World Journal of Pharmaceutical Sciences
ISSN (Print): 2321-3310; ISSN (Online): 2321-3086
Available online at: https://wjpsonline.com/
Research Article

Formulation and evaluation of Lamivudine floating tablets using Carbopol & Eudragit S 100

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Received: 01-02-2022 / Revised Accepted: 28-02-2022 / Published: 01-03-2022

ABSTRACT

Lamivudine comes under class II drugs according to BCS classification. It is poorly water-soluble drug. It has maximum solubility in pH 1.2 and therefore it will be beneficial to retain the drug in stomach for longer period of time for better absorption. Hence, it was found necessary to develop a gastric retentive dosage form containing Lamivudine in order to increase the gastric residence time to enhance its absorption and they're by its oral bioavailability. Also, the slow release of the drug in stomach may avoid the stomach pain associated with immediate release of the drug. The ultimate aim was to design, develop and optimize the floating tablets containing Lamivudine in order to increase its gastric retention time for enhancing absorption in stomach as well as to produce a controlled release of the drug for a longer time using polymers such as Carbopol, and Eudragit S100.

Keywords: Carbopol, Eudragit S 100, Lamivudine, Microcrystalline cellulose

INTRODUCTION

Conventional dosage forms can thus result in a drug regimen in which the drug concentration oscillates between alternating periods of drug overdose and drug inefficiency. Controlled release formulation is expected to remove the peaks and valleys in the drug concentrations in the blood, thus providing for a more effective regimen(1,2). New drug delivery technologies are revolutionizing the drug discovery, development and creating R&D focused pharmaceutical industries to increase the momentum of global advancements. In this regard novel drug delivery systems (NDDS) have many benefits, which includes improved therapy by increasing the efficacy and duration of drug activity, increased patient compliance through decreased dosing frequency and convenient routes of administration and improved site-specific delivery.[4]Lamivudine is a BCS Class I active anti-retroviral agent which belongs to non-nucleoside reverse transcriptase inhibitor. It is generally prescribed in the dose of 100-150 mg twice a day, and is well absorbed in the upper gastrointestinal tract with a short biological half-life of 5-7 h (3,4). By decreasing the dosing frequency to once a day systemic side effects can be decreased and the patient compliance can be improved [4]. Floating drug delivery systems have a bulk density less than gastric fluids and so remain buoyant in the stomach without affecting gastric emptying rate for a prolonged period of time. While the system is

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How to Cite this Article: Kalaiselvi C, Jothimanivannan C, Gomathi M, Praveen Kumar M. Formulation and evaluation of lamivudine floating tablets using Carbopol & Eudragit S 100. World J Pharm Sci 2022; 10(03): 267-272; https://doi.org/10.54037/WJPS.2022.100304

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floating on the gastric contents, the drug is released slowly at a desired rate from the system. After the release of drug, the residual system is emptied from the stomach. This results in an increased gastric retention time and a better control of the fluctuations in plasma drug concentration (5,6). The ultimate aim of this work was aimed at the formulation of Lamivudine floating tablets using two different polymers in different concentrations, in order to decrease the dosing frequency, by sustaining the drug release for 24 hrs and to evaluate the prepared formulations.

MATERIALS AND METHODS (7,8)

Lamivudine is a gift sample from MSN laboratories Ltd., POLYOX WSR 303 was supplied by Colorcon Asia Pvt Ltd (Goa, India), CARBOPOL 971 P was supplied by Lubrizol, Sodium bicarbonate, Citric acid from SD Fine Chemicals, Mumbai, Avicel and Magnesium stearate were procured from commercial sources. All other materials were of Laboratory grade(3,4).

Calibration of Lamivudine:(9)

The stock solution was serially diluted to get solution in the range of 2-10ug/ml using pH 1.2 buffer solution and λ_{max} of the solution was found out.

Micromeritic studies: The powder blends of all the formulations were evaluated for Bulk density, Tapped density, Carr's index, Hausner ratio, angle of repose, and drug content. Similarly the prepared floating tablets were evaluated for hardness, thickness, diameter, friability. (10,11)

Determination of Bulk density

$$\text{Bulk density} = \frac{\text{Mass of powder (gm)}}{\text{Bulk volume(ml)}}$$

Determination of Tapped density

$$\text{Tapped density} = \frac{\text{Mass of powder(gm)}}{\text{Tapped volume (ml)}}$$

Determination of Carr's index(12,13)

$$\text{Carr's index} = \frac{\text{Tapped density} - \text{bulk density}}{\text{Tapped density}} \times 100$$

Determination of Hausner ratio

$$\text{Hausner ratio} = \frac{\text{Tapped density}}{\text{Bulk density}}$$

Determination of Angle of repose

$$\tan \phi = h/r$$

$$\emptyset = \tan^{-1} h/r$$

h= height of Pile (cm)

r= radius of pile (Cm).

