

DESIGN FORMULATION AND EVALUATION OF GASTRORETENTIVE FLOATING TABLETS OF STAVUDINE

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Abstract: The purpose of the present research work was to design, formulate and evaluate the floating tablets of Stavudine, a gastro retentive drug delivery system. Direct compression was used to prepare the tablets using HPMC K4M, HPMC K15M and Carbopol 974(p) as polymers. Formulations were prepared by varying the amount of polymers. The compatibility of drug with the polymers is identified by using FTIR studies. Gastric floating of Stavudine tablets results from effervescence produced by the reaction between sodium bicarbonate and hydrochloric acid in stomach. Twelve formulations of floating tablets were prepared using direct compression technique with polymer such as carbopol974 (p), HPMC grades, Xanthium gum, Guar gum, chitosan in different ratios. The evaluation results revealed that all formulations comply with the specification of official pharmacopoeias and/or standard reference with respect to general appearance, content uniformity, hardness, friability and buoyancy. Out of all the formulation developed, formulation F8 containing of Carbopol showed in vitro drug release of 97.8% up to desired time period of i.e., 24 hours. Thus it is summarized; carbopol grades can be used in formulation of gastro retentive floating drug delivery system. The compatibility of drug with polymers is identified by FT-IR studies. The results obtained showed that the drug is compatible with all the polymers used. The prepared tablets (F1-F12) were evaluated for both pre-compression and post-compression parameters. The results obtained showed that the drug is compatible with all the polymers used.

Keywords: Stavudine, HPMC K4M, HPMC K15M, Carbopol 974.

1. INTRODUCTION:

Oral drug delivery is the most widely utilized route of administration among all the routes that have been explored for systemic delivery of drugs via pharmaceutical products of different dosage form. Oral route is considered most natural, uncomplicated, convenient and safe due to its ease of administration, patient acceptance and cost-effective manufacturing process¹.

Oral delivery continues to be the most popular route of administration due to its versatility, ease of administration and probably most importantly patient compliance.^{2,3} Oral controlled release drug delivery have recently been of increasing interest in pharmaceutical field to achieve improved therapeutic advantages, such as ease of dosing administration, patient compliance and flexibility in formulation. Drugs with short half-lives and drugs that easily absorbed from gastrointestinal tract (GIT) are eliminated quickly from the systemic circulation. For these types of drugs the development of oral sustained-controlled release formulations is an attempt to release the drug slowly into the gastrointestinal tract (GIT) and maintain an effective drug concentration in the systemic circulation for a long time. After oral administration, such a drug delivery would be retained in the stomach and release the drug in a controlled manner, so that the drug could be supplied continuously to its absorption sites in the gastrointestinal tract (GIT).⁴ But oral sustained drug delivery formulations show some limitations connected with the gastric emptying time; variable and too rapid gastrointestinal transit could result in incomplete drug release from the device into the absorption window leading to diminished efficacy of the administered dose.⁵ Floating drug delivery system is an approach to prolong gastric residence time, thereby targeting site-specific drug release in the upper gastrointestinal tract (GIT) for local or systemic effects. This drug delivery system not only prolongs GI residence time but does so in an area of the GI tract that could maximize drug reaching its absorption site in solution and hence ready for absorption.⁷

Gastro retentive Dosage Form (GRDF)⁵:

It is evident from the recent scientific and patient literature that an increased interest in novel dosage forms that are retained in stomach for a prolonged and predictable period of time exists today in academic and industrial research groups. One of the most feasible approaches for achieving a prolonged and predictable drug delivery in the GI tract is to control the gastric residence time (GRT), i.e. gastro retentive dosage form (GRDFs or GRDS).

GRDFs extend significantly the period of time over which the drugs may be released. They not only prolong dosing intervals, but also increase patient compliance beyond the level of existing controlled release dosage form.

Approaches to Gastric Retention

Various approaches have been pursued to increase the retention of an oral dosage form in the stomach. These systems include: Floating systems, Bio adhesive systems, swelling and expanding systems, High density systems, Modified systems.

Floating Drug Delivery Systems (FDSS) have a bulk density lower than gastric fluids and thus remain buoyant in the stomach for a prolonged period of time, without affecting the gastric emptying rate. While the system is floating on the gastric contents, the drug is released slowly at a desired rate from the system. After the release of the drug, the residual system is emptied from the stomach. This results in an increase in the GRT and a better control of fluctuations in the plasma drug concentrations.

