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Original Article

Formulation and Evaluation of Stavudine Floating Tablet

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ABSTRACT

The present study was conducted to develop floating matrix tablets of Stavudine with the objective of extending its gastric retention time and evaluating the effect of various polymers on drug release behavior. Tablets were formulated using the melt granulation method, incorporating beeswax as a hydrophobic binder. Hydroxypropyl methylcellulose (HPMC) was used as the matrix-forming polymer, sodium bicarbonate as the effervescent agent to induce buoyancy, and ethyl cellulose as a floating enhancer. Compatibility and interaction between the drug and excipients were studied using Differential Scanning Calorimetry (DSC) and Fourier Transform Infrared Spectroscopy (FTIR).

Keywords: Stavudine, floating drug delivery, melt granulation, HPMC, beeswax, buoyancy, sustained release

INTRODUCTION

Floating Drug Delivery Systems

Floating drug delivery systems (FDDS) are formulated to remain buoyant in the stomach for extended durations. This approach is especially beneficial for drugs that are absorbed in the upper part of the gastrointestinal tract or those that degrade in the intestinal environment. By maintaining prolonged gastric residence, these systems improve drug bioavailability. FDDS achieve flotation by releasing gas upon contact with gastric fluids, which helps the dosage form float while gradually releasing the drug. After the therapeutic agent is released, the system is eventually expelled from the stomach.

MATERIALS AND METHODS

Drugs and Excipients

Active Pharmaceutical Ingredient: Stavudine

Polymers and Additives: Hydroxypropyl methylcellulose (Methocel K15M), Carbopol 940P, Gum Copal, Gum Karaya, Microcrystalline Cellulose (Avicel PH 102), Sodium Bicarbonate, and Citric Acid

Quantification of Stavudine

Both spectrophotometric and chromatographic methods are available for determining Stavudine concentration. Studies show less than 10% variation between UV spectrophotometry and HPLC, indicating comparable accuracy. For this study, a simple, sensitive, and reproducible UV spectrophotometric method was chosen to quantify Stavudine at its maximum absorbance wavelength (λmax) of 266 nm.

Preparation of Stock Solution

A 100 mg quantity of Stavudine was accurately weighed and dissolved in 0.1N hydrochloric acid.

Preparation of Calibration Standards

Aliquots from the stock solution were used to prepare standard dilutions of 2, 4, 6, 8, and 10 µg/mL in 0.1N HCl. The absorbance of each dilution was measured at 266 nm using a UV-VIS spectrophotometer (ELICO). These values were used to construct a calibration curve, which served as a reference for estimating the drug content in formulations.

Stability Study in Acidic Medium

To evaluate the chemical stability of Stavudine in acidic conditions, a known quantity of the drug was dissolved in 0.1N HCl and left undisturbed for 24 hours. Samples were withdrawn at specific time

Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

intervals, diluted to a concentration of 6 µg/mL, and analyzed using UV spectrophotometry at 266 nm. The absorbance readings were used to determine the drug's stability over time.

Preformulation Studies

Compatibility between Stavudine and the selected excipients was assessed by observing physical changes, analyzing drug content, and conducting thermal characterization using Differential Scanning Calorimetry (DSC).

Formulation of Controlled Release Floating Tablets

Each formulation contained a fixed amount of drug, while the quantity of polymers was varied. Microcrystalline cellulose was used to adjust tablet weight. All ingredients were sieved (mesh #60), weighed, and blended in a double cone mixer for uniformity. Sodium bicarbonate and citric acid were added sequentially to enable gas generation. The powder mixtures were evaluated for flow characteristics such as angle of repose and compressibility index. After blending with 1% talc and magnesium stearate, the formulations were compressed into tablets using 6 mm flat punches on a 10-station rotary tablet press. Consistent processing parameters were maintained across all batches.