Preparation of Floating Tablets of Lamivudine: (14,15)

The formulations containing 300 mg of Lamivudine were fabricated using direct compression method using formulae mentioned in **Table 1**, required quantities of Drug, Polymer and other excipients except magnesium stearate were passed through 30# sieve together and blended for 10 minutes. The powder blend was lubricated with magnesium stearate (pre-sifted through 60# sieve) and blended for 5 minutes. Then the powder blend was compressed into tablets of 900 mg by using 17.5 x 8.75 mm, caplet shaped punches.

Evaluation of Lamivudine floating tablets:(16,17)

Weight variation test: 20 tablets were selected at random and weighed individually. The average weight of each batch of tablet was calculated. Individual weights of the tablets were compared with the average weight. Since the tablet weighed around 250mg, IP specifies that the tablets pass the test if not more than two of the individual weights deviate from the average weight by more than 7.5%.

Percentage deviation allowed under weight variation test	
Average weight of tablet	**Percentage deviation**
< 80mg	**10%**
80-250mg	**7.5%**
250mg	**5%**

Thickness

Thickness was measured during tablet compression using Vernier caliper.

Hardness test

Tablet hardness was measured by Pfizer tablet hardness tester. The tablets were held vertically in between the jaws which were pressed with hand until the tablet broken. The reading was noted from the needle of pressure dial which may be expressed in kilograms.

Friability test

This is performed to evaluate the ability of tablet to withstand abrasions. Ten number of tablets were weighed and placed in the tumbling chamber rotated for 100 revolutions.

The tablets were again weighed and the loss in weight indicated the friability.

$$\% \text{ Friability} = \frac{A-B}{B}$$

Where A=Initial weight of tablet

B=Weight of tablet after 100 revolution.

Drug content (18,19)

Ten tablets were randomly weighed and crushed. Calculated the average weight and taken the powder equivalent to 10 mg of Lamivudine base in

a 100 ml volume flask. Add 20ml methanol and sonicated for 10 minutes. Then volume made up to 100 ml with 0.1N HCL (pH1.2). The 1ml of resultant solution diluted to 100 ml with 0.1N HCL buffer. Measure the asorbance of above solution in UV spectrophotometer at280nm.

In vitro-dissolution studies(20)

Lamivudine release from different formulations was determined using a USPXIX paddle apparatus 2 under sink condition. The dissolution medium was 900 ml HCl at pH (1.2) at 37 ±0.2 °C; paddle speed 50 rpm, to simulate in *vivo* conditions. All experiments were done in triplicate and average values were taken. The formulation was subjected to dissolution tests for 12 hrs. Sample (10 ml) was withdrawn at predetermined time intervals, filtered through Whatmann filter paper and replaced by an equal volume of dissolution medium. Drug content in the dissolution sample was determined by UV spectrophotometer at 280nm.

Floating Behaviors

Floating behavior studies were performed on the prepared floating tablets, carried out in a USP paddle apparatus 2 at a paddle speed 50 rpm in 900 ml 0.IN HCI (pH 1.2) at 37 +0.2 °C for 8hrs to mimic in *vivo* conditions. The following parameters were determined, the time needed to go upward and float on the surface (floating lag time), floating duration and relative matrix integrity. The latter parameter was determined on the basis of visual inspection after the floating studies.(21)

RESULTS AND DISCUSSION

A calibration curve for Lamivudine was constructed in 0.1N HCL by scanning the diluted drug solution at 280 nm using UV Spectrophotometer. The linearity of the Calibration curve was found to be in the range of 2 to 10 µg/ml shown in **Figure 1**. A regression coefficient value of 0.9997 was noticed for Lamivudine. All the prepared formulations were evaluated for bulk density, tapped density, carr's index, Hausner ratio, and angle of repose were shown in **Table 2**. The present study was aimed at preparing floating tablet containing Lamivudine for sustained release of drug and study the effect of swellable release retardant polymer on rate of release and floating lag time. After compression, the tablets were evaluated for weight variation, hardness, thickness, friability, drug content and the results were shown in **Table 3**. Lamivudine is more soluble in acidic pH and hence it will be beneficial to increase its gastric residence time in order to improve its oral absorption as well as by controlling the release rate, the side effects associated with burst release of the drug can be eliminated. In this study, Carbopol was chosen as the swellable polymer and Eudragit S100 was chosen as release retardant polymer. A total of 9 formulations were made with Carbopol and Eudragit S100 combination at three different proportions. Since Eudragit S100 is not soluble in acidic pH, it may reduce the permeability of the fluid inside the matrix and hence may have caused the reduction in drug release. Although all the formulations showed complete release, the time taken was found to be very short which is not suitable for sustained release effect. Formulation F9 with 90mg carbopol and 60mg Eudragit S100 showed a better sustained effect with the complete release of the drug spreading over 12h and hence chosen as a best formulation. The results of *in vitro* dissolution studies were shown in **Figure 2.**