However, besides a minimal gastric content needed to allow the proper achievement of the buoyancy retention principle, a minimal level of floating force (F) is also required to keep the dosage form reliably buoyant on the surface of the meal. Many buoyant systems have been developed based on granules, powders, capsules, tablets, laminated films and hollow microspheres.^{5,6} Different dosage forms of FDSS with examples of various drugs. Factors Affecting Gastric-retention of Dosage Forms The most important parameters controlling the gastric retention time (GRT) of oral dosage forms include: density, size and shape of the dosage form, food intake and its nature, caloric content and frequency of intake, posture, gender, age, sex, sleep, body mass index, physical activity and diseased states of the individual (e.g. chronic disease, diabetes etc.) and administration of drugs with impact on gastrointestinal transit time.^{2, 3, 5, 8} Dosage forms having a density lower than the gastric contents can float to the surface, while high density systems sink to bottom of the stomach.¹⁵ A density of < 1.0 gm/ cm³ is required to exhibit floating property.⁸ In most cases, the larger the dosage form the greater will be the gastric retention time (GRT) due to the larger size of the dosage form would not allow this to quickly pass through the pyloric antrum into the intestine.¹⁶ Dosage forms having a diameter of more than 7.5 mm show a better gastric residence time compared with one having 9.9 mm. The presence of food in the gastrointestinal tract (GIT) improves the gastric retention time (GRT) of the dosage form and thus, the drugs absorption increases by allowing its stay at the absorption site for a longer period. Females have slower gastric emptying rates than male. The effect of posture does not have any significant difference in the mean gastric retention time (GRT) for individuals in upright, ambulatory and supine state. In case of elderly persons, gastric emptying is slowed down.¹⁶ local activity in the stomach, narrow absorption window in gastrointestinal tract (GIT), instability in the intestinal or colonic environment, disturbance of normal colonic microbes, low solubility at high pH values are some conditions for floating drug delivery system.

Classification of Floating Drug Delivery Systems (FDSS)

Floating drug delivery systems are classified depending on the use of two formulation variables: effervescent and non-effervescent systems.

Effervescent Floating Dosage Forms These are matrix types of systems prepared with the help of swellable polymers such as methylcellulose and chitosan and various effervescent compounds, e.g., sodium bicarbonate, tartaric acid and citric acid. They are formulated in such-a-way that when in contact with the acidic gastric contents, carbon dioxide is liberated and gets entrapped in swollen hydrocolloids, which provides buoyancy to the dosage forms.^{3,5}

Non-effervescent Floating Dosage Forms Non-effervescent floating dosage forms use a gel forming or swellable cellulose type hydrocolloids, polysaccharides, and matrix-forming polymers like polycarbonate, polyacrylate, polymethacrylate, and polystyrene. The formulation method includes a simple approach of thoroughly mixing the drug and the gel-forming hydrocolloid. After oral administration this dosage form swells in contact with gastric fluids and attains a bulk density of < 1. The air entrapped within the swollen matrix imparts buoyancy to the dosage form. The so formed swollen gel-like structure acts as a reservoir and allows sustained release of drug through the gelatinous mass.^{2, 3, 5, 8, 11}

Raft Forming Systems The formation of a viscous cohesive gel in contact with gastric fluids, wherein each portion of the liquid swells forming a continuous layer called a raft. This raft floats on gastric fluid because of the low bulk density created by the formation of CO₂. The system contains a gel forming agent and alkaline bicarbonates or carbonates responsible for the formation of CO₂ to make the system less dense and able to float on the gastric fluids.¹⁷

Advantages of Floating Drug Delivery System^{2, 5, 11, 17}

The gastroretentive systems are advantageous for drugs absorbed through the stomach. E.g. Ferrous salts, antacids. Acidic substances like aspirin cause irritation on the stomach wall when come in contact with it. Hence HBS formulation may be useful for the administration of aspirin and other similar drugs. Administration of prolongs release floating dosage forms, tablet or capsules, will result in dissolution of the drug in the gastric fluid. They dissolve in the gastric fluid would be available for absorption in the small intestine after emptying of the stomach contents. It is therefore expected that a drug will be fully absorbed from floating dosage forms if it remains in the solution form even at the alkaline pH of the intestine. The gastroretentive systems are advantageous for drugs meant for local action in the stomach. E.g. antacids. When there is a vigorous intestinal movement and short transit time as might occur in

certain type of diarrhoea, poor absorption is expected. Under such circumstances it may be advantageous to keep the drug in floating condition in stomach to get a relatively better response.

Disadvantages of Floating Drug Delivery System^{5, 17}

Floating system is not feasible for those drugs that have solubility or stability problem in G.I. tract. These systems require a high level of fluid in the stomach for drug delivery to float and work efficiently-coat, water. The drugs that are significantly absorbed through out gastrointestinal tract, which undergo significant first pass metabolism, are only desirable candidate. Some drugs present in the floating system causes irritation to gastric mucosa.

