Formulation of Gastroretentive Floating Tablet Using Cross-linked Sterculia foetida gum

[1]L.P. Kothari*, [2]A.S. Mundada

Shriman Sureshdada Jain College of Pharmacy, Neminagar,
Chandwad, Dist-Nasik, INDIA.

Abstract: Semi synthetic or Natural materials have been gaining lot of interest in the field of drug delivery as they are readily available, cost effective, eco-friendly and compatible due to their natural origin. The purpose of the present research was to develop gastroretentive floating tablets of Diltiazem hydrochloride using modified Sterculia foetida gum. Physicochemical characterization like Viscosity, pH, X-ray diffraction of modified SFG was done. A 3^2 full factorial design (nine runs) was utilized to optimize the formulation wherein the concentration of modified SFG (X1) and concentration of effervescent agent(X2) were taken as independent variables and Cumulative % drug release upto 12hr (Y1) and buoyancy lag time (BLT) (Y2) were taken as dependant variables. The quantitative, as well as qualitative influence of factor on the response, was thoroughly investigated using Design Expert® software (version 13; Stat-Ease, Inc., Minneapolis, MN, USA).. Software generated polynomial equations were utilized to understand the significant interaction among the factors and responses. The Optimized formulations of the tablets were compared with the tablets prepared with natural SFG. The results revealed that, the modified SFG gum has higher drug release retarding capacity than that of natural SFG. The FTIR results indicated that there were no interactions of modified SFG with Diltiazem hydrochloride. It can be concluded from the outcome of the present investigation that modified SFG has good potentials for formulating gastroretentive floating drug delivery system.

Keywords: Sterculia foetida gum (SFG), floating drug delivery system (FDDS), Diltiazem hydrochloride (DH), Buoyancy lag time (BLT), full factorial design etc.

INTRODUCTION

The floating drug delivery system (FDDS) or hydrodynamically balanced system was first described by Davis [(1)]. It is possible to prolong the gastric residence time (GRT) of drugs using this system. Other approaches to prolong GRT include swelling, bioadhesive, altered density, and magnetic and extendable or expandable hydrogel systems [(1)]. FDDS float as their bulk density is lower than the gastric contents or due to the gaseous phase formed inside the system in the gastric environment [(2).] They remain buoyant in the stomach for a prolonged period of time without affecting the gastric emptying rate of other contents. A floating dosage form is useful for those drugs that act locally in the upper parts of gastrointestinal tract (GIT), or are poorly absorbed in the intestine[(2).].

Hydrophilic polymers are widely used in the formulation of floating oral dosage forms. Their convenience and ease of manufacture cut down the cost of the final product. Besides, hydrophilic polymer matrix system offers several additional advantages over other technologies for floating drug delivery system [(4, 5)]. The mechanism of, and the influence of various technological and formulation variables on, the drug release from hydrophilic systems have been well studied and reviewed by many authors [(3-5)]. Large number of natural and synthetic polymers single or in combinations, have been listed as hydrophilic matrix excipients till date. Natural gums (like Xanthan gum, guar gum) have also been examined as matrices for the floating sustained drug release [(6, 7)].

Natural gums or Semi synthetic are often preferred over synthetic materials due to their non-toxicity, low-cost and easy availability. It is the usual balance of economics and performance that determines the commercial realities [(8)]. Sterculia foetida gum (SFG) seems to be an interesting polymer for preparation of hydrophilic tablets. Sterculia gum is expected to retard drug release due to its higher swelling index [(9).]

The goal of the present research work was to prepare floating tablet of diltiazem hydrochloride (DH) using modified SFG. DH is a calcium channel blocker used as an antihypertensive as well as anti-anginal was selected as the model drug for the present study. It has short biological half-life of around 3.5 h and has an absorption window in upper part of GIT [(10, 11)]. A 3^2 factorial design was employed to investigate the effect of two independent variables (factors), *i.e.* concentration of modified SFG and concentration of effervescent agent, on drug release after 12h and BLT.

MATERIALS AND METHODS

Materials

DH was received as a gift sample from Wockhardt Limited, Aurangabad and Sterculia foetida gum (SFG) was received as a gift samples from Medicinal natural products research laboratory, University Institute of Chemical Technology, Mumbai, India, All other chemicals were of analytical grade and purchased from local vendor.

Methods

Synthesis of Modified Sterculia foetida Gum

Sterculia foetida gum was cross-linked with tri-sodium tri-metaphosphate (STMP) as follows: STMP (1g) was dissolved in 50ml of 0.1N NaOH in a 200ml beaker with 1g of SFG in a 50ml of water then added slowly with stirring. The reaction mixture was stirred for 2h, poured into each of 5 petridish (20ml each) & dried at 60^0c for 24 h.The dried complex(modified gum) was powdered, passed through a 60u aperture sieve & used for formulation of tablets[(12).]

Drug-Excipients Compatibility Study

The drug-excipients interaction study was conducted using FTIR spectrophotometer (Jasco IR spectrophotometer, Model: 4100). The IR spectrum of pure DH, SFG, modified SFG and physical mixture of DH: SFG were recorded using KBR pellet method [13].

Characterization of Modified SFG

Initially modified SFG was passed through 160# and used subsequently for characterization studies. Solubility of SFG in water and alcohol was determined. 1 g of modified SFG was dissolved in various amounts of water for solubility determination and for viscosity determination 1% solution was prepared by dissolving 1 g of modified SFG in 99 g of water and pH of the solution was also noted [9,13].

Preparation of Tablets

The granules were prepared by wet granulation method as per formulae given in the Table 1. The drug Diltiazem hydrochloride, modified polymer, effervescent agent sodium bicarbonate and lactose, were passed through sieve 40# separately and blended thoroughly. After proper mixing then slowly adds the binding solution containing PVP K-30 in IPA till fine uniform granules were obtained. The wet mass was passed through sieve 16# and dried at 50°C for 30 minutes to get the moisture content less than one. Then lubricate the dried granules with magnesium stearate which were already passed through sieve 40#. Then lubricated granules were compressed using a karnavati rotary tablet press using 10-mm biconvex punch [14].

TABLE 1: COMPOSITION OF BATCHES F1- F9

INGREDIENTS	F1	F2	F3	F4	F5	F6	F7	F8	F9
DH	15	15	15	15	15	15	15	15	15
Modified Gum	30	30	30	40	40	40	50	50	50
$NaHCO_3$	10	12.5	15	10	12.5	15	10	12.5	15
Lactose	35	32.5	30	25	22.5	20	15	12.5	10
PVP K-30	8	8	8	8	8	8	8	8	8
Magnesium Stearate	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
Talc	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
Total % (W/W)	100	100	100	100	100	100	100	100	100

***In Vitro* Buoyancy Studies**

The *in vitro* buoyancy was determined by floating lag time, duration of buoyancy as per the method described by Rosa *et al.* [16]. The tablets were placed in a 100 mL beaker containing 0.1N HCl. The time required for the tablet to rise to the surface and float was determined as floating lag time.

