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DESIGN, DEVELOPMENT AND EVALUATION OF GASTRORETENTIVE FLOATING TABLETS FOR LAMIVUDINE

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ABSTRACT

OBJECTIVE: The objective of the study was development, evaluation of theLamivudine floating tablets with natural polymers

Method: Lamivudine floating tablets were developed by physical method ofcompression using Guar Gum and Xanthane gum as Natural polymers and Sodium bicarbonate. The tablet formulations are developed and assessed for physicochemical parameters, floating study, drug content, dissolution,Kinetic models and stability studies.

Results: The obtainedresultswerefollowed within the suitable limits for all formulations and among all the formulations F4 shown the good floating behaviour, better drug release. The formulation (F4) was follows Higuchi kinetics and it was more stable at various temperature conditions.

Conclusion: Lamivudine floating tablets were developed successfully by natural polymers and were stable for three months.

Keywords: Lamivudine ;floating technique,Gaurgum, Xanthan Gum andBuoyancy

INTRODUCTION

The most convenient, desired, preferable givenroute ofdrugs is oral route because of less cost involved in the production, ease of administration, compliance of patient[1-3]. This route of hadgained much popularity than the other routes of drugadministration[4-6].

In the floating technology, developed with the intention of better gastric retentiontime, specifically non-soluble drugsor notstable in intestinet so that we can enhance the bioavailability for drugs[7-10]

The drug Lamivudine is a cytidine analog that can be used as an antiretroviral agent, by blocking reverse transcriptase enzyme and control the both types-1 and type 2 HIV conditions and it alsoacts against Hepatitis B.The dose of the Lamivudine is usuallygiven in two times a day.The biological half-life of Lamivudine is 5-7 hours and it shows good absorption from the stomach [11]Because these characters, weselected the Lamivudine in this study.

MATERIALS AND METHODS

Lamivudinewas purchased from Mylon Laboratory, India. Guar gum, Sodium bicarbonate,Xanthan gum,Crospovidone, stearates, PolyVinylPyrolidine k-30 and Dicalcium phosphate were procured from S.D. Fine-Chemicals.Ltd., Mumbai, India.

Formulation development ofLamivudine floating tablets: Quantity sufficient ofDrug, excipients are taken,passed individually by using sieve no ≠ 40.Then they are subjected for mixing for 15 minutes. Then the lubricant, talcwas added to powder mass. Finally the powdered mass was compressed usingwith 10 mm punch. The composition of various formulations arementioned in table 1.

Table 1:Composition of the Lamivudine floating tablets.

Ingredients (mg)	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**	**F10**
Lamivudine	100	100	100	100	100	100	100	100	100	100
Guar gum	20	40	60	80	100	-	-	-	-	-
Xanthan gum	-	-	-	-	-	20	40	60	80	100
$NaHCO_3$	40	40	40	40	40	40	40	40	40	40
DCP	90	70	50	30	10	90	70	50	30	10
Crospovidone	30	30	30	30	30	30	30	30	30	30

Mg.Stearate	5	5	5	5	5	5	5	5	5	5
PVP K-30	15	15	15	15	15	15	15	15	15	15
Total tablet weight (mg)	300	300	300	300	300	300	300	300	300	300

Study of DSC:

The compatibility studies fordrug and other excipient were conducted using DSC and recorded thermo grams for pure drug and other recipients.

Evaluation of physicochemical properties:

The *in vitro* characterization tests were conducted on developed tablets which includes variation in weight, hardness,thickness, friability,*in vitro* floating of lag time and total floating time and stability study of the drug.

Study of weight variation: Electronic digital balancewas used to check all the twenty tablets weightsindividually and mean and deviation were calculated.

Hardness test: This test was performed to know hardness for 6 tablets with hardness testing deviceand mean and standard deviation were determined.

Thickness: Take randomly selected ten tablets and calculated the thickness of the tablets with the help of verniercalipers. Mean, SD were determined.

Friability: Take randomly selected ten tablets and weighed and placed in the friabilator. This study was conducted by using Roche friabilator.

Assay: select ten tablets randomly and made them powder by crushing. Then place 10 mg of Lamivudinepowder inl volumetric flask (100ml).To this, add 0.1N HCl and sonicated it up to 15 minutes and the final volume was makeupby0.1N HCl.,and check its absorbance of drug solution with spectrophotometer at 283 nm.

Buoyancy study: The floating behaviour was performed by putting the tablet in the beaker consisting of 0.1N HCl and note down the time taken for the raise up of tableton the top of surface was considered as FLT and how long the tablet remains floated was considered as total floating time (TFT) [12-15].