2. MATERIALS AND METHODS:

Materials:

Stavudine from Aarti drug Laboratories, Ltd. Thane. HPMC K15M, Xanthium gum and guar gum, MCC from S.D. Fine Chem. Ltd, Mumbai, India. HPMCK100M and Magnesium stearate from Degussa India Pvt Ltd., Mumbai L.R. Carbopol-974, Sodium CMC and Aerosol from Merck Specialties Pvt Ltd, Mumbai, India.

Methodology

Preformulation studies

Floating tablets of Stavudine were determined by the parameters like identification of pure drug by IR spectra, solubility, drug excipients, compatibility studies, angle of repose, bulk density, tapped density, Hausner ratio, Carr's index were evaluated

Fourier Transform infra-red (FTIR) spectroscopy:

Infrared spectroscopy is a useful analytical technique utilized to check the chemical interaction between the drug and excipients used in the formulation. 1-2 mg of solid fine powder of Stavudine and 200-300 mg of dry powder of KBr (IR grade) were taken in a mortar and mixed well with the help of a spatula. Spectrum measurement was carried out using KBr disk method in the wavelength region of 4000-400cm⁻¹ by FTIR spectrophotometer. The IR spectrum of the physical mixture was compared with that of the pure drug to check any possible drug-excipient interaction.

Preparation of stock solution:

Standard stock solution of Stavudine was prepared by dissolving 10mg of Etodolac in 10ml of methanol which gives 1000µg/ml solution. Preparation of working solution From the above stock solution 1ml was transferred into 10ml volumetric flask and The volume made was up to mark with 0.1N Hcl to give 100µg/ml. from this 2ml was pipetted out in to 10ml volumetric flask and made up to mark with 0.1N Hcl to give 20µg/ml Stavudine was scanned with UV is spectrophotometer in the range 200-400nm against methanol as blank and the wavelength corresponding to maximum absorbance was noted which is its max i.e., at 265nm.

Preparation of calibration curve:

0.2 ml-1ml of 100µg/ml solution were diluted and the volume was made up to 10ml using methanol to produce 2-10µg/ml solutions respectively. The absorbance calibration curves were plotted by taking concentration on x-axis and absorbance on y-axis, which shows a straight line. This straight line obeyed linearity in the concentration range of 2-10µg/ml. The correlation was found to be 0.999.

Formulation:

Direct Compression Method:

The drug and all other excipients were sifted through #40 sieves and mixed thoroughly. The above blend was pre lubricated with Carbopol-974, MCC and lubricated with magnesium stearate. Aerosol was used as glidant. Micro crystalline cellulose was used as diluent. Finally the powder mix was subjected to compression after mixing uniformly in a polybag. The above lubricated blend was compressed using standard flat faced punch on a sixteen station rotary tablet punching machine.

Evaluation Parameters:

The properties of the Floating tablet, such as hardness, friability, weight variation, drug content were determined standard procedures. Briefly, hardness was determined using Monsanto hardness tester. Friability was determined by using Roche friability testing apparatus. Weight variation and drug content were performed according to IP procedures.

3. RESULTS AND DISCUSSION:

Fig 4.6: Comparative FTIR Interpretation of Stavudine with Excipients

The wave number of mixture of drug with excipients is within the range of wave number of pure drug. This implies that the excipients are compatible with the drug since their combination did not alter the functional groups of pure drug. The comparative FTIR interpretation of Stavudine with excipients were shown in fig

Preformulation Studies

Standard graph of Stavudine in 0.1N Hcl:

The scanning of the volumetric solution of Stavudine in the ultraviolet range (200-400nm) against 0.1 N Hcl blank gave the λ_{\max} as 265nm.

The slope and intercept values were found to be **0.057** and **0.004** and the Coefficient of Correlation (R^2) was found to be 0.999. From the slope and intercept values it was found that the curve is having a positive slope and intercept. As the coefficient of correlation value is 0.999 the values are acceptable. The standard graph of Stavudine in 0.1N Hcl were shown in fig.

Flow properties:

Precompression parameters: The results were shown in Table 3. The values for angle of repose were found in the range of 25^0 - 30^0 . Bulk densities and tapped densities of various formulations were found to be in the range of 0.41 to 0.50 (gm/cc) and 0.50 to 0.58 (gm/cc) respectively. Carr's index of the prepared blends fall in the range of 13.06% to 18.18%. The Hausner ratio fall range of 1.14 to 1.22. From the result it was concluded that the powder blends had good flow properties and these can be used for tablet manufacture.

Post compression parameters:

The tablets were evaluated for weight variation, thickness, hardness, friability, swelling index, floating lag time, floating duration, drug content and *in-vitro* drug release study (table 6, fig 1-2). All the formulations passed the evaluation tests and showed comparable satisfactory results.

