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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 the Lamivudine floating tablets with natural polymers

Method: Lamivudine floating tablets were developed by physical method of compression 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 obtained results were followed 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, Gaugum, Xanthan Gum and Buoyancy

[illegible]

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 for drug 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 balance was used to check all the twenty tablets weights individually and mean and deviation were calculated.

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

Thickness: Take randomly selected ten tablets and calculated the thickness of the tablets with the help of vernier calipers. 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 Lamivudine powder in volumetric flask (100ml). To this, add 0.1N HCl and sonicated it up to 15 minutes and the final volume was made up by 0.1N 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 tablet on 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: The developed Lamivudine floating tablets subjected for dissolution studies by Paddle type dissolution apparatus. (900 ml buffer, Temp: $37 \pm 0.5^\circ\text{C}$; 50 rpm). At definite time periods, 5 ml of drug sample was collected and subjected it for analysis at 283 nm, with UV spectrophotometer.

Release kinetic analysis:

The release kinetics of drug release data was applied to different kinetic models such as first 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 formulation by placing into desiccators (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: The DSC studies revealed that Lamivudine exhibited 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 with physical direct compression method by natural polymers. All ten formulations followed specific pharmacopoeial specifications. The developed floating tablets thickness was lies between 3.11mm - 3.8mm. The Friability and Hardness 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 remained floated on the surface above 12 h (Table 2 & 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 various amounts 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-F10 formulations developed by using various amounts of natural polymer, xanthan gum, was lies between 27-53 sec.

Drug release studies: The release studies are conducted on all developed tablets of Lamivudine in acidic buffer. Formulations such as F1-F5 developed by using various quantity of Guar gum whereas formulations such as F6-F10 developed by using various quantity of xanthan gum. Dissolution profiles for F1-F5 formulations were depicted in Figure 3. 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 notably[20-21].F4 formulation was elected as a best and good formulation. Dissolution profiles for F6-F10 formulations developed with xanthan gum were shown in Fig.4. From this series of formulations, F9 formulation was chosen as the best and good formulation.

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

Stability study:

F4 formulation was elected as a best one among all, after all studies and it was subjected for stability study for 3 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 days period 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	98.25%	99.35%	96.24%
Uniformity			
Color Change	No	No	No