***In Vitro* Drug Release Studies**

The *in vitro* drug release studies were conducted using USP type II apparatus (TDT-08 L, Electro lab, Mumbai, India). The dissolution media used was 900 mL of 0.1 N Hydrochloric acid (pH 1.2) kept at 37.0 ± 0.5 ^{0}C and 100 rpm. An aliquot of 5 mL sample was withdrawn and replenished with fresh dissolution medium at various time intervals. The contents of DH in sample were determined by measuring absorbance at 237.5 nm in a UV-Visible spectrophotometer (Jasco UV-630). The dissolution data so obtained was then treated using different kinetic models to understand the mechanism of the drug release [17]. The release study was performed in triplicate.

Full Factorial Design

A 3^2 randomized full factorial design was used in this study. In this design two factors, the Concentration of modified gum (X_1) and Concentration of effervescent agent (sodium bicarbonate) (X_2) were selected as independent variables, each at 3 levels and experimental trials were performed at all 9 possible combination. The buoyancy lag time and drug release after 12h were selected as dependent variables. All data of optimization study is compiled into Design Expert® software (Design Expert trial version 13) to get one desirable formulation [18- 20]. Table 2 summarizes dependent and independent variables and the resultant formulations are listed in table 3.

TABLE 2: EXPERIMENTAL DESIGN: FACTORS AND RESPONSES

Factors (independent variables)	Levels used			Responses (dependent variables)
	-1	0	1	
X1. Concentration of Modified Sterculia foetida gum (% w/w)	30	40	50	Y1= Buoyancy lag time(BLT)
X2. Concentration of effervescent agent (% w/w)	10	12.5	15	Y2= Q_{12} (% of drug releases upto 12h)

TABLE 3: COMPOSITION OF EXPERIMENTAL FORMULATIONS (RUNS)

Batch No.	Concentration of modified Sterculia foetida gum (%w/w)	Concentration of sodium bicarbonate (%w/w)
F1	30	10
F2	30	12.5
F3	30	15
F4	40	10
F5	40	12.5
F6	40	15
F7	50	10
F8	50	12.5
F9	50	15

Water uptake studies

The percentage of water uptake of Gastroretentive floating tablet was determined by placing a tablet in a USP dissolution test apparatus (basket assembly). (900 mL of 0.1N HCL, maintained at 37 ± 0.5 °C and 50 rpm). At predetermined time points, the tablets were removed from the dissolution medium, carefully blotted with tissue paper to remove surface water, weighed and then placed back in the medium and was done so till tablet ruptured. The percentage of water uptake was calculated as follows:

$$\% \text{ Water uptake} = \frac{(Wt - W_0) \times 100}{W_0}$$

Where, Wt is the weight of a wet tablet at a time point and W_0 is the weight of a dry tablet [21].

Comparative studies

Optimized final batch was decided using Design Expert® software. Formulation F6 containing modified 40% of SFG (X_1) and 20 % Sodium bicarbonate (X_2) was selected based on the results from the Design Expert® software for further comparative study with natural polymers SFG.The batches were prepared as shown in formulation Table 4.

TABLE 4: COMPOSITION OF COMPARATIVE BATCHES OF & NF

INGREDIENTS	OF(F6)	NF
Diltiazem hydrochloride	**15**	**15**
Modified SFG	40	-
SFG	-	40
Sodium bicarbonate	20	20
PVP K-30	8	8
Lactose	10	10
Magnesium stearate	1.5	1.5
Talc	0.5	0.5
Total % (W/W)	**100**	**100**

Stability Study

Tablets were packed in aluminium foil and placed in the stability chamber at 40 ^{0}C and 75% RH for a period of 4 weeks. At the end of 4 weeks *in-vitro* drug release study and *in-vitro* floating behavior were performed [22].

RESULTS

Drug Excipients Compatibility Study:

The IR spectrum of the pure DH, SFG, Modified SFG and physical mixture was recorded to check the possible Drug-Excipients interaction. Pure SFG are associated with 0H group & COO^{-} groups of oleic acid residue. In modified SFG, OH group has been disappears & appearance of new peaks which are absent in Sterculia gum are ascribe to phosphate-I(-C=O Stretching) & phosphate-II(-C-0 bending) of the phosphate group of STMP confirms cross linking reaction. The FTIR Spectra of drug as well as formulation shows characteristics peak of both shows no interaction between drug & excipients.

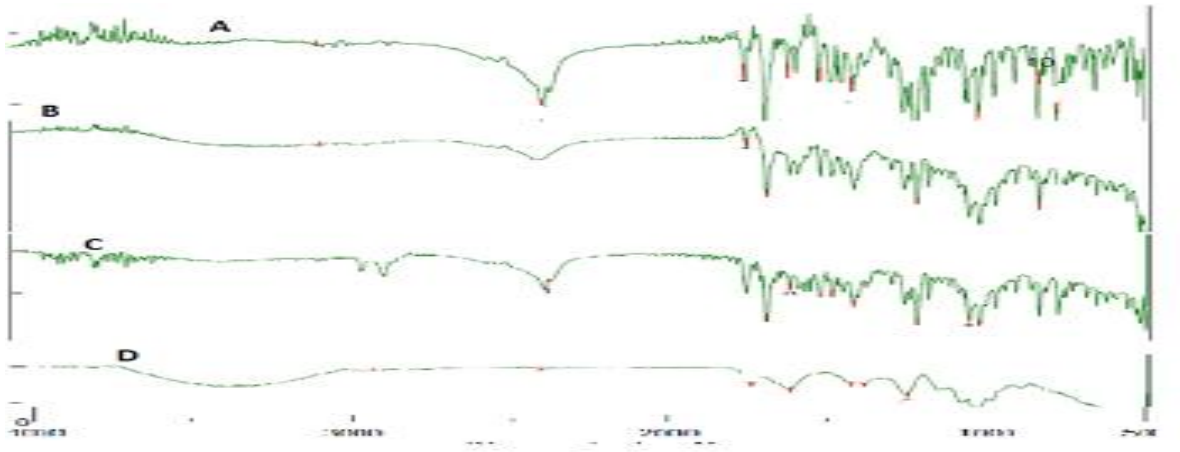

Fig 1: FT-IR spectra of A)Pure drug B) Unmodified Sterculia foetida gum C)Modified Sterculia foetida gum D) Optimized formulation.

Characterization of modified SFG

Modified SFG is sparingly soluble in water and it dissolves with hydration. It is practically insoluble in absolute ethanol. The viscosity of 1% SFG was found to be 950 centipoises and pH in range of 4–5.

Evaluation Parameters of Factorial Design Batches

The result reveal that the all the evaluation parameters were within the limits as per IP.