The thickness of all tablets was found to be in the range of 5.35-6.52 mm and hardness was found to be in the range of 10-11kg/cm² in all the formulations, the MCC and carbopol974 together showed good binding properties. In all the formulations, the %friability was (0.37-0.72) below 1% as per USP.

The average weight was found to be 999-1002mg which will be within the given limits. Hence all the tablets were found to show less weight variation.

The drug content of all formulations ranged from 99% to 100%, which is within the specified IP limits.

Swelling index was found to range from 30% to 45% within two hours' time period, which shows that the formulations swell to a certain degree after coming in contact with the simulated gastric medium. Also the swelling index of tablets containing xanthium showed lower % swelling index than that of the tablets with carbopol974 because of the fact that the polymer carbopol974 is a more viscous in nature. The results of formulations containing carbopol974 showed more values of swelling index than that of the ones containing xanthium because of the fact that the carbopol974 showed good swelling properties in the later periods of time and that the CO₂ evolved by NaHCO₃ was entrapped by the fast hydrating polymer, thus maintaining the tablet integrity for longer periods of time, enhancing the floating duration time to be 12hrs.

The floating lag time of the dosage forms made of carbopol974 and 20% of gas evolving agent were found to be satisfactory and were <5 min because carbopol974 is a hydrophilic polymer and that it swells fast when it comes in contact with 1.2 pH acidic buffer. But the tablets made of xanthium showed lesser FLT as its viscosity is less and that the polymer took even lesser time to form a matrix that could accommodate the evolved gas and also the entrapped gas bubbles during compression are more than that or the gas bubbles in matrices of carbopol974, a more viscous polymer. The tablets containing carbopol974 alone showed longer FLT as the tablets tend to disintegrate due to the fast release of CO₂ gas. Carbopol974(P) were such that the gas released by the bicarbonate could facilitate the floating of the tablets, which was aided by the fast matrix forming polymer and highly viscous gel forming polymer at the later stage of the drug dissolution, which is evident in the tablets showing a floating duration up to 12 hrs.

The % Cumulative drug release of all the formulations F₁, F₂, F₆, and F₇ were not sustained the drug release for 12 hrs. F₃, F₉ and F₁₀ formulations showed good integrity for 10 hrs. F₈ formulation was optimised based on the floating behaviour. The optimized formulation F₈ showed a % drug release of 97.8% for 12hrs which shows greater release compare to all other formulation.

Optimized formulations for preparation of Floating tablets:

Out of all formulations of floating tablets with Carbopol-974 as polymer, based on the results it was found that **F8** had optimum flow properties. Thus **F8** was selected as the optimized formulation among the Floating tablets with Carbopol-974 polymer for the preparation of Stavudine floating tablets.

Kinetic Analysis of Dissolution Data:

The results of dissolution data were fitted to various drug release kinetic equations (Table7, fig 3-6). Regression coefficient (R^2) value was highest for Korsmeyer-peppas release equation in formulation F₈, F₉ and F₁₀. The kinetics of dissolution data with R^2 value obtained from formulation F₁, F₂, F₃, F₄, F₅, F₆, F₇, F₈, F₉, F₁₀, F₁₁, F₁₂ were tabulated in table.

Formulation F8 plots of Zero order, First order, Higuchi and Korsmeyer-peppas are depicted. The Zero order drug release graph is plotted time taken on x-axis and the cumulative percentage of drug released on y-axis.

The First order drug release graph is plotted between by time taken on x-axis and the log cumulative percentage of drug remaining on y-axis. Higuchi's graph is plotted between the square root of time taken on x-axis and the cumulative percentage of drug released on y-axis. Korsmeyer-peppas drug release graph is plotted between the log time taken in x-axis and the log cumulative percentage of drug released on y-axis.

Among the various formulations studies, formulations F8 is considered as ideal formulation which exhibited 97.8% of drug release in 12 hours. The R^2 values of Korsmeyer-peppas model are found to be highest among all other models for these three formulations.

4. SUMMARY AND CONCLUSION:

To modulate the GI transit time so that the drug delivery system developed can be transported to a target site or to absorption site and reside there for a prolonged period of time to maximize the delivery of a drug dose. Conventional oral controlled dosage forms suffer from mainly two adversities. The short gastric retention time (GRT) and unpredictable gastric emptying time (GET).

The present work is carried out on anti-viral drug on gastro retentive drug delivery system, based on floating system by preparing floating tablets.

Floating dosage systems form important technological drug delivery systems with gastric retentive behavior and offer several advantages in drug delivery. To Improved drug absorption, because of increased GRT and more time spent by the dosage form at its absorption site Controlled delivery of drugs for local action in the stomach.