CONCLUSION

Gastro retentive dosage forms are gaining more importance in the field of drug delivery research especially for those drugs whose absorption and oral bioavailability can be improved when it is delivered in acidic conditions. In this study we have successfully developed oral floating tablets of Lamivudine with the use of polymers like carbopol and eudragitS100. The formulations showed excellent floating characteristics with good matrix integrity and sustained release of the drug spread over 12 hrs. Since the gastric residence time of the drug can be substantially increased by these types of sustained release formulations, it can be expected that drug will have complete absorption and improved bioavailability and also a reduction in the frequency of drug administration because of the sustained release effect. This may also decrease the stomach pain associated with repeated administration of conventional Lamivudine tablets. From this research work we have concluded that oral floating systems can be developed successfully using a combination of carbopol and Eudragit S100.Further studies using animal model will throw more light on the effectiveness of the formulation *in vivo.*

ACKNOWLEDGEMENT

The authors would like to express their sincere thanks to the management and Principal of SS Institute of Pharmacy for their encouragement and providing necessary facilities in carryout the research work.

Table 1: Composition of Lamivudine floating tablets:

Formulation	1	2	3	4	5	6	7	8	9
Drug	100	100	100	100	100	100	100	100	100
Carbopol	60	90	120	60	90	120	60	90	120
Eudragit S100	0	0	0	30	30	30	60	60	60
$NaHco_3$	55.5	55.5	55.5	55.5	55.5	55.5	55.5	55.5	55.5
Magnesiumsterate	5	5	5	5	5	5	5	5	5
Talc	5	5	5	5	5	5	5	5	5
MCC	144.5	114.5	84.5	114.5	84.5	54.5	54.55	54.5	54.5
Total	370	370	370	370	370	370	370	370	370

Table 2: Micromeritic properties of directly compressible powder

Matrix material	**Formula code**	**Angle of repose**	**Bulk density (gm/ml)**	**Tapped density (gm/ml)**	**C.I(%)**	**Hausner ratio**
Carbopol	F1	$32^{O}\ 41^{'}$	0.481	0.532	9.5%	1.11
	F2	$31^{O}\ 23^{'}$	0.485	0.535	9.3%	1.10
	F3	$34^{O}\ 53^{'}$	0.483	0.533	9.3%	1.10
	F4	$30^{O}\ 27^{'}$	0.484	0.531	8.8%	1.09
	F5	$33^{O}\ 34^{'}$	0.482	0.534	8.85%	1.08
	F6	$32^{O}\ 26^{'}$	0.485	0.535	9.7%	1.09
	F7	$35^{O}\ 38^{'}$	0.480	0.531	9.6%	1.10
	F8	$32^{O}\ 31^{'}$	0.483	0.534	9.5%	1.09
	F9	$35^{O}\ 34^{'}$	0.485	0.531	8.6%	1.08

Table 3: Evaluation of prepared tablets:

Polymer	Formula code	Thickness (mm)	Hardness	Friability (%)	Average weight(mg)	Drug content (%)	Floating lag time (Sec)
Carbopol	F1	4.25	2-3kg/cm	0.45	370±2	96.45	8
	F2	4.36	2-3kg/cm	0.58	370±4	97.21	9
	F3	4.68	2-3kg/cm	0.76	370±1	94.55	13
	F4	4.71	2-3kg/cm	0.48	370±3	97.23	10
	F5	4.44	2-3kg/cm	0.28	370±5	95.34	16
	F6	4.32	2-3kg/cm	0.47	370±4	96.56	21
	F7	4.56	2-3kg/cm	0.35	370±2	95.21	21
	F8	4.78	2-3kg/cm	0.56	370±1	98.66	24
	F9	4.71	2-3kg/cm	0.47	370±3	97.88	27