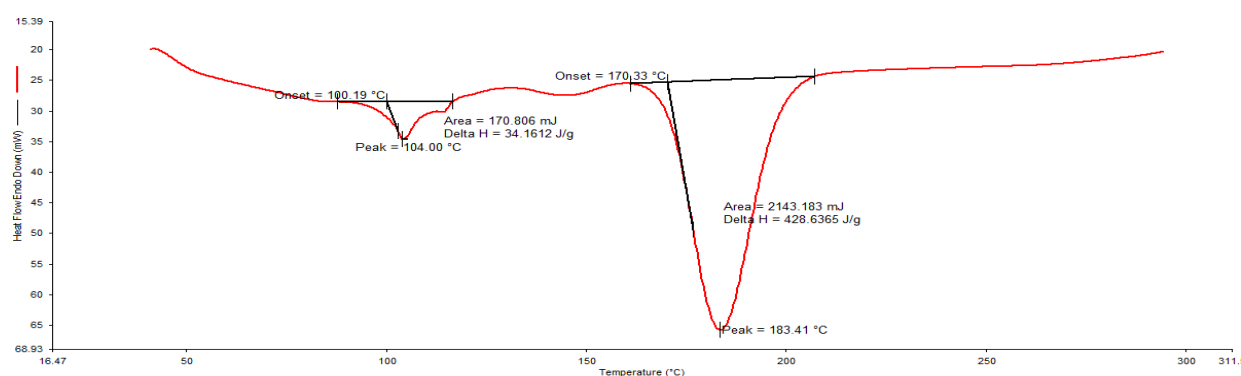


Fig 1: DSC spectra for pure drug+Excipients

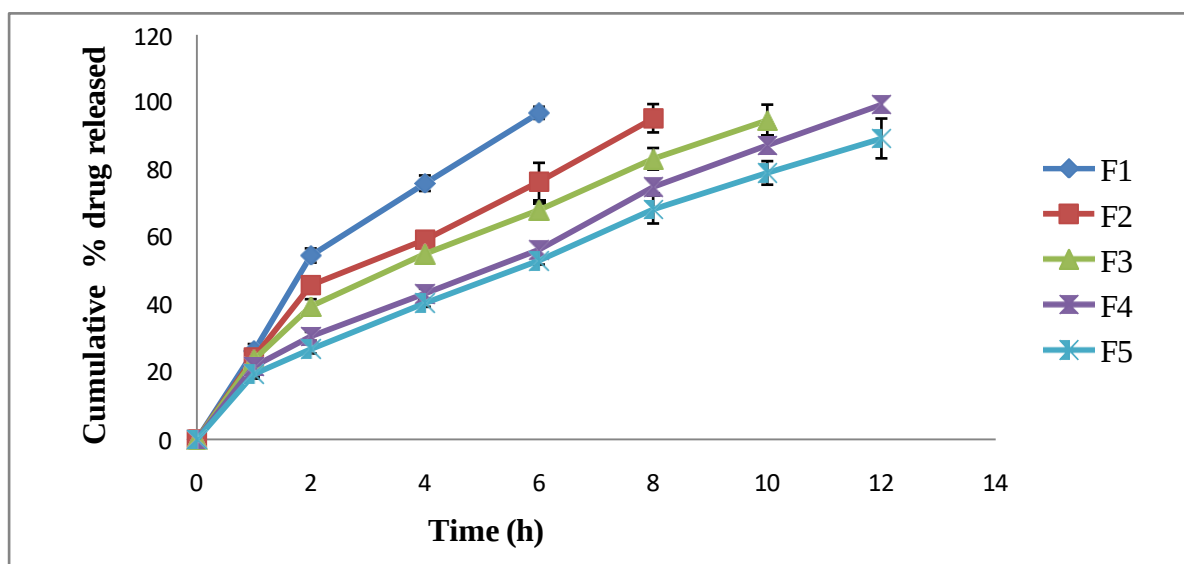


Fig 3: Drug release profiles of Lamivudine floating tablets composed of guar gum

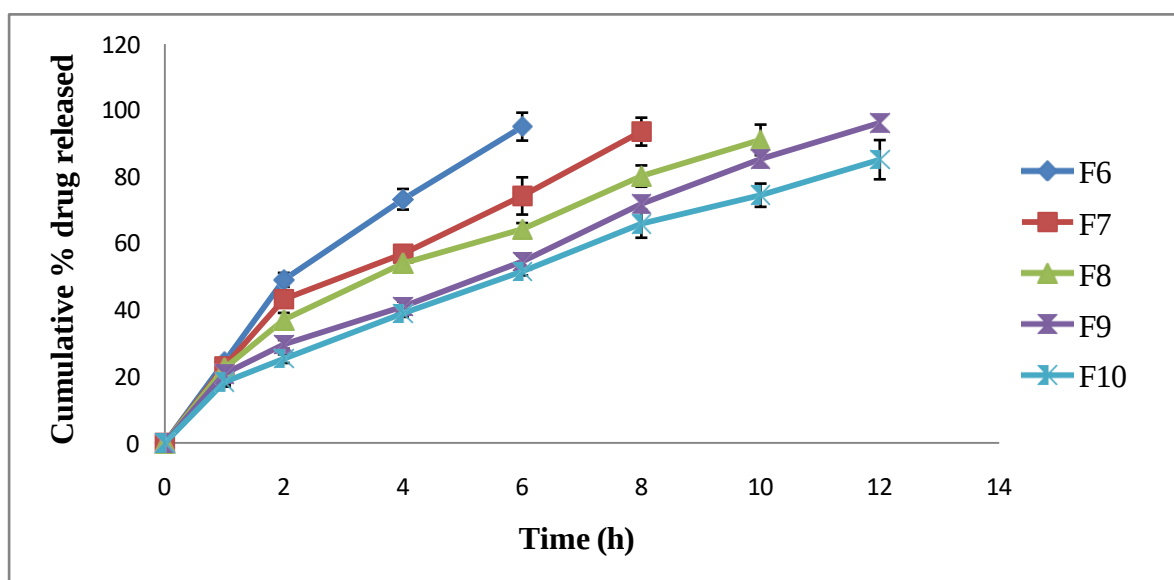


Fig 4: Drug release profiles of Lamivudine floating tablets composed of xanthan gum

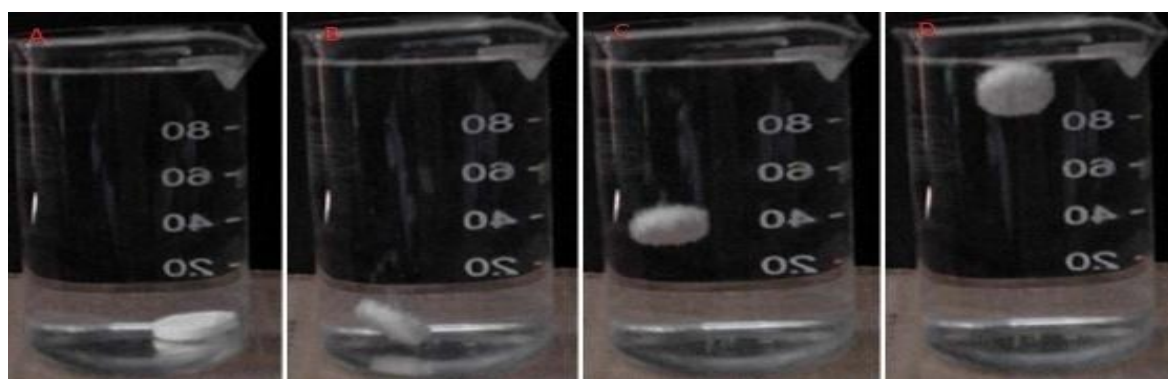


Figure 5: In-vitro buoyancy of Lamivudine floating tablets in 0.1N HCl at 0sec, 5sec, 15sec and 12th h.

CONCLUSION

Gastro retentive Lamivudine floating tablets are developed successfully with floating technology. Based on several studies, F4 formulation was chosen as good and optimized formulation. The F4 was considered stable for 90 days as there was no color change in outward appearance, floating properties, content of drug at 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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