Results shown in table5:

Table 5: Evaluation data for floating tablets for formulations F1-F9

All values are expressed is mean ± SD, n=3

PARAMETERS	F1	F2	F3	F4	F5	F6	F7	F8	F9
Tablet weight (mg)	600±5	600±5	600±5	600±5	600±5	600±5	600±5	600±5	600±5
Hardness (Kg/cm^2)	5.5±0.46	5.7±0.53	6.0±0.32	5.5±0.89	5.8±0.32	6.0±0.42	5.5±0.62	5.8±0.23	6.0±0.62
Friability (%)	0.35	0.36	0.33	0.31	0.31	0.43	0.48	0.51	0.66
Thickness (mm)	6.02	6.01	6.04	6.06	6.03	6.01	6.04	6.02	6.06
Diameter (mm)	10±0.1	10±0.1	10±0.1	10±0.1	10±0.1	10±0.1	10±0.1	10±0.1	10±0.1
Drug content uniformity (%)	97.51	97.93	98.57	98.67	99.92	99.88	97.88	100.22	97.19
BLT(Seconds)	66	43	29	82	71	55	127	103	89
Duration of buoyancy (h)	8	8	8	12	12	12	12	12	12

***In- Vitro* Buoyancy of Factorial Design Batches**

The result of *in vitro* buoyancy study of optimized batch F6 shown in Figure 3 & 4. The figure clearly indicates that the floating lag time (1 min) of modified SFG tablets and the floating and swelling tendency of the formulation. The *in vitro* buoyancy study was also conducted at an elevated pH condition (~4.5). The floating tendency remained unaltered at higher pH.

Figure 2: Picture representation of tablet floating behavior for floating tablet at various time intervals

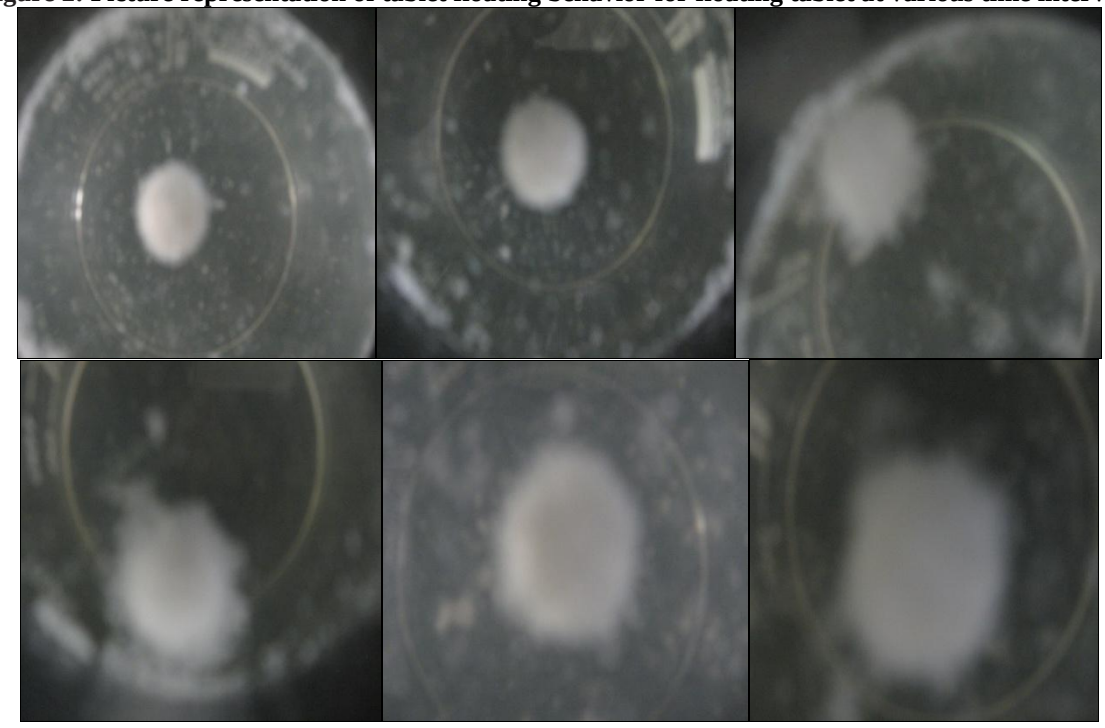

Figure 3: Picture representation of tablet swelling ability for floating tablet at various time intervals

Factorial design

A 3^2 full factorial design was constructed to study the effect of the concentration of modified SFG (X_1) and effervescent agent (X_2) on the drug release as well as buoyancy lag time for the tablets. The two dependent variables chosen were selected i.e. drug release upto 12hr (Q_{12}) and buoyancy lag time(BLT).The results were compiled in Table 5**.**

TABLE 5: LAYOUT OF DESIGN ACTUAL

STD	*RUN*	*FACTOR 1* **A: CONCENTRATION OF MODIFIED GUM**	*FACTOR 2* **B: CONCENTRATION OF EFFERVESCENT AGENT**	*RESPONSE1 BLT SECONDS*	*RESPONSE2 % CUMULATIVE DRUG RELAEASE UPTO 12HR*
8	1	40	15	55	98.77
2	2	40	10	82	96.66
6	3	50	12.5	103	79.7
7	4	30	15	29	
4	5	30	12.5	43	
1	6	30	10	66	
9	7	50	15	89	82.4
5	8	40	12.5	71	97.71
3	9	50	10	123	77.3

Response surface methodology (RSM) is a widely practiced approach in the development and optimization of drug delivery devices. Based on the principle of design of experiments (DoE), the methodology encompasses the use of various types of experimental designs, generation of polynomial equations, and mapping of the response over the experimental domain to determine the optimum formulation(s). The technique requires minimum experimentation and time, thus proving to be far more effective and cost-effective than the conventional methods of formulating dosage forms.

Various computations for the current optimization study were performed using Design Expert® software (Design Expert trial version 13; State-Ease Inc., Minneapolis, MN, USA). A two-factor three-level full factorial design was used for systemic study of modified (SFG) and gas generating agent (sodium bicarbonate). A 3^2 full factorial design was constructed where the concentration of modified SFG (X1) and concentration of effervescent agent (X2) were selected as the independent variables i.e. factors. The levels of these factors were selected on the basis of initial studies and observations. All the other formulation aspects and processing variables were kept invariant throughout the study period. Polynomial models including interaction and linear terms were generated for the entire response variable.

Using multiple linear regression analysis (MLRA) approach. The general form of the MLRA model is represented in the Equation

$$Y = b_0 + b_1X_1 + b_2X_2 \text{ ---------- (1)}$$

Where Y is the dependent variable; b_0 is the arithmetic average of all the quantitative outcomes of nine runs.b_1, b_2, b_{12} are the estimated coefficients computed from the observed experimental response values of Y and X_1 and X_2 are the coded levels of the independent variables. The interaction term (X_1X_2) shows how the response values change when two factors are simultaneously changed. The polynomial terms (X_1^2, X_2^2) are included to investigate nonlinearity.

The polynomial equations can be used to draw conclusion after considering the magnitude coefficient and the mathematical sign that the coefficient carries. A high positive or negative value in the equation represent that by making a minor change in the setting of that factor one may obtain a significant change in the dependent variable.

