

“Formulation and Evaluation of Floating Tablets”

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Abstract- The drug delivery system aims to provide a therapeutic amount of drug to the desired site in the body and maintain the desired plasma concentration of the drug for a particular period of time. Lamivudine, an anti-viral drug, choice in the treatment of HIV has been chosen as a model drug in the formulation of controlled drug delivery systems for the present work. Various studies reported the absolute bioavailability of Lamivudine (86%) when administered orally with a half-life of 4-6 hrs. A microparticulate floating drug delivery system was planned for Lamivudine as such a system release for a prolonged period of time and the drug would be available in the dissolved form. This would lead to improvement in the bioavailability of the drug. In this way, it stands an advantage over conventional dosage forms. Floating tablet formulations were prepared using HPMCK4M and Xanthan Gum. The prepared floating tables were characterized by their pre- and post-compression parameters. Almost all the formulations showed fairly acceptable values for all the parameters evaluated. Further, the analysis of the release mechanism was carried out by fitting the drug diffusion data to various kinetic equations. The overall curve fitting into various mathematical models was found to be average and best fitted into the zero-order kinetic model. A stability study was conducted for the prepared batch of F4-selected formulations for 60 days. There was no significant change in the drug entrapment and in-vitro release study of the floating tablet.

Keywords: Antiviral, Floating tablet, Lamivudine.

INTRODUCTION:

Oral Drug Delivery System

Drug delivery system represents a pure crude form of the drugs either in solid, liquid, or semi-solid form. It should be therapeutically safe, efficient, and stable enough to deliver a required amount of the drug to the specified site of body to reach instantly, to achieve the desired concentration and then retain the adapted concentration. Many of the drug delivery systems are commercialized oral drug delivery systems [1]. Due to low treatment costs, increased patient compliance, and easy to administration of oral drug delivery is mostly preferred. Despite multiple benefits, the frequency of dosing of medication should be increased as it gets easily emptied from the stomach [2]. To overcome these barriers, the delivery of drugs must provide a prolonged duration of gastric residence. The time of drug release is improved, drug waste is reduced, and the solubility of drugs that are less soluble in high ambient pH is improved because to gastro retention [3]. Many drugs released in the stomach have the greatest therapeutic impact as they are continuously delayed and controlled in a release. This type of drug delivery method would have comparatively fewer side effects and would eliminate the need for repeated dosages [4]. In pharmaceutical dosage, the formulation of drugs in multilayered tablets is an innovative approach for providing the loading dose and maintenance dose in a tablet. This design enables the preparation of extended-release by placing a component of the drug for quick release in the first layer and a portion for extended release in the second, maintaining a sustained blood level. The immediate release portion, which delivers the initial dose of medication for immediate action and where the matrix layer largely remains intact as it passes through the intestine, gradually dissolves from its exposed phases in this path, helping to maintain the blood level that was initially reached [5], will disintegrate quickly after absorption. Conventional controlled-release dosage forms often delay the beginning of effect following oral administration and prolong drug release. Accordingly, the layered tablets provide a pharmacokinetic benefit over the conventional controlled-release dosage forms as the drug is rapidly released from the rapid-release layer leading to a rapid increase in drug plasma concentration accompanied by a continued release of the drug from the sustained release layer [6].

Floating System

FDSDS or Hydro-dynamically balanced systems (HBS) (**Figure 1**) are low-density systems having a sufficient tendency to float over the gastric contents and remain in the stomach for an extended period of time that releases the drug component at the desired rate, while floating over the gastric contents it contributes to optimize gastro-retention time and reduced fluctuation. FDSDS is the mechanism of a gastro-retentive drug delivery system that which controls the pharmacokinetic release rate of a drug to a specific site to achieve its pharmacological action [7].



Figure 1: Floating Drug Delivery System

Classification of Floating Dosage Systems

I. Single Unit Floating Dosage Systems

- a. Effervescent Systems
- b. Non-effervescent Systems

II. Multiple Unit Floating Dosage Systems

- a. Non-effervescent Systems
- b. Effervescent Systems
- c. Hollow Microspheres [8]

III. Raft Forming Systems

Advantages of FDDS

The following are the advantages of the Floating Drug Delivery System [8].