EVALUATION

1. Angle of Repose

The angle of repose was assessed to evaluate the powder's flow characteristics using the fixed funnel technique. A funnel with a 10 mm internal diameter was secured at a height of 2 cm above a flat surface. Roughly 10 grams of the powder blend was gently poured down the funnel wall until a pile formed and touched the funnel's tip. The base of the pile was outlined, and the radius was measured to calculate the angle. Results are recorded in Tables 25–26 and 29–30.

2. Compressibility Index (Carr's Index)

To assess the flow properties of the powder, both bulk and tapped densities were measured. Carr's Index was calculated using the formula:

Carr's Index (%) = [(Tapped Density - Bulk Density) / Tapped Density] × 100

This value reflects the compressibility and potential flow behavior of the powder during tablet manufacturing.

3. Weight Variation Test

Their average weight was calculated and compared with each individual tablet's weight to check for consistency. According to Indian Pharmacopoeia (IP) standards, no more than two tablets should deviate beyond the permissible limits to pass the test, ensuring uniformity in tablet weight.

4. Tablet Hardness

Each tablet was placed between two jaws, and pressure was gradually increased until the tablet broke. The force required (in kg/cm²) was recorded. Hardness depends on factors like tablet weight, punch setting, and compression force applied during tablet formation.

5. Friability Test

Tablet friability was tested using a Roche friabilator. During rotation, tablets were repeatedly lifted and dropped from a fixed height, simulating mechanical stress. Tablets with weight loss below 1% were considered to have acceptable friability.

6. Drug Content Uniformity

For drug content analysis, tablets from each batch were crushed and dissolved in 0.1N HCl in a 250 mL volumetric flask. The solution was shaken intermittently for 30 minutes and the volume was adjusted to 250 mL. After allowing the mixture to settle, the supernatant was filtered through Whatman filter paper, further diluted, and analyzed using UV spectroscopy. Lamivudine was measured at 280 nm and Stavudine at 266 nm. Each batch was tested six times (n=6), with findings presented in Tables 27–28 and 31–32.32.

IN VITRO DISSOLUTION STUDIES

Dissolution studies on lamivudine floating matrix tablet formulations were performed in a calibrated 8

station test apparatus (LAB INDIA) equipped with paddles (USP apparatus II method) employing 900ml of 0.1N HCl as a dissolution medium. Samples were withdrawn at regular intervals for 12hrs and replaced with equal volume of same dissolution medium to maintain the constant volume throughout the experiment. Samples withdrawn at various time intervals were suitably diluted with same dissolution medium and the amount of drug released was estimated by ELICO double beam spectrophotometer at 280nm. The dissolution studies on each formulation were conducted in triplicate and the average of 3 values were taken for studies. The release values and dissolution profiles for all the formulations were shown in tables 33-37 and graph 5-9 respectively. Dissolution studies on stavudine floating matrix tablet formulations were performed in a calibrated 8 station test apparatus (LAB INDIA) equipped with paddles (USP apparatus II method) employing 900ml of 0.1N HCl as a dissolution medium. Samples were withdrawn at regular intervals for 12hrs and replaced with equal volume of same dissolution medium to maintain the constant volume throughout the experiment. The dissolution studies on each formulation were conducted in triplicate and the average of 3 values were taken for studies. The release values and dissolution profiles for all the formulations were shown in tables 38-42 and graph 10-14 respectively

Swelling Index:

The swelling index of tablets was determined by placing the tablets in the basket of dissolution apparatus using dissolution medium 0.1N HCl at 37±0.50C. After 1, 2,4, 6 and 8 hr's, each dissolution basket containing tablet was withdrawn and blotted with tissue paper to remove the excess water and weighed on the analytical balance (Shimadzu, Ax 120).

Infra- Red Spectroscopy:

I.R Spectral studies were carried out on some selected floating matrix tablets of lamivudine and stavudine by using BRUKER FTIR. FTIR spectrophotometer were used forrecording spectra in the region of 4000 – 400 cm-1 or in some cases down to 200 cm-1. Triturate 1 – 2mg of substance to be examined with 200mg of finely powdered and dried KBr. These quantities were usually sufficient to give a disc of 10-15mm diameter and a spectrum of suitable intensity. FTIR spectra and the interpreted values of various floating matrix tablet formulations were shown in graph 19-26 respectively.

