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FORMULATION DEVELOPMENT AND *INVITRO* EVALUATION OF CONTROLLED RELEASE MATRIX TABLETS OF ABACAVIR

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Abstract:
The aim of the present study was to develop Abacavir controlled release tablets to maintain constant therapeutic levels of the drug for over 12 hrs. Carbopol974P, Xanthan Gum and HPMC K 15M were used as polymers. All the formulations were passed various physicochemical evaluation parameters such as Bulk Density, Tapped Density, Cars Index, Hauser's Ratio, Angle of Repose, Weight Variation, Hardness, Thickness, Friability and Drug Content. From the dissolution studies it was evident that the formulation F5 showed better and desired drug release pattern i.e.,99.16%in` 12hours. It contains the Xanthan Gums polymer.It followed peppas order release kinetics.

Key Words: *Abacavir, Carbopol974P, Xanthan` Gum and` HPMCK` 15M, Controlled` release tablets.*

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INTRODUCTION:

Controlled release tablets are commonly taken only once or twice daily, compared with counterpart conventionalformsthatmayhavetotakethreeorfourti mesdailytoachievethesametherapeuticeffect. The advantage of admin is tiring a single dose of a drug that is released over an extended period of time to maintain a near-constant or uniform blood level of a drug of ten translates into better patient compliance, as well as enhanced clinical efficacy of the drug for its intended use.

The first Controlled release tablets were made by Howard Pressing New Jersey in the early 1950's. The first tablets released under his process patent were called 'Nitroglyn' and made under license by Key Corp.in Florida.

Controlled release, prolonged release, modified release, extended release or depot formulations are terms used to identify drug delivery systems that are designed to achieve or extend therapeutic effect by continuously releasing medication over an extended period of time after administration of a single dose. The goal in designing Controlled or Controlled delivery systems is to reduce the frequency of the dosing or to increase effectiveness of the drug by localization at the site of action, reducing the dose required or providing uniform drug delivery. So, Controlled release dosage form is a dosage form that release one or more drugs continuously in predetermined pattern for a fixed period of time, either systemically or to a specified target organ.

Controlled released dosage forms provide a better control of plasma drug levels, less dosage frequency, less side effect, increased efficacy and constant delivery. There are certain considerations for the preparation of extended release formulations:

- ✓ If the active compound 'has a 'long half-life, it is Controlled on its own,
- ✓ Ifthepharmacologicalactivityoftheactiveisnotdire ctlyrelatedtoitsbloodlevels,
- ✓ If the absorption of the drug involves an active transport and
- ✓ If the active compound has very short half-life then it would require a large amount of drug to maintain a prolonged effective dose.

The above factors need serious review prior to design.

Introduction of matrix tablet as Controlled release (SR) has given a new breakthrough for novel drug delivery system in the field of Pharmaceutical technology. It excludes complex production procedures such as coating and Pelletization during manufacturing and drug release rate from the dosage form is controlled mainly by the type and` proportion of polymer used in` the preparations. Hydrophilic polymer matrix is widely used for formulating an SR dosage form. Because of increased complication and expense involved in marketing of new drug entities, has focused greater attention on development of Controlled release or controlled release drug delivery systems. Matrix systems are widely used for the purpose of Controlled release. It is the release system which prolongs and controls the release of the drug that is dissolved or dispersed.

In fact, a matrix is defined as a well-mixed composite of one or more drugs with gelling agent i.e. hydrophilic polymers. By the Controlled release method therapeutically effective concentration can be achieved in the systemic circulation over an extended period of time, thus achieving better compliance of patients. Numerous SR oral dosage forms such as membrane controlled system, matrices with water soluble/insoluble polymers or waxes and osmotic systems have been developed, intense research has recently focused on the designation of SR systems for poorly water soluble drugs.