Drug release studies: Thedeveloped Lamivudine floating tablets subjected for dissolution studies byPaddle type dissolution apparatus. (900 ml buffer, Temp: 37±0.5^{o}C; 50 rpm). At definite time periods, 5 m of drug sample was collected and subjected it for analysis at 283 nm,with UVspectrophotometer.

Release kinetic analysis:

The release kinetics of drug release data was applied to different kinetic models such asfirst order, Higuchi,zero order[16] and Peppas kinetic models [17]. The best fitting one was selected based on the model exhibiting high correlation value.

Stability studies: The physical stability study performed on best formulationby placing intoadesiccators (75% RH). After 3 months, the tablets were subjected for content of drug and release studies.

RESULTS & DISCUSSION

Lamivudine solubility was performed in various media. It concludes that the drug has highest solubility in 0.1 N HCl and as pH increases, there was a decrease in solubility.

Drug-Excipient compatibility study: TheDSC studies revealed that Lamivudineexhibited a sharp peak at 177-180°C which corresponds to its M.P(Figure.1) and there was no deviations were found in this peak shape, which is obtained with drug and excipient mixture when compared to the pure drug peak (Fig.2). So this study concluded that no interaction was found in the formulation powder mixture.

***In vitro* characterization of Lamivudine floating tablets:**

The Lamivudine floating tablets are developed withphysical direct compression method by natural polymers.Allten formulations followed specificpharmacopoeial specifications.The developed floating tablets thickness was lies between 3.11mm - 3.8mm. The Friability andHardness was lies between 4.8-5.3kg/cm2 to 0.12-0.33% it denotes that tablets had proper mechanical strength and variation of the weight of developed tablets falls in prescribed standard limits. The assay of drug was followed acceptable range between 97.23-99.26% [20]. All the developed formulations were remainedfloated on the surface above 12 h (Table2& Fig 5) and all formulations were raise up to the surface within less than one minute (Table.2). The FLT (Floating lag time) of the F1-F5 formulations developed by using variousamounts of natural polymer, guar gum and equal quantity of effervescent agent[18-19], sodium bicarbonate ratio, was lies in the range of 16 to 32 sec, while F6-F10formulations developed byusing variousamounts of natural polymer, xanthan gum, was lies between27-53 sec.

Drug release studies: The release studies are conducted on all developed tablets of Lamivudinein acidic buffer. Formulationssuch as F1-F5 developed by using various quantity of Guar gum whereas formulationssuch as F6-F10developed by using various quantity of xanthan gum. Dissolution profiles for F1-F5 formulations were depicted in Figure3. The influence of concentration of Guar gum on the drug release rate was evaluated and concluded that, the guar gum amount increases, the release rate of the developed floating tablet was

decreased notanbly[20-21].F4 formulation was elected as a best and goodformulation. Dissolution profiles for F6-F10formulations developed with xanthan gum were shown in Fig.4. From this series of formulations, F9 formulation was chosen as the best and goodformulation.

The release kinetic studies were applied on the F4 formulation and it follows Higuchi model (Table 3).

Stability study:

F4 formulationelected as a bestone among all,after all studies and it was subjected for stability study for3 months period of time and after 3 months, the F4 tablets were tested for physical outward appearance, content of drug and release studies. The obtained results concluded that No considerable change was found in color of tablet, content of drug and drug release (Table 4). Hence,it was said that, F4 was stable for 90 daysperiod at various temperature conditions.

Table 2: Physical parameters of floating tablets of Lamivudine

Formulation	Weight variation (mg)	Hardness (kg/cm^2)	Thickness (mm)	Friability (%)	Drug content (%)	FLT (sec)	TFT (h)	Drug release (%)
F1	301	5.1±0.21	3.5±0.08	0.24	97.23	22 ± 1	>12	98.16
F2	302	5.3±0.11	3.7±0.18	0.33	98.32	24 ± 3	>12	97.25
F3	299	5.2±0.15	3.6±0.25	0.24	98.04	25 ± 1	>12	90.01
F4	300	5.0±0.37	3.5±0.12	0.31	99.26	16 ± 2	>12	99.93
F5	301	4.8±0.15	3.8±0.25	0.25	98.14	32 ± 3	>12	98.14
F6	303	5.2 ±0.23	3.7±0.45	0.31	98.14	43 ± 6	>12	91.15
F7	301	4.8±0.10	3.8±0.01	0.12	97.25	45 ± 4	>12	73.23
F8	302	5.1±0.22	3.1±0.03	0.15	98.52	53± 2	>12	69.51
F9	301	5.2±0.25	3.5±0.04	0.21	99.06	27 ± 3	>12	96.12
F10	302	5.20±0.28	3.7±0.08	0.25	98.16	45 ± 1	>12	85.13