Differential Scanning Calorimetry:

method representing the rate of heat uptake. About 10mg of sample was weighed in a standard open aluminium pans, were scanned from 0-450oC, at a heating rate of 10oC/minute while being purged with dry nitrogen. DSC thermograms and their interpreted values for the optimized formulations were shown in graph

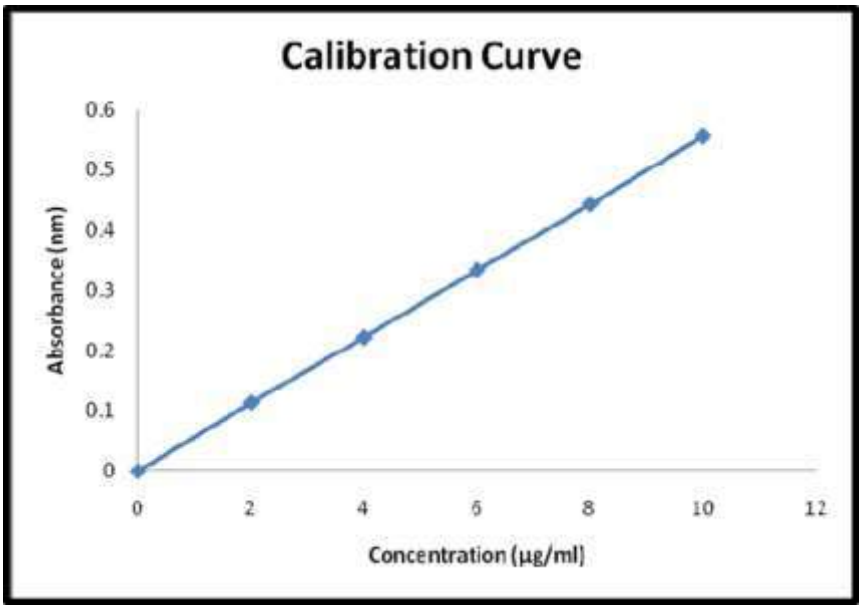
RESULTS AND DISCUSSION

Estimation of Stavudine

The λmax of Stavudine was found to be 266 nm, in the college laboratory, by using UV Spectrophotometer. Thus, in the present investigation a simple, sensitive accurate spectrophotometric method was used for the estimation of Stavudine at a λmax of 266nm 0.1N HCl as a medium. and their corresponding absorbance values were given in table 14. The absorbance values were plotted against concentrations of Stavudine and the corresponding calibration curve was shown in graph 3. The calibration curve values obtained were used to estimate Stavudine in the present investigation

Table: Calibration Curve for the Estimation of Stavudine in 0.1N HCl

S.No	Concentration (µg/ml)	Absorbance*
1	2	0.114
2	4	0.222
3	6	0.334
4	8	0.443
5	10	0.556



Graph: Calibration Curve for the Estimation of Stavudine in 0.1N HCl

DISCUSSION:

Stavudine in 0.1N HCl was estimated by spectrophotometric method at a wavelength of 266 nm. The method used for estimation of Stavudine was found to be liner with the Beers law in the concentration range of 0-10µg/ml.

Pre-formulation Studies on Stavudine:

Table: Preformulation Studies on Stavudine

S. No	Description	Method Evaluated	0^{th} day	1 month	3 months
1	Stavudine	Physical Evaluation	White powder	White powder	White powder
2	Stavudine + HPMC K15M	Physical Evaluation	White powder	White powder	White powder
3	Stavudine + HPMC K15M +MCC	Assay by UV method	complied	Complied	complied
4	Stavudine	DSC Studies	Melting isotherm was observed at 173.5^0C	Complied	complied
5	Stavudine + HPMC K15M	DSC Studies	Melting isotherm was observed at 176.1^0C	Complied	complied
6	Stavudine	FTIR Studies	3425 cm^{-1} 1115.2 cm^{-1}	Complied	complied
7	Stavudine + Excipients	FTIR Studies	3425 cm^{-1} 1115.2 cm^{-1}	Complied	complied