Statistical validity of the polynomials was established on the basis of analysis of variance (ANOVA) provision in the Design Expert software. Level of significance was considered at $p < 0.05$. The best-fitting mathematical model was selected based on the comparison of several statistical parameters, including the coefficient of variation (CV), the multiple correlation coefficient(R^2), the adjusted multiple correlation coefficient (adjusted R^2), and the predicted residual sum of squares (PRESS), provided by the software. PRESS indicates how well the model fits the data, and for the chosen model, it should be small relative to the other models under consideration. The 3-D response surface graphs and the 2-D contour plots were also generated by the Design Expert® software. These plots are very useful to see interaction effects of the factors on responses.

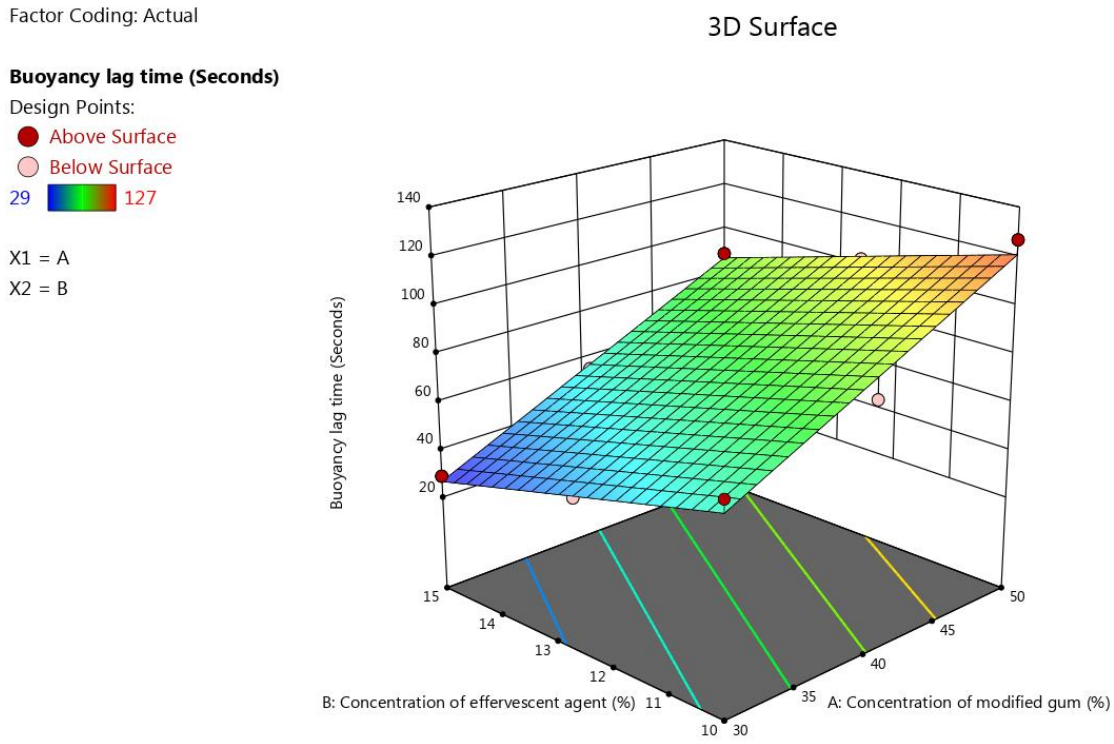

Figure 4: 3D response curve of BLT for GRDDS Floating system

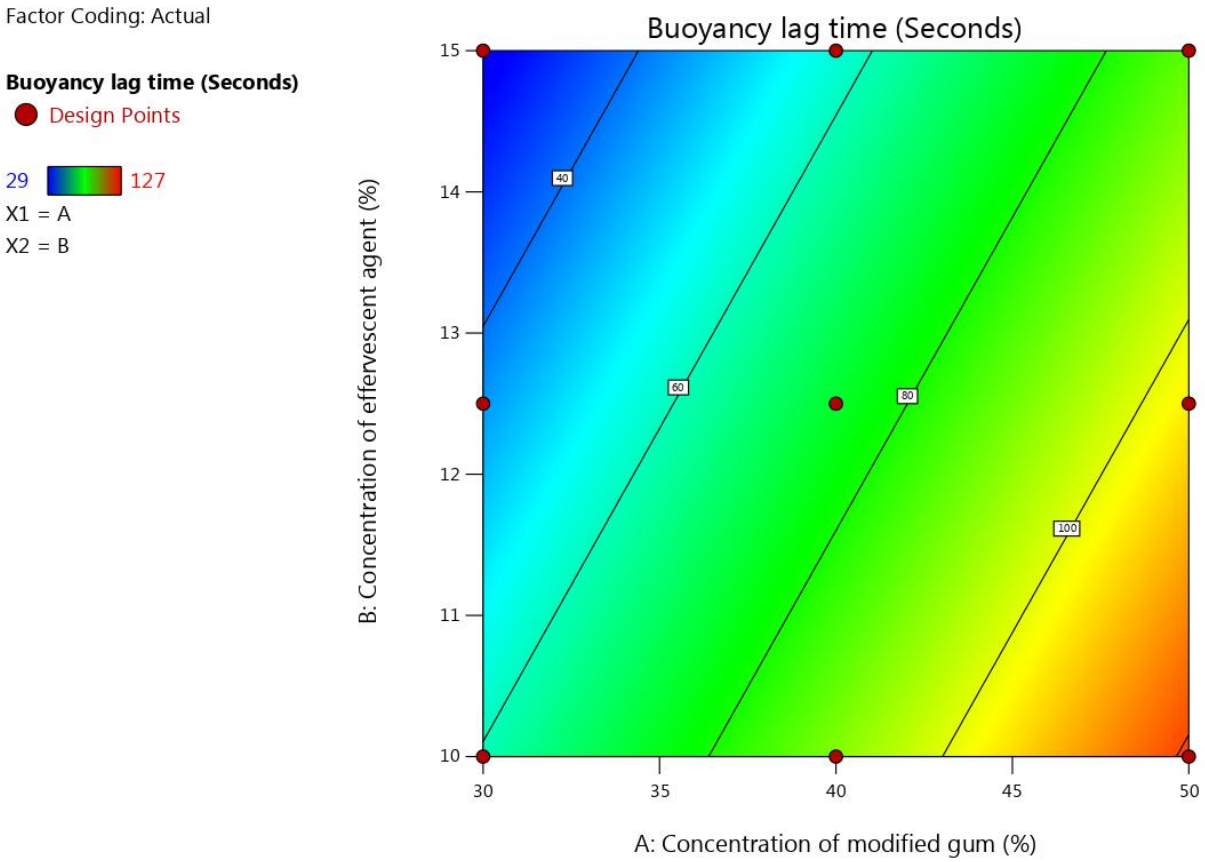

Figure 5: Contour plot of BLT for GRDDS Floating system

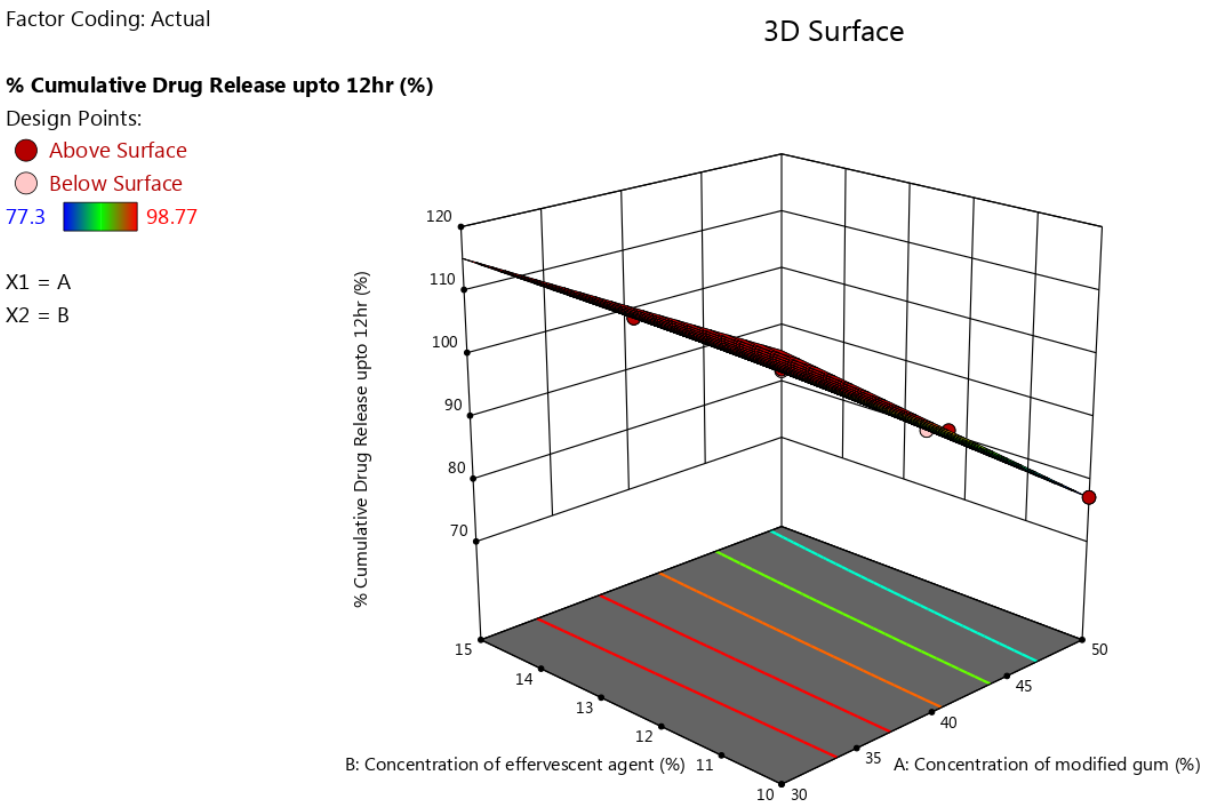

Figure 6: 3D response curve of Q_{12} for GRDDS floating system

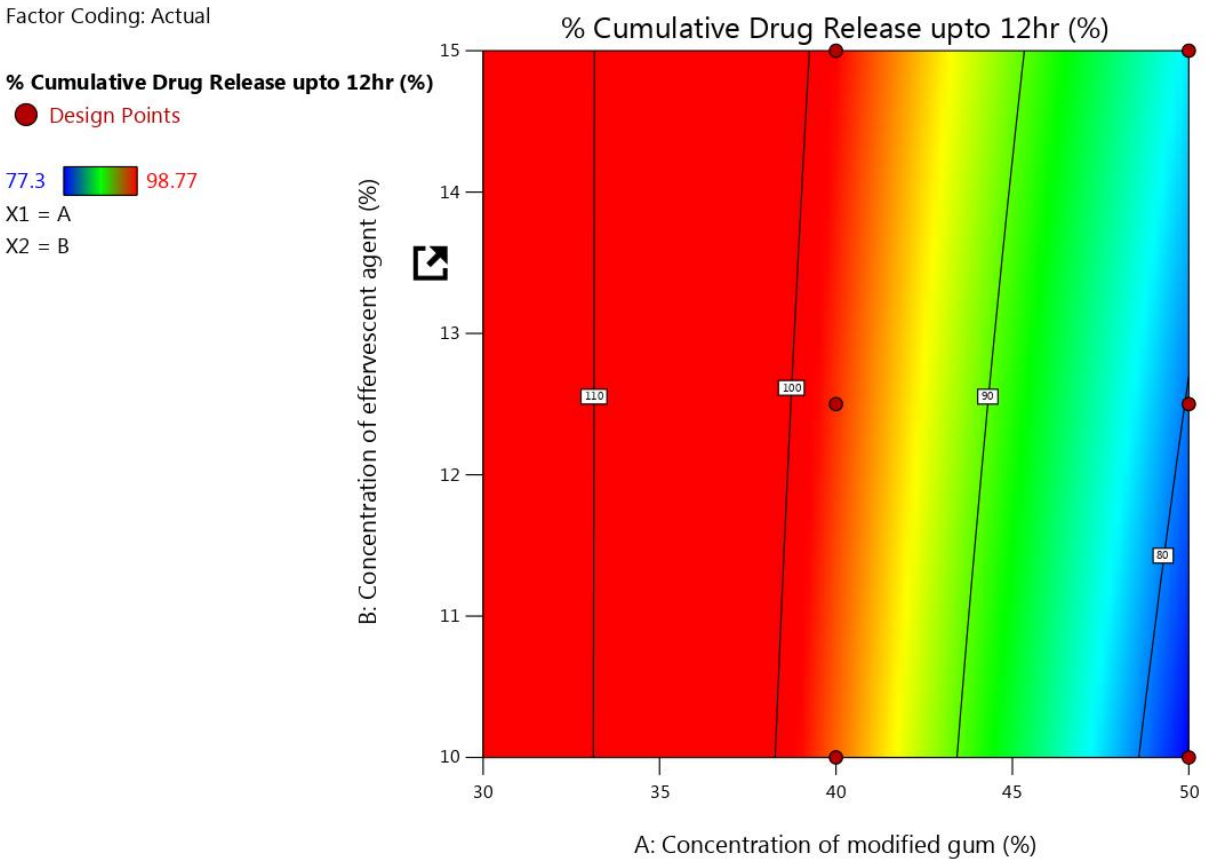

Figure 7: Contour plot of Q_{12} for GRDDS Floating system

Full and Reduced Model assessment for the dependent variables

A) Full Model for buoyancy lag time (BLT):

Full model equation

BLT =73.89+30.17A-17.00 B

Statistical validation of the polynomial equations generated by Design Expert and estimation of significance of the models was established on the basis of analysis of variance provision of the software as shown in Table 6.