- FDDS can remain in the stomach for several hours and thereby prolonging the gastric retention time of various drugs.
- Advantageous for drugs that are meant for local action in the stomach e.g., Antacids.
- Formulation of FDDS is useful in intestinal movement and in diarrhea to hold the drug in a floating state in the stomach in order to get a comparatively better response.
- By decreasing the dosing frequency FDDS improves patient compliance.
- Treatment of gastrointestinal disorders such as gastroesophageal reflux.
- Despite of first-pass effect the bioavailability since the plasma drug concentration is avoided.
- HBS/FDDS formulations may be useful for the administration of aspirin and other similar drugs since these drugs are acidic and cause irritation on the stomach wall

Disadvantages of FDDS

The following are the disadvantages of the Floating Drug Delivery System [9, 10-13].

- The drug substances which are unstable in the acidic environment of the stomach are not suitable candidates for integration into the systems.
- In these systems the presence of food is usually required to prolong gastric emptying.
- It is not suitable for drugs which are having stability or solubility problem in GIT.
- The drugs which undergo first-pass effect and the drugs which are significantly absorbed throughout the gastrointestinal tract are the only desirable candidate.

Methods of Developing a Floating Drug Delivery System

1. **Direct compression technique:** It means compressing tablets directly from powder content without altering the substance's physical structure itself. the most widely used carriers are Dicalcium trihydrate phosphate, tricalcium phosphate, etc. [11].
2. **Effervescent Technique:** An effervescent reaction between organic acid (citric acid) and bicarbonate salts will fill the floating chamber of the drug delivery system with inert gas [11-12].
3. **Wet granulation technique:** Involves wet powder massaging, milling or drying. Wet granulation shapes the granules by binding the powders together with an adhesive rather than compacting them [13].
4. **Iontropic Gelation Technique:** Gelation of anionic polysaccharide sodium alginate, the primary polymer of natural origin, was accomplished with oppositely charged calcium ions (counter-ions) with the objective of forming instantaneous microparticles [11, 13].
5. **Solvent evaporation technique:** Continuous phase ability is inadequate to remove the entire amount of liquid dispersal solvent. The solvent evaporates from the dispersal surface to receive hardened [13].

- 6. Spray Drying Technique:** Involves dispersing the core layer into the liquefied coating content and spraying the core coating mixture into the environment so that the coating is solidified by rapidly evaporating in which the coating material is solubilized [12].
- 7. Melt Solidification Technique:** This method involves emulsifying the molten mass in the aqueous phase followed by cooling it to solidify. carriers used for this technique are Lipids, waxes, polyethylene glycol, etc. [11-13].

Preliminary studies:

Preliminary physicochemical properties of Lamivudine powder were investigated by performing a test for the organoleptic properties of the drug, the Test of purity. The result of characterizations of pure drugs is shown in (Table).

Table Organoleptic properties of Lamivudine powder

Sr. No	Parameters	Observation/Result
1	Colour	off-white
2	Odour	Odourless
3	Appearance	Amorphous

Table Solubility of Lamivudine powder

Sr. No	Solubility	Observation/Result
1	Water	Soluble
2	Methanol	Slightly Soluble
3	0.1N HCL	Soluble

Table Melting point of Lamivudine powder

Sr. No	Melting point	Observation/Result
1	Lamivudine powder	160°C
2	Lamivudine powder	161° C
3	Lamivudine powder	162°C
Average		161°C

DISCUSSION

Based on the above physical characterization of Lamivudine, The Organoleptic, the solubility of the drug and melting point matches with the reference data which confirms the purity of the drug.

EVALUTION OF PREPARED TABLET

Precompression evaluation:

1) Angle of Repose:

The precise weight powder mix was taken in the channel. The tallness of the pipe is balanced in such a way the tip of the pipe simply touched the zenith of the powder mix. The powder mix is permitted to move through the pipe uninhibitedly onto the surface. The distance across the powder cone is estimated and the point of rest is ascertained utilizing the accompanying condition.

$$\tan \theta = h/r$$

Where,

h= hight and r = readius of the powder cone.