Preformulation studies on Stavudine and excipients were carried out for a period of three months at an ambient storage condition. The drugs and excipient interaction were observed physically and by thermal methods. Physical evaluation indicated that there were no physical changes in the colour and amorphous nature of the drug and its excipient blends even after 3 months of storage. UV Spectrophotometric methods exhibited the similar absorbance values of drug alone and excipient indicated that there were no drug excipient interactions. FTIR spectral studies exhibited the same peaks even in the presence of excipients and DSC studies showed the same melting isotherms with or without the presence of excipients indicated both the drugs selected for the study, Stavudine was stable and hence suitable for further formulation development.

Preparation of Stavudine Controlled Release Floating Matrix Tablets Controlled release floating matrix tablets for Stavudine were prepared by direct compression method using Elite 10 station mini press. The direct compresion process used for the preparation of matrix tablets was found to be ideal and is easy to reproduce. As many of the polymers and the excipients used are hydrophilic, the involvement of water or moisture makes the wet granulation process highly problematic. Hence the dry process such as direct compression technique was employed in the present investigation for the preparation of controlled release floating matrix tablets.

Table: Composition of Various Stavudine Controlled Release Floating Matrix Formulations

Ingredients (mg)	S1	S2	S3	S4	S5
Stavudine	40	40	40	40	40
HPMC K15M	40	--	--	--	--
Carbopol 940P	--	40	--	--	--
Copal gum	--	--	40	--	--
Dammar gum	--	--	--	40	--
Gum Karaya	--	--	--	--	40
MCC	116	116	116	116	116
Magnesium stearate	2	2	2	2	2
Talc	2	2	2	2	2
Total tablet weight (mg)	200	200	200	200	200

The direct compression process used for the preparation of matrix tablets was found to be ideal and is easy to reproduce. Polymers such as Hydroxy Propyl Methyl Cellulose (HPMC K15 M), Carbopols, gum Karaya, gum dammar and copal gum were used in the preparation of matrix tablets with incorporation of Sodium bicarbonate as a gas generating agent and combination of sodium bicarbonate and citric acid as effervescent agents. These polymers were found to be ideal for the preparation of controlled release matrix tablets. Twenty-five floating matrix tablet formulations were prepared with Stavudine by employing various polymers at different concentrations.

Evaluation of Powder Flow Characteristics of Stavudine Controlled Release Floating Matrix Tablets

Table: Flow Properties of Powder Blends of Stavudine Floating Tablets

S.NO	Formulation	Angle of repose (θ)	Hausner's ratio	Compressibility Index (%)
1	S1	23.90	1.12±0.03	14.23
2	S2	22.34	1.12±0.03	12.17
3	S3	24.54	1.12±0.02	11.87
4	S4	23.18	1.12±0.04	11.41
5	S5	22.77	1.12±0.03	13.67
14	S14	23.43	1.11±0.02	12.08

Table: Flow Properties of Powder Blends of Stavudine Floating Tablet

S.NO	Formulation	Angle of repose (θ)	Hausner's ratio	Compressibility Index (%)
1	S15	22.57	1.12±0.03	13.63
2	S16	21.36	1.12±0.03	11.57
3	S17	25.74	1.12±0.02	13.37
4	S18	22.14	1.12±0.04	12.61
5	S19	21.74	1.12±0.03	12.27

Evaluation of Physical Properties of Stavudine Controlled Release Floating Tablets