TABLE 6: ANALYSIS OF VARIANCE FOR RESPONSE Y1 (BLT)

SOURCE	SUM OF SQUARES	DF	MEAN SQUARE	F VALUE	P-VALUE PROB > F	SIGNIFICANCE
Model	*770.83*	*2*	*385.42*	*730.26*	< 0.0001	*S*
A-Modified SFG	*682.67*	*1*	*682.67*	*1293.47*	< 0.0001	*S*
B-NaHCO3	*88.17*	*1*	*88.17*	*167.95*	< 0.0001	*S*
Residual	*3.17*	*6*	*0.53*			-
Cor Total	*774.00*	*8*				-

The Model F-value of 730.26 implies the model is significant. There is only a 0.01% chance that a "Model F-Value" this large could occur due to noise. Values of "Prob > F" less than 0.0500 indicate model terms are significant. In this case A, B are significant model terms. Values greater than 0.1000 indicate the model terms are not significant. If there are many insignificant model terms (not counting those required to support hierarchy), model reduction may improve your model.

It is observed from the Figure of the response curve of BLT for floating system that as the concentration of modified SFG in the formulation increases from -1 level to 0 and +1 level, the BLT of diltiazem hydrochloride tablet increases significantly. The factor modified SFG showed threefold positive increase effect on the buoyancy lag time as compared to sodium bicarbonate. The sodium bicarbonate influences negative effect on the BLT. It is observed that as the concentration of sodium bicarbonate level in the in the formulation increases from -1 to +1 level, the BLT of diltiazem hydrochloride tablet decreases significantly.

B) Full Model for Q_{12}:

Full model equation

Q_{12} =97.71-17.91A+1.05B+1.50AB

Statistical validation of the polynomial equations generated by Design Expert and estimation of significance of the models was established on the basis of analysis of variance provision of the software as shown in Table 7.

TABLE 7: ANALYSIS OF VARIANCE FOR RESPONSE Y2 (Q_8).

SOURCE	SUM OF SQUARES	DF	MEAN SQUARE	F VALUE	P-VALUE PROB > F	SIGNIFICANCE
Model	*401.44*	*2*	*202.67*	*1825.56*	< 0.0001	*s*
A-Modified SFG	*390.75*	*1*	*393.98*	*3554.06*	< 0.0001	*s*
B-NaHCO3	*10.69*	*1*	*11.36*	*97.26*	< 0.0001	*s*
Residual	*0.33*	*3*	*0.073*			
Cor Total	*401.77*	*5*				

The Model F-value of 1825.56 implies the model is significant. There is only a 0.01% chance that a "Model F-Value" this large could occur due to noise. Values of "Prob > F" less than 0.0500 indicate model terms are significant.

In this case A, B are significant model terms Values greater than 0.1000 indicate the model terms are not significant. If there are many insignificant model terms (not counting those required to support hierarchy), model reduction may improve your model.

It is observed from the figure of the response curve of Q_{12} that as the concentration of modified SFG in the formulation increases from -1 level to 0 and +1 level, the Q_{12} of Diltiazem hydrochloride tablet decreases significantly. The factor modified *SFG* showed tenfold negative effect on the drug release as compared to sodium bicarbonate. The sodium bicarbonate influences positive effect on the drug release. It is observed that as the concentration of sodium bicarbonate level in the in the formulation increases from -1 to +1 level, Q12 of DH tablet increases significantly. After analysis of both independent variables (i.e. factor) and dependant variables (i.e. response) Design Expert® software gives 2 solutions which are shown in Table 8.

Table 8: Solutions for optimized batch

NUMBER	*MODIFIED SFG*	NAHCO3	BLT	Q_{12}	DESIRABILITY
1	*40*	*15*	*56.88*	*98.76*	*1.00*

2	*43.50*	*15*	*66.69*	*93.43*	*1.00*

***n- Vitro* Buoyancy of Factorial Design Batches**

The entire factorial design batch shows good in vitro buoyancy study. The result of *in vitro* buoyancy study of optimized batch F6 shown in Figure 8. The figure clearly indicates that the floating lag time (55sec) of modified SFG tablets and the floating and swelling tendency of the formulation. The figure also indicates that the tablet remained buoyant for 12 h, but the tablet actually floated throughout the entire study. The *in vitro* buoyancy study was also conducted at an elevated pH condition (~4.5). The floating tendency remained unaltered at higher pH.

Figure 8: *In vitro* buoyancy study of Optimized batch F6.

***In Vitro* Drug release studies of Factorial Design Batches**

The results of the *in vitro* drug release studies of the factorial design batches are given in figure 8. The results in case of drug release indicate that as the concentration of modified SFG in the formulation increases the drug release of diltiazem hydrochloride tablet decreases significantly. The SFG showed tenfold negative effect on the drug release as compared to sodium bicarbonate. The sodium bicarbonate influences positive effect on the drug release. It is observed that as the concentration of sodium bicarbonate level in the in the formulation increases, the drug release of diltiazem hydrochloride tablet increases significantly.