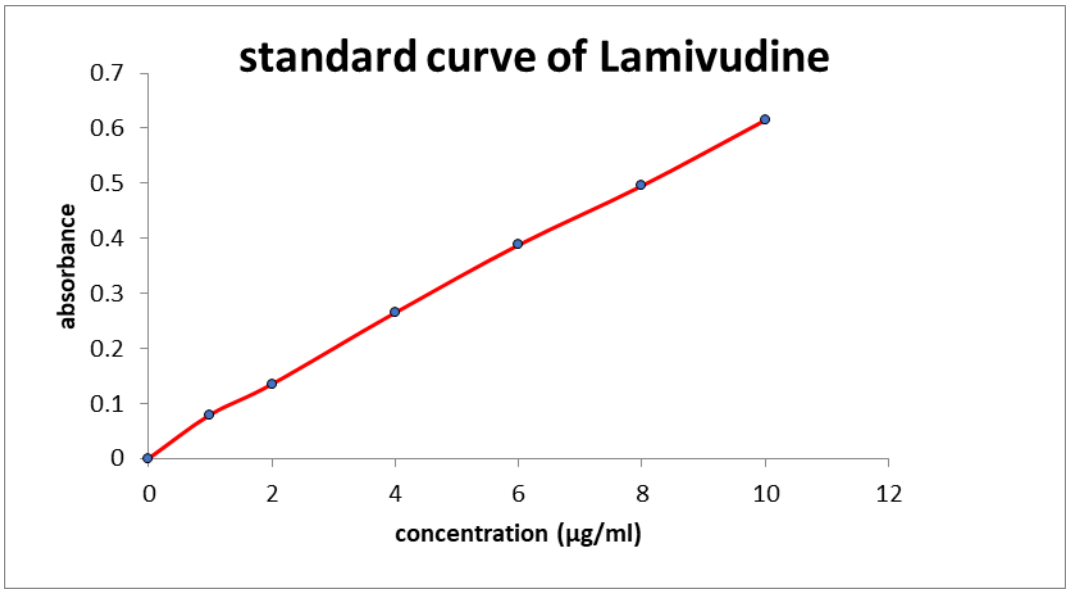

Figure: 1. Standard curve of Lamivudine.

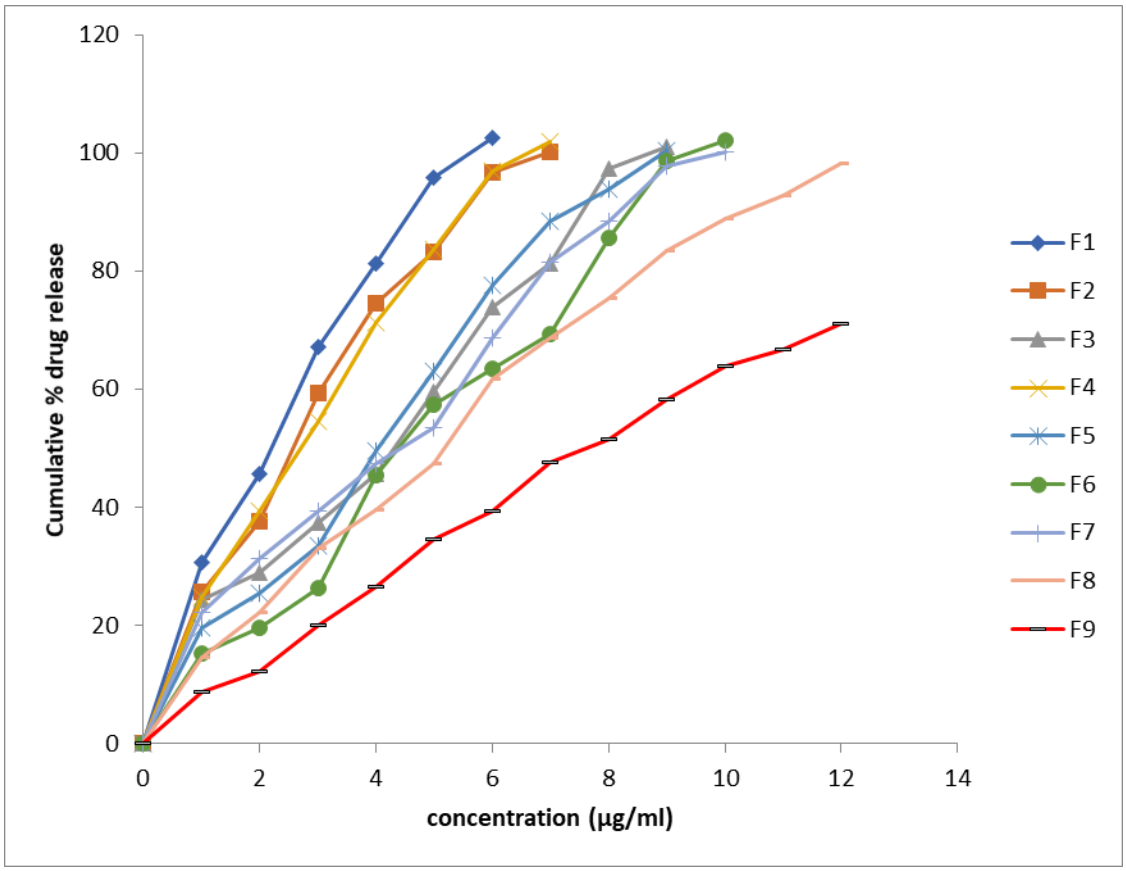

Figure: 2 *In vitro* dissolution studies of Lamivudine floating tablets (F1-F9).

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