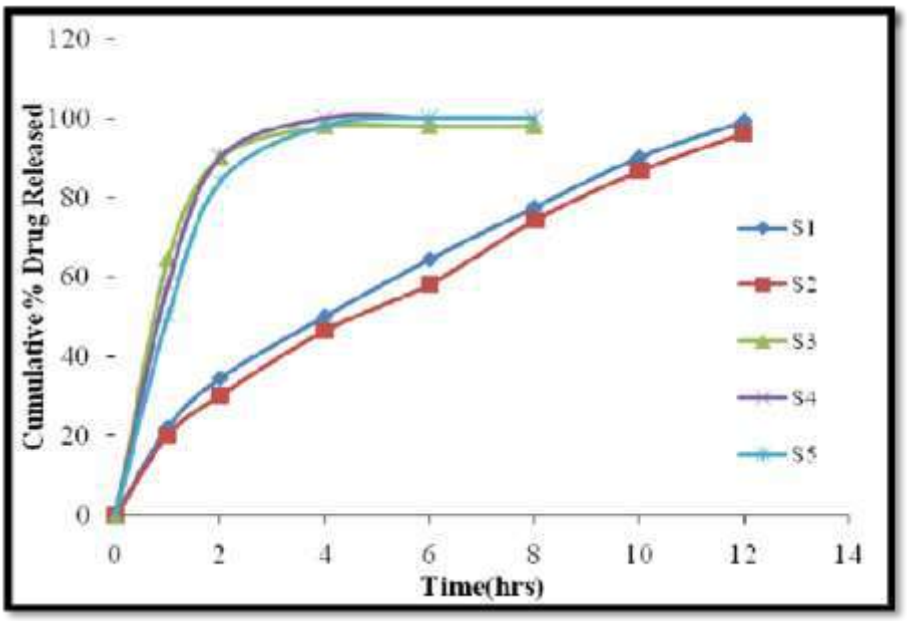
Table: Physical Properties of the Stavudine Floating Matrix Tablets

S.NO	Formulation	Weight uniformity(mg)	Hardness (kg/cm^2)	Friability (%)	Drug content (mg/tablet)
1	S1	203±2.0	6.0±0.3	0.12	39.2±0.5
2	S2	204±2.0	6.0±0.3	0.12	40.2±0.5
3	S3	202±2.0	6.0±0.3	0.18	36.4±0.5
4	S4	200±2.0	6.0±0.3	0.17	39.9±0.2
5	S5	200±2.0	6.0±0.3	0.15	41.2±0.3

In Vitro Dissolution Studies of Stavudine Floating Matrix Tablet Formulations

Table: Drug Release Profile of Stavudine Floating Matrix Tablet

Time(hrs)	Cumulative % Drug Release from Various Formulations				
	S1	S2	S3	S4	S5
0	0	0	0	0	0
1	22.24	20.24	64.66	58.24	50.24
2	34.66	30.26	90.24	90.22	84.22
4	50.24	46.56	98.12	100.00	98.25
6	64.56	58.22	98.14	100.11	100.0
8	77.66	74.22	98.32	100.12	100.0
10	90.24	86.66	---	---	---
12	99.26	96.12	---	---	---



Graph: Release Profiles from Various Controlled Release Floating Matrix Tablet Formulations of Stavudi