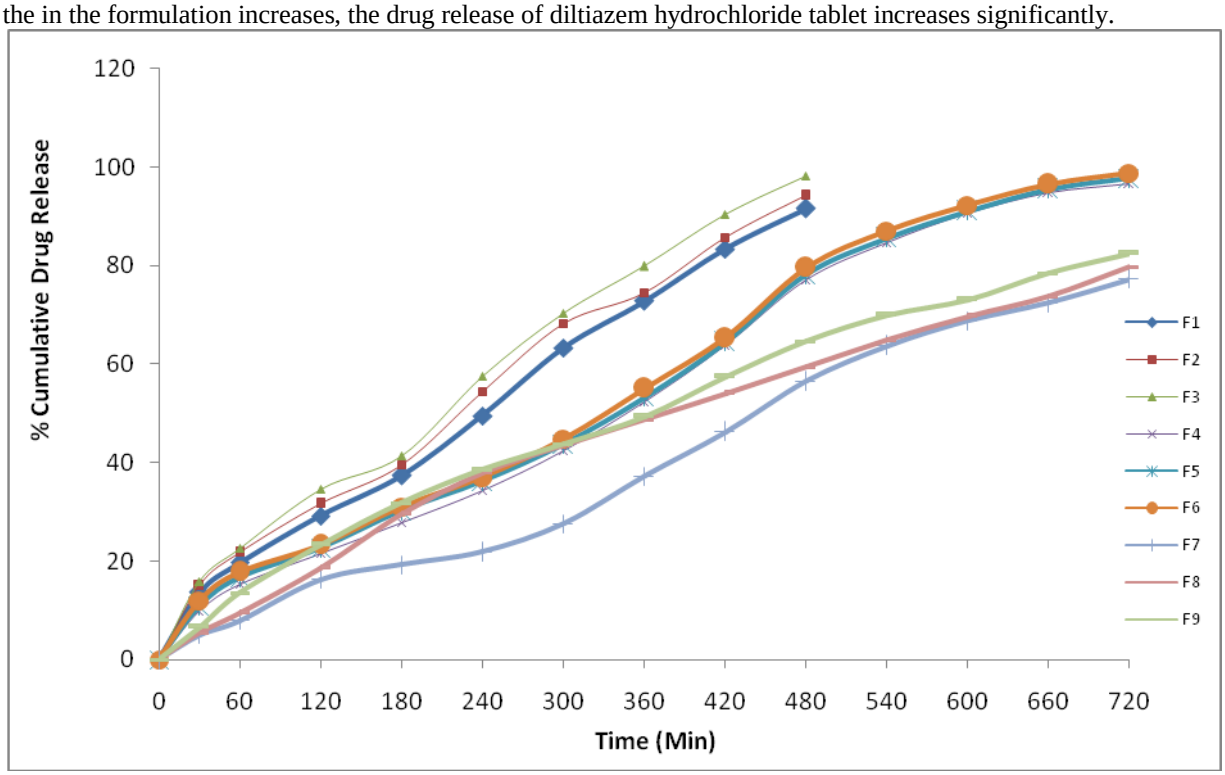

Figure 9: Dissolution profile of Optimized Batches F1 – F9

The results in case of buoyancy lag time indicate that that as the concentration of modified SFG in the formulation increases, the BLT of DH tablet increases significantly. The modified SFG showed threefold positive increase effect on the BLT as compared to sodium bicarbonate. The sodium bicarbonate reveals negative influences on the BLT. It was observed that as the concentration of sodium bicarbonate level in the formulation increases, the BLT of DH tablet decreases significantly. Dissolution data was then treated using various kinetic models and it was found that the drug release of the optimized formulations follows korsemeyer-peppas model.

Water uptake studies of optimized batches

The results of the water uptake studies are shown in figure 10. The results revealed that intially water penetration in tablets increase rapidly which results in increase in the tablets weights very rapidly, but as the time passes drug is released through the tablet an automatically there is tremendous decrease in tablets which was shown in figure 10.

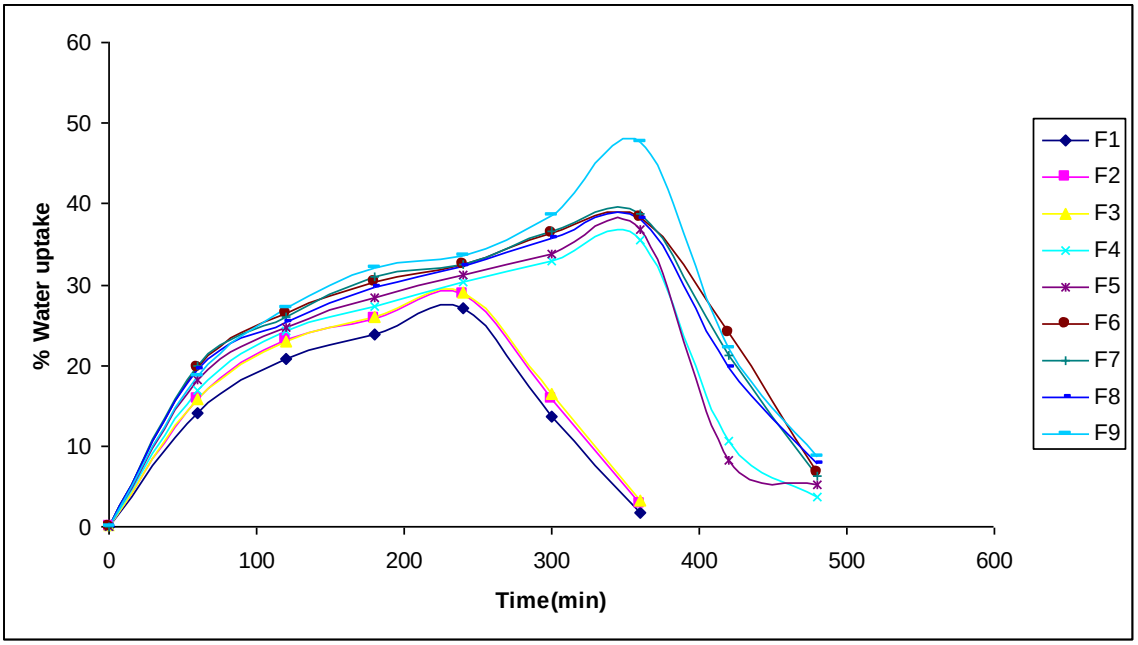

Figure 10: Water uptake study (F1-F9)

***In Vitro* Buoyancy studies of comparative batches C1-C2**

All the developed tablets showed required hardness and thickness. The result of the *in vitro* buoyancy studies of the comparative batches are given in Table 9.

Table 9: *In vitro* floating evaluation of comparative batches C1-C2

Formulations	OF(F6)	NF
Buoyancy lag time(Sec)	55	70
Duration of buoyancy(h)	12	8

The results indicated that, the tablets prepared with modified SFG shows less BLT and more duration of buoyancy as compared to the tablets prepared with Natural polymers such as SFG.

***In Vitro* Drug release study of comparative batch**

The result of *in vitro* drug release is given in figure 10. The results revealed that the floating tablets prepared with modified SFG had higher drug release retarding capacity than that of floating tablets prepared with natural polymer SFG.

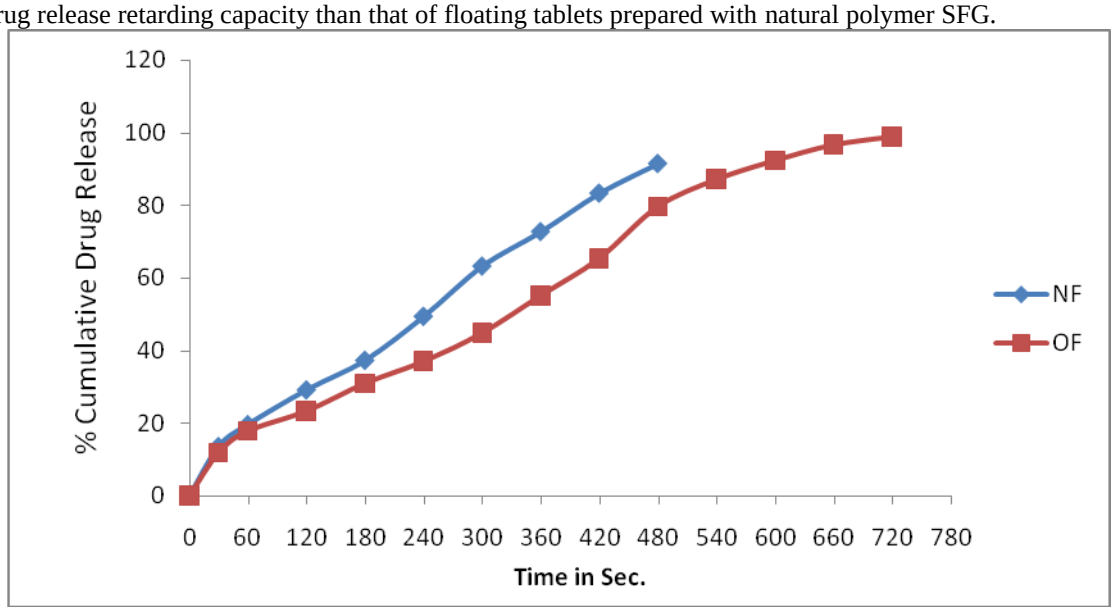

Figure 10: Dissolution profile of the batches NF(Natural gum formulation) & OF(Optimized formulation)

Stability Study

There was no significant change observed in the drug release and BLT of floating tablets of optimized batch after 4 weeks.