FDDS have a bulk densities than gastric fluids and so remain buoyant in the stomach without affecting the gastric emptying rate for a prolonged period of time. While the system is floating on the gastric contents, the drug is released slowly at the desired rate from the system. After release of drug, the residual system is eliminated from the stomach. This results in an increased GRT and a better control of the fluctuations in plasma drug concentration.

Floating tablets were prepared by direct compression method with drug: polymer ratios of Stavudine and Carbopol974 and the evaluation parameters of floating tablets were within the limits. The optimized formulation F8 showed the cumulative % drug release of 97.8%.

All the formulations were prepared by direct compression method. The prepared tablets of all the formulations were evaluated for physical characters, tablet density, hardness and friability, swelling index, floating lag time, total floating time, drug content and *in-vitro* drug release. The main aim was to optimize the formulation for 24 hrs. *in-vitro* release with the use of polymers.

Optimized formulation F₁₀ containing carbopol 974 was considered as the best product with respect to *in-vitro* drug release for 24 hrs. release and total floating time. Tablets of batch F₈ possessed quick buoyancy lag time and good total floating time of 24 hrs. The results showed that the drug release rate was decreased by increasing viscosity of the polymer.

S.No.	Concentration (µg/mL)	Absorbance (nm)
0	0	0
1	2	0.101
2	4	0.233
3	6	0.342
4	8	0.463
5	10	0.567
6	12	0.693

Table no: 1 Calibration curve for the estimation of Stavudine

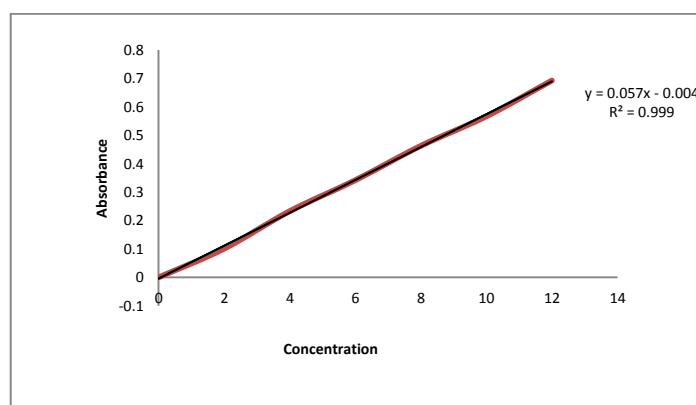


Fig no: 1 Standard graph of Stavudine in 0.1N HCl

Table 2: Composition of Formulations of Stavudine Containing HPMC (F1-F6)

Ingredients	F1(mg)	F2(mg)	F3(mg)	F4(mg)	F5(mg)	F6(mg)
Stavudine	30	30	30	30	30	30
HPMC K15m	30	60	-	-	-	-
HPMC K100m	-	-	30	60	-	-
Xanthium gum	-	-	-	-	30	60
Sod. bicarbonate	35	35	35	35	35	35
Magnesium stearate	2.5	2.5	2.5	2.5	2.5	2.5
Aerosil	2.5	2.5	2.5	2.5	2.5	2.5
MCC	100	70	100	70	100	70
Total weight	200	200	200	200	200	200

Table 3: Composition of Formulations of Stavudine containing (F7-F12)

Ingredients	F7(mg)	F8(mg)	F9(mg)	F10(mg)	F11(mg)	F12(mg)
Stavudine	30	30	30	30	30	30
Carbopol-974(p)	30	60	-	-	-	-
HPMC K4M	-	30	60	-	-	-
Sodium CMC	-	-	30	60	-	-
Guar gum	-	-	-	-	30	60
Sod. bicarbonate	35	35	35	35	35	35
Magnesium Stearate	2.5	2.5	2.5	2.5	2.5	2.5
Aerosol	2.5	2.5	2.5	2.5	2.5	2.5
MCC	100	70	100	70	100	70
Total weight	200	200	200	200	200	200

Table no: 4 Pre-Compression parameters:

Formulation	Angle of repose(ϕ)	Bulk density (gm/cm ²)	Tapped density (gm/cm ²)	Carrs index (%)
F1	25.71	0.51	0.66	14.33
F2	23.40	0.52	0.63	15.40
F3	26.12	0.58	0.68	16.35
F4	27.79	0.56	0.71	15.66
F5	27.79	0.53	0.64	16.96
F6	26.58	0.54	0.63	14.43
F7	30.11	0.52	0.63	17.93
F8	27.33	0.55	0.64	17.32
F9	25.85	0.53	0.65	17.48
F10	27.17	0.52	0.64	15.07
F11	26.55	0.54	0.67	19.19
F12	24.72	0.53	0.66	15.55

Table no: 5 Post compression parameters:

Formulation	Average weight(mg)	Thickness (mm)	Hardness (kg/cm ²)	Friability (%)	Floating Duration	Swelling index	Floating Lag Time
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F1	200	8.6±0.03	3.5±0.27	0.96±0.34	> 12hrs	30.66	12min
F2	199	8.1±0.09	3.0±0.13	0.95±0.38	>12hrs	33.91	8min
F3	200	8.5±0.20	3.3±0.25	0.95±0.41	<12hrs	40.33	10min
F4	200	8.6±0.22	3.3±0.13	0.93±0.37	>30min	33.11	4min
F5	201	8.8±0.17	3.5±0.25	0.95±0.31	<30min	30.18	10min
F6	199	8.0±0.05	3.8±0.13	0.94±0.27	<30min	43.55	7min
F7	201	8.4±0.18	3.9±0.22	0.94±0.23	>6hrs	45.65	2min
F8	200	8.0±0.15	4.4±0.14	0.98±0.32	>12hrs	41.75	1min
F9	201	8.6±0.20	4.1±0.31	0.91±0.25	<6hrs	43.44	25sec
F10	199	8.4±0.17	4.0±0.23	0.95±0.22	<6hrs	38.81	53sec
F11	199	8.1±0.05	3.9±0.45	0.95±0.54	>30min	37.52	59sec
F12	200	8.5±0.22	3.7±0.54	0.96±0.31	>30min	35.32	6min

Table no: 6 In vitro drug release study:

Table no: 6.1 Cumulative percentage drug release of F1, F2, F3, F4, F5, F6 formulation

Time(mins)	F1	F2	F3	F4	F5	F6
0	0	0	0	0	0	0
30	22.0	14.0	19.6	14.5	10.2	21.3
60	26.4	15.9	22.7	15.6	25.8	35.7
120	33.7	21.5	34	19.3	36.9	38
240	36	33.9	36.9	33.9	48	50.1
360	57	37.3	55.2	54	54.6	54.6
480	64.5	59.1	58.5	69.6	64.5	58.2
600	72.6	80.7	74.7	79	69.3	66.3
720	90.3	91.2	81.9	89.0	75.9	76.8

Table no: 6.2 Cumulative percentage drug release of F7, F8, F9, F10, F11, F12 formulations

Time(mins)	F7	F8	F9	F10	F11	F12
0	0	0	0	0	0	0
30	25.4	29.6	27.0	31.6	30.3	34.2
60	33	37.5	36.9	38.2	33.6	37.0
120	36.3	57.3	53.4	48	36.3	50.4
240	50.4	68.4	56.1	53.4	38.3	57.3
360	58.2	76.8	63.6	58.3	56.7	65.1
480	65.1	86.1	73.8	65.1	62.7	70.8
600	75	91.2	80.7	73.5	73.5	74.7
720	82.8	97.8	90.3	81.9	78.3	79.2

5 KINETIC ANALYSIS OF DISSOLUTION DATA:

Table no: 7 Kinetic analysis of dissolution data

Formulation code	Zero-order		First-order		Higuchi		Korsmeyer-Peppas		Best fit model
	Slope	R ²	slope	R ²	slope	R ²	slope	R ²	
F1	0.104	0.943	-0.001	0.896	3.025	0.962	0.428	0.932	Higuchi
F2	0.117	0.973	-0.001	0.877	3.255	0.910	0.599	0.928	Zero Order
F3	0.099	0.943	-0.000	0.962	2.899	0.976	0.452	0.960	Higuchi
F4	0.120	0.984	-0.001	0.962	3.418	0.956	0.631	0.939	Zero order
F5	0.094	0.888	-0.000	0.974	2.866	0.984	0.560	0.933	Higuchi
F6	0.082	0.837	-0.000	0.932	2.517	0.958	0.348	0.957	Higuchi
F7	0.093	0.892	-0.000	0.971	2.829	0.983	0.362	0.980	Higuchi

F8	0.112	0.828	-0.001	0.949	3.483	0.970	0.374	0.986	Peppas
F9	0.098	0.837	-0.001	0.946	3.027	0.962	0.348	0.971	Peppas
F10	0.083	0.801	-0.000	0.932	2.595	0.939	0.277	0.977	Peppas
F11	0.087	0.872	-0.000	0.953	2.604	0.945	0.304	0.872	First
F12	0.083	0.762	-0.000	0.926	2.637	0.932	0.274	0.985	Peppas

CUMULATIVE (%) RELEASE Q	TIME (T)	ROOT (T)	LOG (%) RELEASE	LOG (T)	LOG (%) REMAIN
0	0	0			2.000
29.6	30	5.477	1.471	1.477	1.848
37.5	60	7.746	1.574	1.778	1.796
57.3	120	10.954	1.758	2.079	1.630
68.4	240	15.492	1.835	2.380	1.500
76.8	360	18.974	1.885	2.556	1.365
86.1	480	21.909	1.935	2.681	1.143
91.2	600	24.495	1.960	2.778	0.944
97.8	720	26.833	1.990	2.857	0.342

