethyl-tamarind	60	60	60	70	70	70	80	80	80	81.8
HPMC K100M	20	20	20	20	20	20	20	20	20	20
$NaHCO_3$	25	30	35	25	30	35	25	30	35	25.04
MCC	37	32	27	27	22	17	17	12	7	15.16
Talc	2	2	2	2	2	2	2	2	2	2
Mg. St.	2	2	2	2	2	2	2	2	2	2
PVPK-30	20	20	20	20	20	20	20	20	20	20
IPA	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s
TOTAL WEIGHT(mg)	200	200	200	200	200	200	200	200	200	200

Table 2: Micromeritics properties of powder blend of different formulation (F1-F10)

Batch Code	Angle of repose (θ)	Bulk density (gm/cm^3)	Tapped density (gm/cm^3)	% compressibility	Hausner's ratio
F1	26.14±0.46	0.36±0.0099	0.40 ±0.012	10.17 ±0.303	1.10 ±0.003
F2	25.77±0.40	0.35±0.0091	0.38 ±0.010	9.68 ±0.274	1.09 ±0.007
F3	25.27±0.16	0.36±0.0099	0.40 ±0.012	10.17 ±0.303	1.10 ±0.003
F4	26.32±0.09	0.35±0.0091	0.38 ±0.010	9.68 ±0.274	1.09 ±0.002
F5	26.18±0.21	0.39±0.0100	0.43 ±0.013	10.91 ±0.337	1.10 ±0.003
F6	26.54±0.57	0.41±0.0120	0.46 ±0.015	11.54±0.377	1.11 ±0.003
F7	25.94±1.00	0.37±0.0090	0.41 ±0.012	10.35±0.303	1.10 ±0.003
F8	26.89±0.18	0.41±0.0121	0.46 ±0.015	11.54 ±0.377	10.72±0.337
F9	26.82±0.27	0.38±0.0100	0.42 ±0.013	10.72 ±0.337	1.10 ±0.003
F10	20.93±0.20	0.35±0.0090	0.38±0.010	9.68±0.274	1.09±0.002

Table 3: Physicochemical and buoyancy properties of the tablets of different formulations (F1 to F10)

Batch Code	Hardness (kg/cm^2)	Weight variation (mg)	Friability (%)	Content uniformity (%)	Floating lag time (sec)	Floating time (h)
F1	5.33 ±0.28	201.09±1.7	0.46 ±0.10	95.74±0.1	152.3±1.5	7
F2	5.66 ±0.57	198.76±2.8	0.36 ±0.22	97.70±0.1	114.6±2.0	8
F3	5.66 ±0.76	201.23±2.1	0.33 ±0.12	96.55±0.3	82.0±2.0	8
F4	6.33 ±0.28	198.56±2.4	0.38 ±0.02	99.56±0.1	133.6±2.0	9
F5	5.16 ±0.28	199.12±1.7	0.36 ±0.07	98.62±0.3	72.6±1.1	11
F6	6.16 ±0.28	198.89±1.5	0.34 ±0.17	96.78±0.1	58.3±1.5	11
F7	6.00±0.00	201.92±2.8	0.38 ±0.14	97.93±0.3	90.0±1.7	12
F8	5.66±0.288	199.33±2.4	0.23 ±0.02	98.85±0.1	67.3±1.5	12
F9	6.16±0.288	201.66±2.4	0.33 ±0.05	95.86±0.3	48.0±2.0	12
F10	6.33±0.28	199.12±1.7	0.33±0.12	99.26±0.1	46.33±2.08	12