Table 3: The correlation coefficient (R2) values for optimized formulation

Zero order	First order	Higuchi	Peppas
0.9721	0.8124	0.9916	0.8813

Table 4: Stability studies optimized batch

Parameters	Storage conditions		
	At 2-8°C	Room temperature	At 40°C
% Cumulative Drug Release	97.21%	98.82	95.13%
Drug Content Uniformity	98.25%	99.35%	96.24%
Color Change	No	No	No

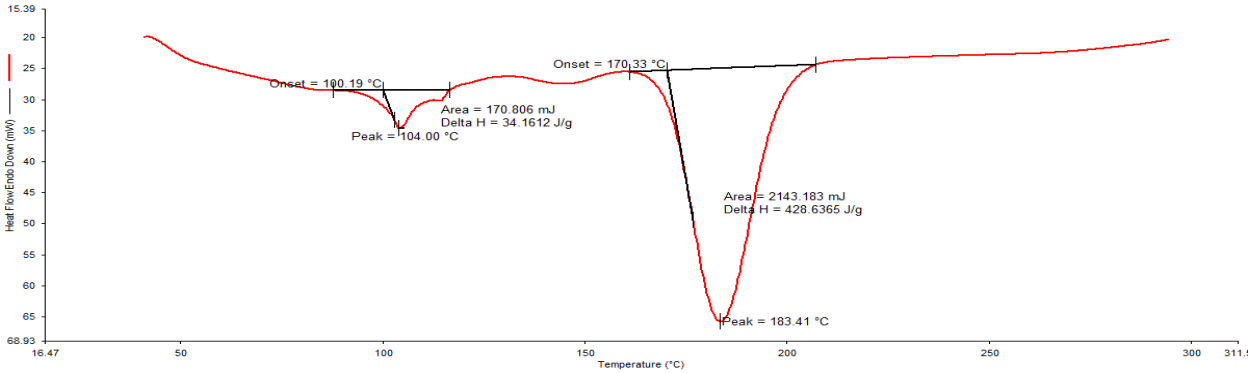

Fig 1: DSC spectra for pure drug+Excipients

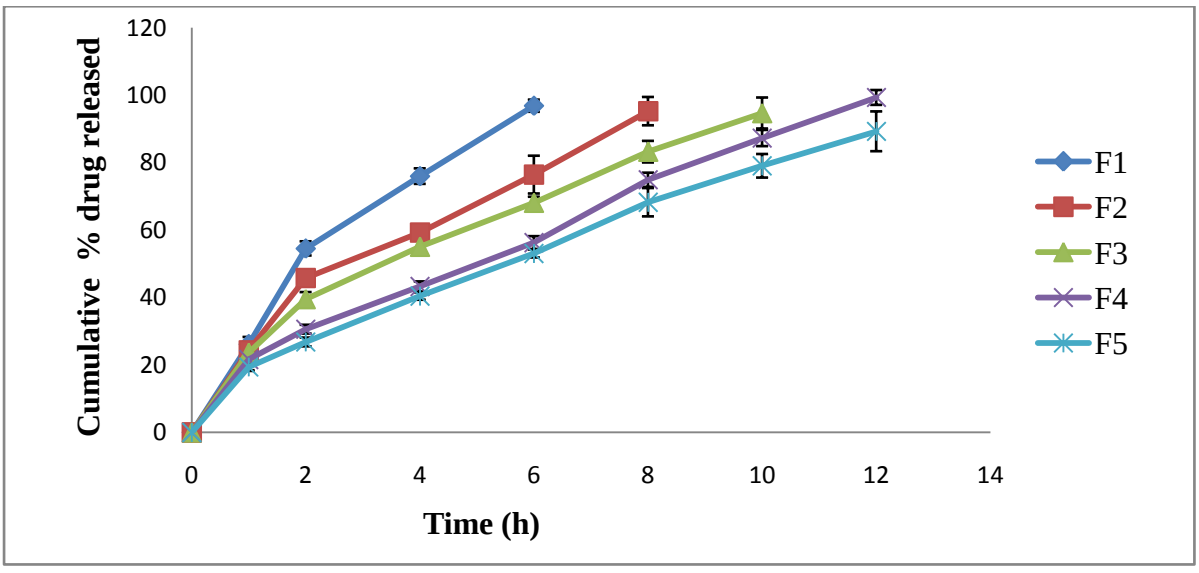

Fig 3: Drug release profiles of Lamivudine floating tablets composed of guar gum

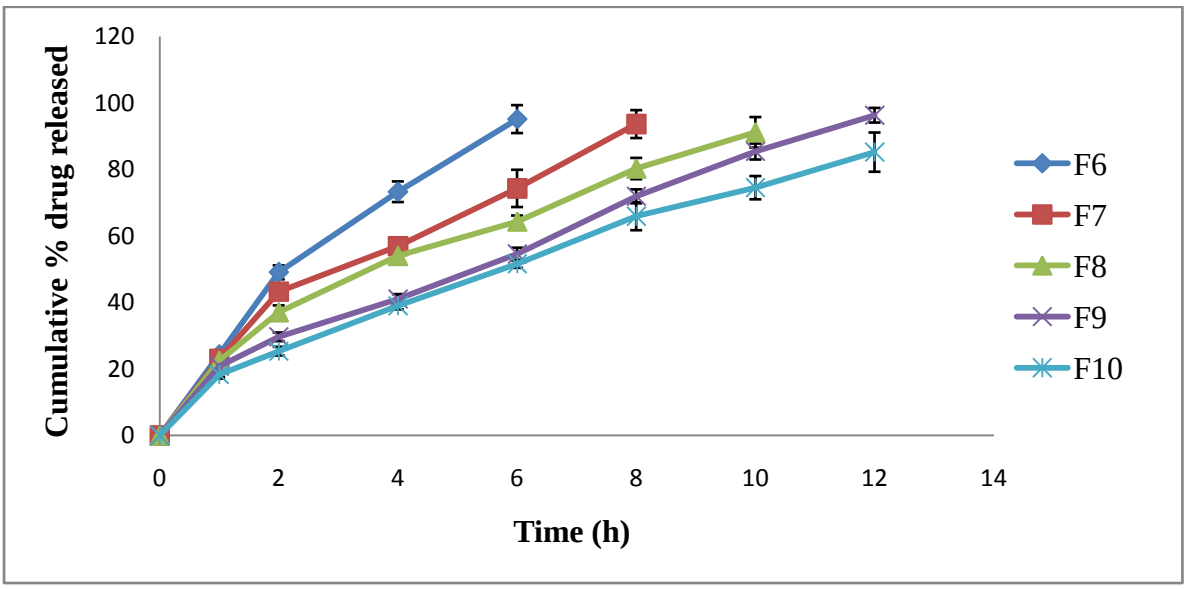

Fig 4: Drug release profiles of Lamivudine floating tablets composed of xanthan gum

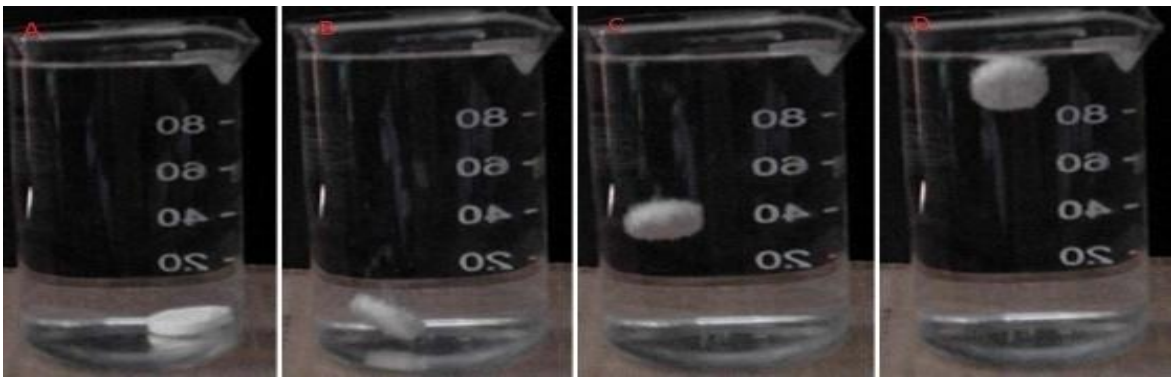

Figure 5:*In-vitro* buoyancy of Lamivudine floating tablets in 0.1N HClat 0sec, 5sec, 15sec and 12th h.

CONCLUSION

Gastro retentive Lamivudinefloating tablets are developed successfully withfloating technology. Based on several studies, F4formulation was choosen as good and optimizedformulation. The F4was considered stable for 90 days as there was no color change in outward appearance, floating properties, content of drugat 40°C/75% RH.

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CONFLICT OF INTEREST

Authors have no conflict of interest.

AUTHOR CONTRIBUTIONS

The authors are involved in working research and writing of the manuscript. The corresponding author is suggested the work and framing up the research design.

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