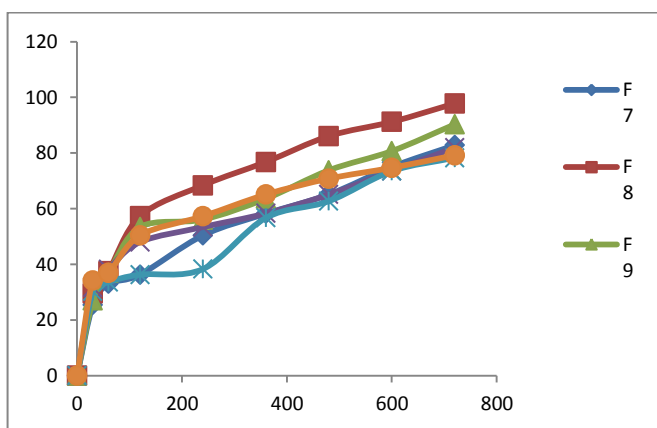
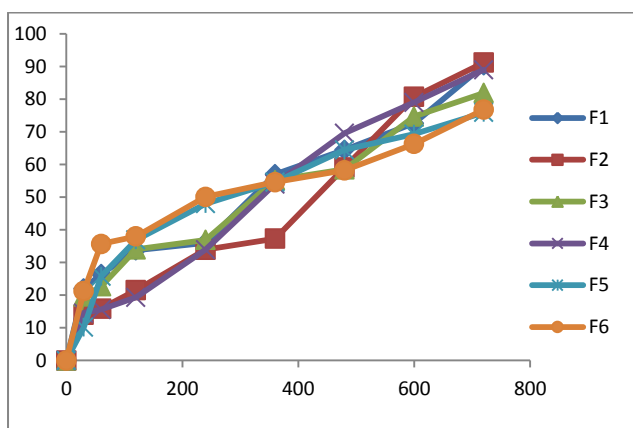