Characterization of optimized Floating Matrix Tablet Formulations of Stavudine

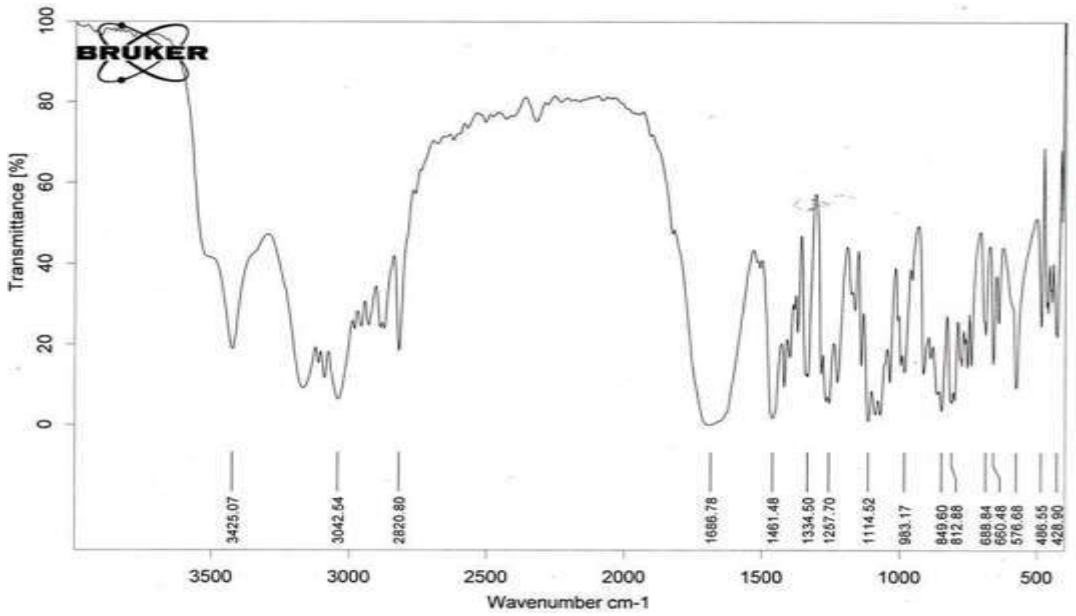


Figure: FTIR Spectra of Stavudine Pure Drug

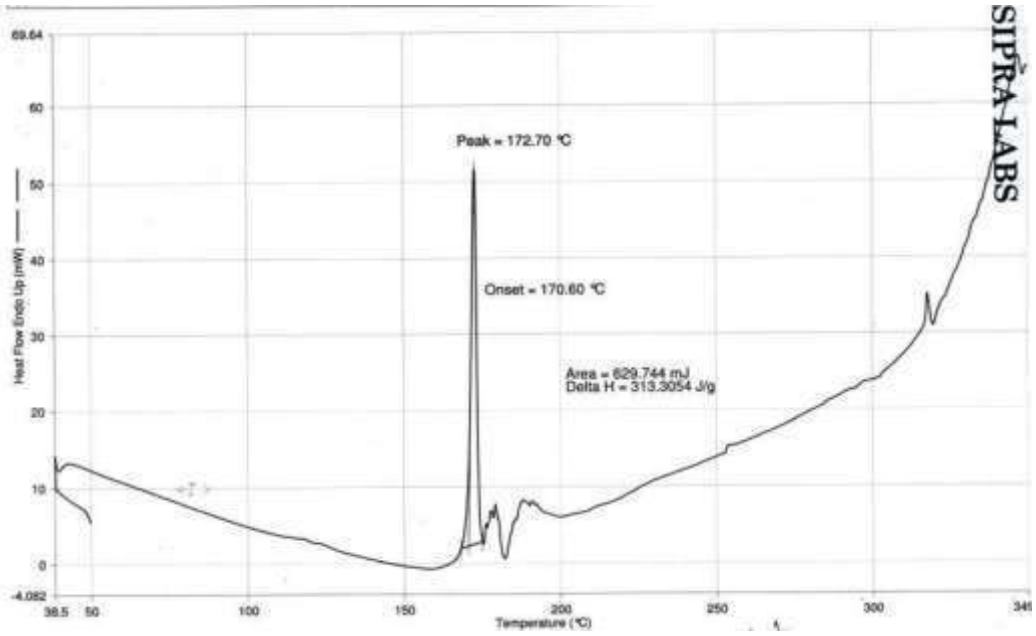


Figure: DSC Thermograms of Stavudine Pure Dru

CONCLUSION

The current study reveals that a great attempt has been made in order to formulate and study the drug release behavior of stavudine tablets with improved rapid release and bioavailability.

From all this experimental work we can conclude;

- A drug can be easily analyzed by using UV-Visible spectrophotometry shows maximum absorption. The value of linear regression coefficient was found to be 0.999, which indicates linear relationship between absorbance and concentration.
- From experimentation we can say that as the concentration of superdisintegrants increases there is increase in disintegration time and drug release behavior.
- Various combinations of superdisintegrants have a great impact on Disintegration time and drug release behavior as it improves both of them.

- The formulated tablets showed compliance for various physicochemical parameters such as disintegration, drug content and in-vitro drug release.

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