Table No.4: %Swelling index of all the tablet formulation

Time (hr)	% Swelling Index (Mean±SD) n=3									
	F1	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**	**F10**
0	0	0	0	0	0	0	0	0	0	0
1	28.6±1.7	27.5±2.0	29.8±1.2	21.6±0.5	22.1±0.7	23.0±0.5	18.3±1.1	19.6±0.2	19.8±0.7	17.83±1.25
2	39.8±1.2	38.6±1.5	41.0±0.8	32.0±0.5	33.3±0.7	32.6±1.2	27.6±0.5	28.5±0.8	29.0±0.8	26.66±0.76
3	54.8±1.0	53.6±0.7	56.0±1.3	48.1±1.6	49.3±1.1	48.8±0.2	36.6±1.1	36.3±0.5	35.8±0.2	34.50±2.17
4	63.6±0.7	62.5±0.8	64.8±0.2	59.5±1.5	58.6±1.5	59.3±1.5	45.6±1.2	44.0±0.5	43.1±0.2	42.83±0.76
5	71.6±1.1	70.0±2.0	72.8±1.5	66.1±1.0	67.5±1.3	68.3±1.1	53.6±1.0	56.1±0.2	56.1±1.2	56.16±1.25
6	78.6±1.0	76.8±1.5	79.8±1.6	70.3±0.5	72.0±1.3	73.6±0.5	62.5±0.8	64.6±0.2	63.6±0.5	63.50±1.80
7	83.6±0.7	82.5±1.0	84.8±0.2	78.0±0.5	78.8±0.7	79.6±0.7	69.3±0.5	76.3±0.5	75.3±0.5	77.16±2.02
8	88.3±1.2	87.1±1.0	89.5±1.3	85.1±0.7	85.3±0.5	86.3±0.2	75.8±0.7	83.0±0.5	82.1±0.2	83.00±1.32
9	90.8±0.7	89.6±0.5	92.0±1.3	90.3±1.0	92.3±1.5	90.0±0.8	82.1±0.2	89.8±0.2	90.1±0.2	89.66±0.76
10	91.6±0.5	90.5±0.5	92.3±1.1	92.3±1.1	93.8±1.0	92.6±0.5	88.1±0.5	84.3±0.5	93.8±0.2	93.66±0.57
11	92.3±0.7	91.1±0.7	92.3±0.7	94.6±1.5	95.6±1.5	93.3±0.5	94.8±1.2	96.1±0.2	95.1±0.7	97.16±0.76
12	92.3±0.7	91.8±0.7	92.8±1.1	95.1±0.7	96.1±0.7	94.0±1.7	96.8±0.7	98.1±1.0	95.5±0.5	98.16±0.28

Table No.5: % Cumulative drug release of all the tablet formulation

Time (hr)	% Cumulative Drug release (Mean±SD) n=3									
	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
0	0	0	0	0	0	0	0	0	0	0
1	28.7±0.9	25.4±1.2	28.0±1.4	26.2±1.3	26.4±2.5	25.7±0.8	24.3±0.7	24.7±0.8	22.5±0.9	18.43±0.66
2	38.7±1.2	37.0±1.3	37.1±1.8	36.9±1.6	38.4±1.2	37.1±1.1	32.8±0.4	32.9±0.5	29.2±0.5	28.77±0.80
3	54.5±0.6	49.0±1.2	46.2±1.5	50.4±1.0	47.0±2.5	44.7±1.3	40.4±0.6	39.9±0.5	36.0±0.5	40.40±0.67
4	62.3±1.1	56.1±1.8	57.7±0.4	57.7±0.9	53.5±2.4	52.4±1.2	49.5±1.0	45.7±0.4	41.6±0.8	54.74±0.96
5	67.7±0.5	62.1±1.8	65.6±0.9	66.8±2.7	63.9±1.9	57.7±0.7	57.0±0.4	53.0±0.4	48.0±0.6	64.13±0.82
6	75.5±1.0	67.3±1.3	72.9±1.1	75.4±2.5	72.2±2.3	65.4±0.5	63.2±1.0	61.5±0.8	57.1±0.6	73.75±0.68
7	77.5±1.4	75.1±1.5	77.3±1.2	81.3±2.3	79.7±1.9	70.8±0.6	68.7±0.5	68.2±0.4	63.7±0.4	83.33±1.3
8	------	79.1±0.9	80.1±1.4	86.5±2.5	85.6±1.5	76.3±0.8	75.2±0.5	76.4±1.1	71.6±0.8	87.84±0.57
9	-------	------	------	90.3±2.4	90.7±1.3	83.7±0.8	82.0±0.3	82.8±0.8	77.8±0.6	91.76±1.09
10	------	------	------	------	93.5±1.5	86.8±1.5	88.3±1.1	89.5±0.4	84.9±0.4	95.34±0.73
11	------	------	------	------	97.6±0.9	94.4±1.4	94.2±0.2	96.4±0.4	91.1±0.4	98.41±0.59
12	-------	------	------	------	------	-------	95.9±0.6	97.7±0.4	95.2±0.5	98.86±0.44

Figures

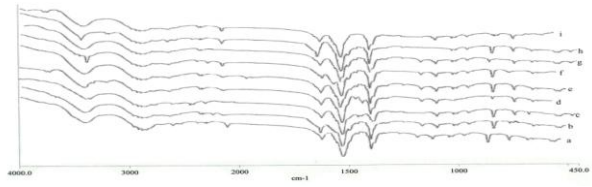

Figure No.1: Overlap FTIR spectra of drug and excipients. Were (a) Baclofen; (b) Baclofen + HPMC K100M; (c) Baclofen + Carboxymethyl-Tamarind; (d) Baclofen + Sodium Bicarbonate; (e) Baclofen + Microcrystalline Cellulose; (f) Baclofen + Magnesium Stearate; (g) Baclofen + Talc; (h) Baclofen + PVP K30; (i) Final Formulation.