2) Bulk and tapped Density:

Both loose bulk density and tapped bulk density are determined. A quantity of 2 gm of powder blend from each formula, previously

shaken to break any agglomerates formed, is introduced into a 10 ml measuring cylinder. After that, the initial volume is noted and the cylinder is allowed to fall under its own weight onto a hard surface from the height of 2.5 cm at second intervals. Tapping is continued until no further change in volume is noted. Loose BD and Tapped DB were calculated using the following equations.

$$\text{LBD} = \text{Weight of the powder blend} / \text{Untapped Volume of the packing}$$

$$\text{TBD} = \text{Weight of the powder blend} / \text{Tapped Volume of the packing}$$

3) Compressibility Index:

The Compressibility Index of the powder blend is determined by Carr's compressibility index. It is a simple test to evaluate the LBD and TBD of a powder and the rate at which it is packed down. Carr's Index formula are as follows:

$$\text{Carr's Index (\%)} = [(TBD-LBD) \times 100] / TBD$$

4) Hausner's Ratio:

It is calculated from bulk density and tap density.

$$\text{Hausner's ratio} = \text{Tapped density} / \text{Bulk density.}$$

Readings less than 1.25 indicate good flow (20% Carr index.) and a value greater than 1.25 indicates poor flow (33% Carr index.). If it is between 1.25-1.5 added glidant normally to improve flows.

Post-compression parameters:

Organoleptic properties Test

Organoleptic properties are a significant factor to be estimated in the prepared sample by observation of color and Texture.

Weight variation Test

From each prepared batch, twenty tablets of the tablet were randomly selected and individually weighed. The average weight of tablets is calculated. Then the individual weight is compared with that of the average weight and the amount of weight variation is determined. If not higher than two the distinct tablet weight differs from the mean weight by further than the percentage according to IP limits.

Thickness Test Tablet thickness can be measured using a simple procedure. Three compressed tablets were taken and their thickness is measured using Vernier calipers. The thickness is measured by placing the tablet between two arms of the Vernier calipers.

Hardness Test

The determination of the tablet's hardness was through using the Monsanto Hardness tester. The force applied to break down each tablet was recorded. The hardness of the tablet was obtained in terms of (kg/cm²).

Friability Test

The Friability test is performed by using the Roche friability. Ten tablets of the tablet were weighed and placed in the friability, then operated for 25 revolutions per minute. After four minutes (100 revolutions) the tablets were dusted and reweighed. The percentage friability is determined using the formula,

$$\text{Percentage friability} = \frac{\text{Initial weight} - \text{Final weight}}{\text{Initial weight}} \times 100$$

Floating Test

The tablets were placed in a 100 ml beaker containing 0.1 N HCl. The time between the introduction of the dosage form and its buoyancy on 0.1 N HCl and the time during which the dosage form remains buoyant were measured. The time taken for the dosage form to emerge on the surface of the medium is called Floating Lag Time (FLT) or Buoyancy Lag Time (BLT) and the total duration of time during which the dosage form remains buoyant is called Total Floating Time (TFT).

Formulation of Floating Tablet

Floating Tablet Formulation Batches of Lamivudine

Tablet Ingredients	F1	F2	F3	F4	F5	F6
Lamivudine	100	100 mg	100 mg	100 mg	100 mg	100 mg
HPMCK4M	95	85	75	---	---	--
Xanthan Gum	--	--	--	95	85	75
Camphor	30	20	10	30	20	10
Magnesium stearate	5	5	5	5	5	5
Talc	5	5	5	5	5	5
Lactose	15	35	55	15	35	55
Total Weight	250mg	250mg	250mg	250mg	250mg	250mg

Procedure:

Lamivudine Floating tablet were prepared using two polymer concentrations (F1-F3) HPMCK4M and Xanthan Gum (F4-F6) by the direct compression method along sublimation method. The formulation data is shown in Table Accurately weighed amount of active pharmaceutical ingredient (lamivudine), polymer (HPMCK4M and Xanthan Gum) in different ratios, and other excipients (Flavouring agent).

Optimization of Prepared formulation for tablet

From all pre-post compression studies, F4 formulation shows acceptable thickness, hardness and friability test and also post compression parameters hence from above all formulations F4 were considered an ideal formulation batch from which F4 batch gives 94.85 drug release in 12 min. hence consider an ideal batch.

CONCLUSIONS:

The Floating of lamivudine was successfully formulated with two different polymers, the prepared tablet was evaluated and characterized for various parameters. The prepared tablet gives ideal result in post and pre-compression evaluation parameters hence based on the all-observation parameters tablets of lamivudine using different excipients was capable of exhibiting all the properties hence, the prepared formulation enhanced the bioavailability of Lamivudine.

FUTURE SCOPE

The present study is to formulate and evaluates floating tablets and gives the following future overall outcome:

- The floating tablet increases its residence time in the stomach without contact with the mucosa.
- Prepared floating tablet will ensure complete release of the drug before the dosage form passes into the non-absorbing zone of the intestine.
- Prepared tablets making the delivery system more efficient.
- Prepare Tablet enhancing bioavailability of Lamivudine.

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