Fig 1: Cum % drug release F1, F2, F3, F4, F5, F6

Fig 2: Cum % drug release of F7, F8, F9, F10, F11, F12

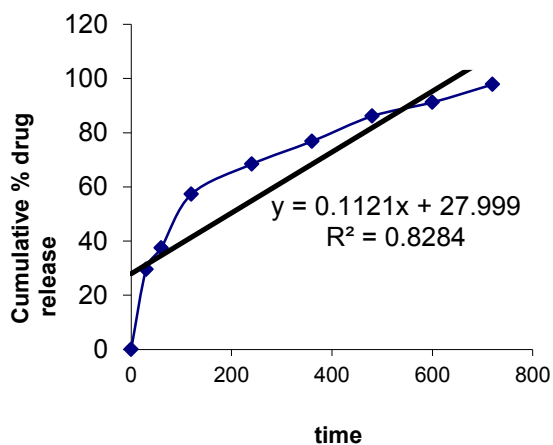


Fig no: 3 Zero order release kinetics graph

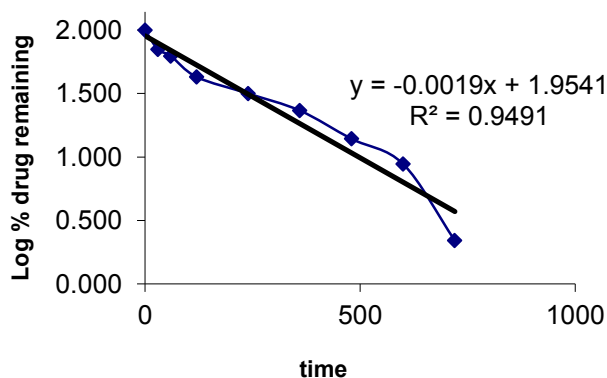


Fig no: 4 First order release kinetics graph

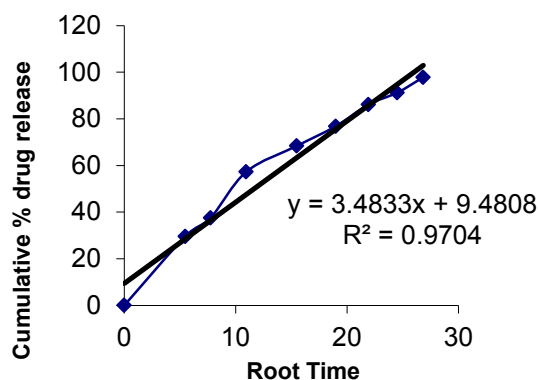


Fig no: 5 Higuchi release kinetics graph

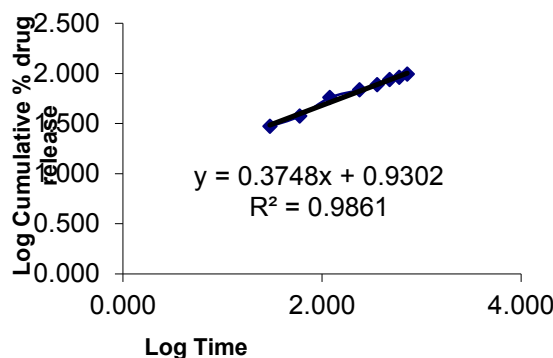


Fig no: 6 korsmeyer-peppas release kinetics graph

FT-IR (Fourier Transform Infrared Spectrophotometry)

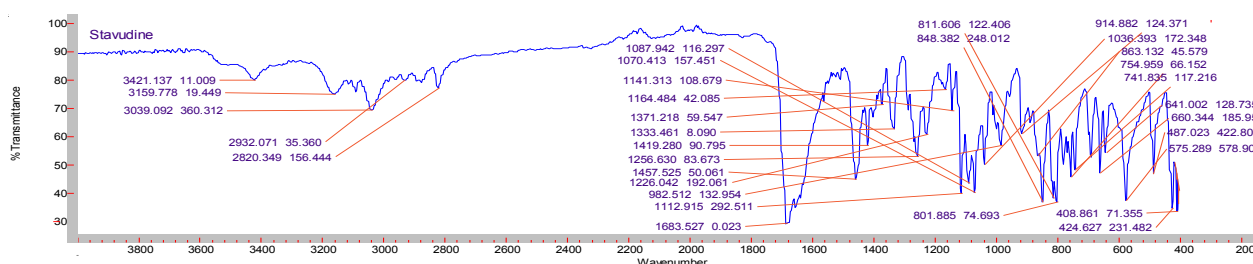


Fig no 7: FTIR spectra of Stavudine

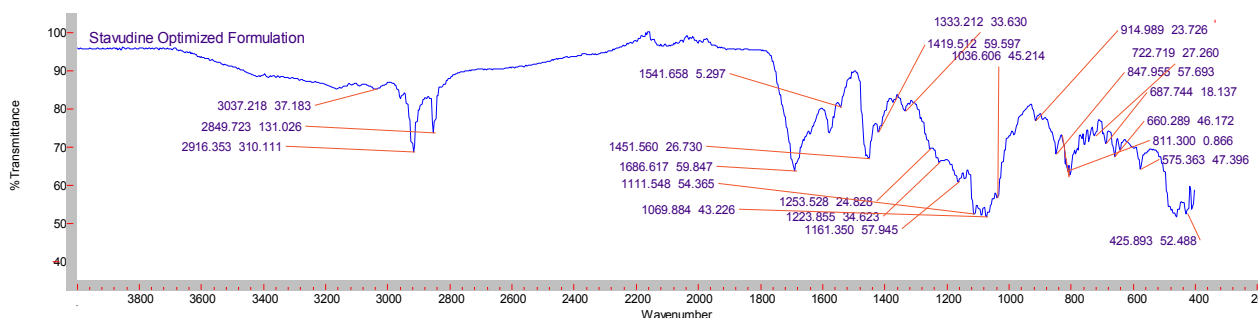


Fig no 8: FTIR spectra of Stavudine with Carbopol-974

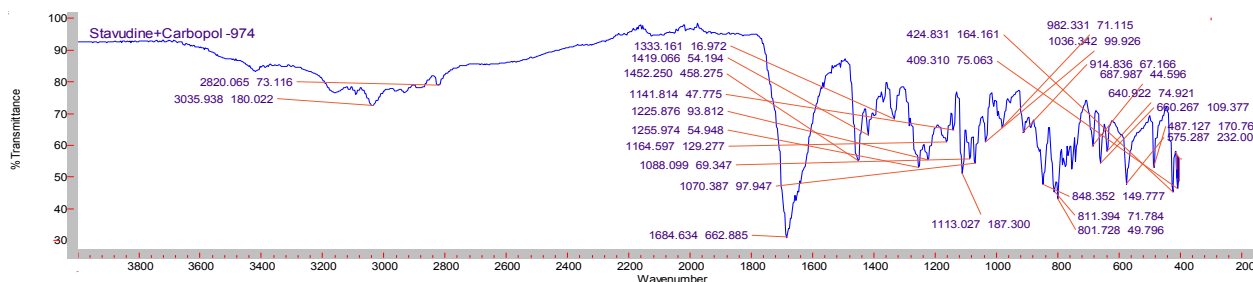


Fig 9: Comparative FTIR Interpretation of Stavudine with Excipients

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