DISCUSSIONS

Gastroretentive floating tablets of DH using modified SFG were prepared by wet granulation method and all the tablets were found to be good without chipping, capping and sticking. The drug content was uniform in all the formulations. The low values of standard deviation indicate uniform distribution of drug within the Gastroretentive floating tablet. Infrared spectroscopic studies indicated that the drug is compatible with the polymers. As the amount of modified polymer in the tablet formulation increases, the drug release rate decreases and as the concentration of gas generating agent increases then drugs release was also found to be increased and floating lag time decreased. Tablets of DH prepared with modified SFG helpful in increasing the bioavailability of drug. Short-term stability studies of optimized formulation OF (F6) indicated that there were no significant changes in drug content and dissolution parameter values after 4 weeks of storage at 40±1 ºC. The results of comparative study revealed that the Gastroretentive floating tablets prepared with modified SFG were better in terms of the retarding drug release as well as providing proper BLT than that of natural SFG. It can be thus concluded that modified SFG has good potentials for formulating gastroretentive floating drug delivery system.

ACKNOWLEDGMENT

Authors wish to acknowledge Wockhard Lab. Ltd. (Aurangabad, India) for providing DH as a gift samples. The authors also thankful to University Institute of Chemical Technology, (Mumbai, India) for providing SFG as a gift sample. Authors wish to thank Principal, S.S.D.J. College of Pharmacy, Chandwad for providing the necessary facilities to carry out this work.

Declaration of interest: The authors report no conflicts of interest.

REFERENCES

1. Sing BN, Kim K. Floating drug delivery system: An approach to oral controlled drug delivery via gastric retention. Journal of Control Release. 2000; 63, 235-59.
2. Arora S, Ali J, Ahuja A, Khar RK, Baboota S. Floating drug delivery system: A review. AAPS Pharm SciTech.2005; 6, 47.doi.org/10.1208/pt060347
3. Bamba M, Puisienx F, Marty JP, Carstensen JT. Release mechanisms in gel forming sustained release preparation. International Journal of Pharmaceutics. 1979; 2,307–315.
4. Lapidus H, Lordi NG. Drug release from compressed hydrophilic matrices. Journal of Pharmaceutical Sciences.1968; 57, 1292–1301.
5. Buri P, Doelker E. Formulation of extended release tablets II hydrophilic matrices. Pharmaceutica Acta Helvetiae. 1980; 55,189–97.
6. Doelker E, Peppas NA. Water-swollen cellulose derivative in pharmacy. In N. A. Peppas (ed.). Hydrogels in Medicine and Pharmacy. CRS Press, Florida. 1987; 2, 115–160.
7. Taukdar MM, Vercammen JP. Evaluation of Xanthan gum as a hydrophilic matrix for controlled release dosage form preparation. Drug Development and Industrial Pharmacy. 1993; 19, 1037-46**.**
8. Smith F, Montgomery R, Hamor WA. The structure of gum exudates. In F. Smith, and R. Montgomery (eds.), The chemistry of plant gums and mucilage and some related polysaccharides. Reinhold Publishing Corporation, New York.1959; 291-293.
9. Nath B, Nath KL. Evaluation of Sterculia urens gum as novel carrier for oral colon targeted drug delivery system. Journal of Advanced Pharmaceutical Science and Technology. 2013; 1(2), 1-15.
10. Kulkarni GS, Swami S. Formulation and evaluation of sustained release floating tablets of an antihypertensive Diltiazem. International Journal of Pharmaceutical Sciences and Technology. 2017; 10(5), 3844-3852.
11. Patel AN, Patel FM, Rathore KS**.** Formulation and characterization of floating tablets of Diltiazem hydrochloride. Journal of Pharmaceutical and Biomedical Sciences. 2011; 9(9), 1-6.
12. Reddy MM, Reddy JD, Moin A, Shivakumar HG. Formulation of sustained- release matrix tablets using cross-linked karaya gum. Tropical Journal of Pharmaceutical Reasearch.2012;11(1),28-35.
13. Sharma YR. Elementary organic spectroscopy, Principles and chemical applications, 3rd ed., S. Chand and Company Limited. 2008; 211,312,321.
14. Ohara T, Kitamura A, Kitagawa T, Terada K. Dissolution mechanism of poorly water-soluble drug from extended release solid dispersion system with ethyl cellulose and hydroxyl propylmethylcellulose. International Journal of Pharmaceutics. 2005; 302:95-102.
15. Kumar R, Patil MB, Patil SR. Formulation and evaluation of effervescent floating tablets of famotidine. International Journal PharmTech Research. 2009; 1(3), 754-763.
16. Rosa M, H Zia, Rhodes T. Dosing and testing in-vitro of a bioadhesive and floating drug delivery system for oral ingestion. International Journal of Pharmaceutics. 1994;105, 65-70.
17. Korsmeyer R, Gurny R, Peppas N. Mechanisms of solute release from porous hydrophilic polymers. International Journal of Pharmaceutics. 1983; 15, 25-35. Shah NH, Asghar S, Choudhry MA, Muhammad SHA, Rehman N, Baksh S. Formulation and evaluation of natural gum-based sustained release matrix tablets of flurbiprofen using response surface methodology. Drug Development and Industrial Pharmacy. 2009; 35, 1470–8.
18. Patil SB, Sawant KK. Development, optimization and in vitro evaluation of alginate mucoadhesive microspheres of carvedilol for nasal delivery. Journal of Microencapsulation. 2008; 1–12.
19. Gohel MC, Parikh RK, Nagori SA, Jena DG. Fabrication of modified release tablet formulation of metoprolol succinate using hydroxypropyl methylcellulose and Xanthan gum. AAPS PharmSciTech. 2009; 10(1), 62-68.doi.org/10.1208%2Fs12249-008-9174-1
20. Surana SJ, Belgamwar VS. Floating bioadhesive drug delivery system using novel effervescent agents. Asian Journal of Pharmaceutics. 2009.
21. Sahoo J, Murthy PN, Biswal S, Sahoo SK. Comparative study of Propranolol hydrochloride release from matrix tablets with Kollidon® SR or Hydroxypropyl methyl cellulose. AAPS Pharm SciTech.2008; 9,577-82**.**