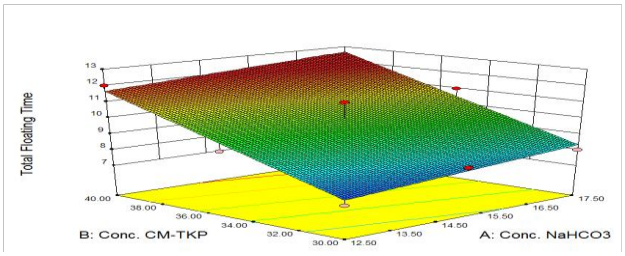

Figure No.2: 3-D Plot of Effect of $NaHCO_3$ and CM-TKP on Y_1

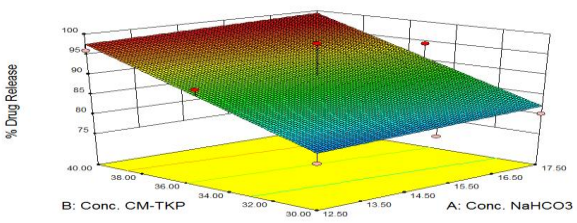

Figure No.3: 3–D plot of Effect of $NaHCO_3$ and CM-TKP on Y_2

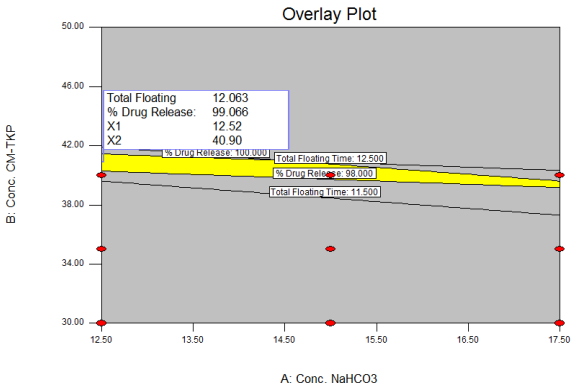

Figure No.4: Overlay Plot of Effect of $NaHCO_3$ and CM-TKP on Total Floating Time and % Drug Release

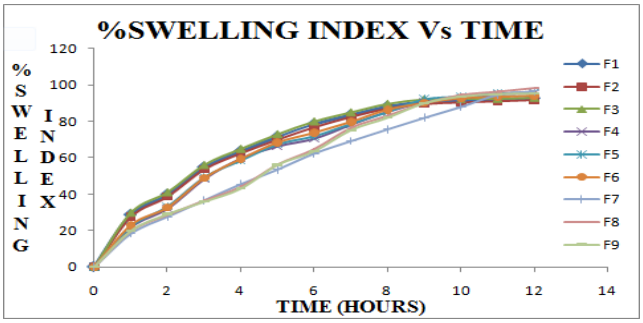

Figure No.5: %swelling index of different batch (f1 to f9)

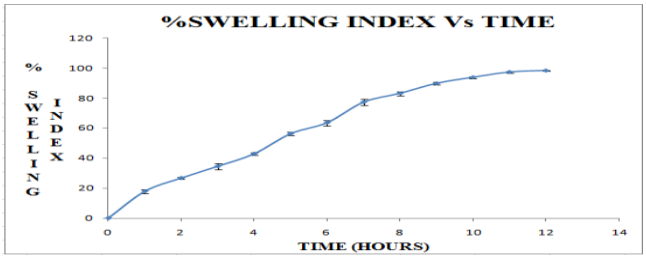

Figure No.6: %swelling index of optimized batch (f10)

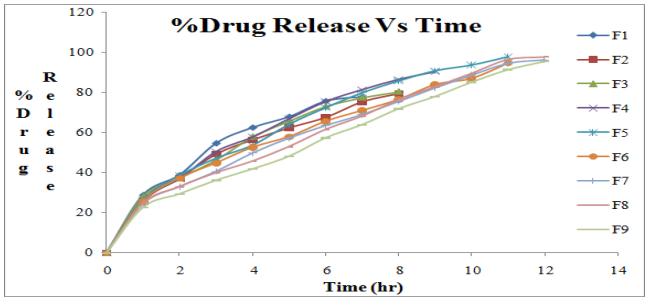

Figure No.7: %Drug release of different batch (f1 to f9)

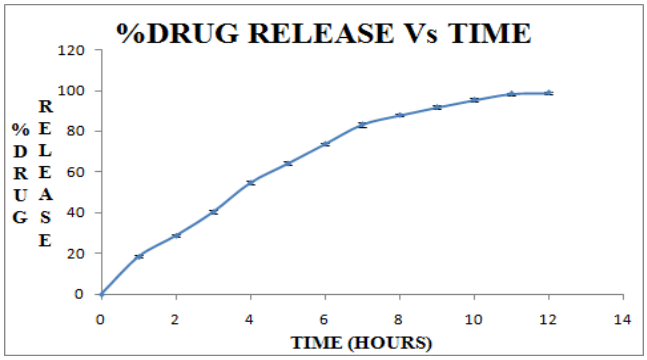

Figure No.8: %Drug release of optimized batch (f10)