RATIONALEFOREXTENDEDRELEASEDOSAGEFORMS[10-12]:

Some drugs are inherently long lasting and require only once-a-day oral dosing to sustain adequate drug blood levels and the desired therapeutic effect. These drugs are formulated in the conventional manner in immediate release dosage forms. However, many other drugs are not inherently long lasting and require multiple daily dosing to achieve the desired therapeutic results. Multiple daily dosing is inconvenient for the patient and can result in missed doses, made up doses, and noncompliance with the regimen. When conventional immediate-release dosage forms are taken on schedule and more than once daily, they cause sequential therapeutic blood level peaks and valleys (troughs) associated with the taking of each dose. However, when doses are not administered on schedule, the resulting peaks and valleys reflect less than optimum drug therapy. For example, if doses are administered too frequently, minimum toxic consent rations of drug may be reached, with toxic side effects resulting. If doses are missed, periods of sub therapeutic drug blood levels or those below the minimum effective concentration may result, with no benefit to the patient. Extended-release tablets and capsules are commonly taken only once or twice daily, compared with counterpart

conventional forms that may have to be taken three or four times daily to achieve the same therapeutic effect. Typically, extended- release products provide an immediate release of drug that promptly produces the desired therapeutic effect, followed by gradual release of additional amounts of drug to maintain this effect over a predetermined period(Fig.1).

The Controlled plasma drug levels provided by extended-release products oftentimes eliminate the need for night dosing, which bene fits not only the patient but the care giver as well.

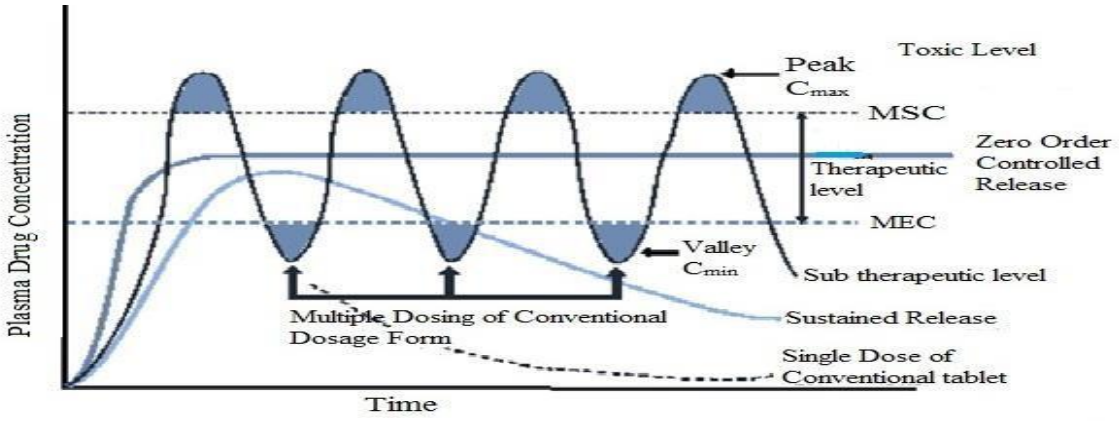

Figure 1.1: Hypothetical plasma concentration-time profile from conventional multiple dosing and single doses of Controlled and controlled delivery formulations.

DrawbacksofConventionalDosageForms[13]:

1. Poor patient compliance, increased chances of missing the dose of a drug with short half-life for which frequent administration is necessary.
2. A typical peak-valley plasma concentration time profile is obtained which makes attainment of steady-state condition difficult.
3. The fluctuations in drug levels may lead to precipitation of adverse effects especially of a drug with small Therapeutic Index (TI) when ever over medication occur.

TERMINOLOGY[14,15]: Modified release delivery systems may be divided conveniently in to four categories.

A) Delayed release
B) Controlled release
✓ Controlled release
✓ Extended release C) Site specific targeting D) Receptor targeting

Delayed Release:
These systems are those that use repetitive, intermittent dosing of a drug from one or more immediate release units incorporated into a single dosage form. Examples of delayed release systems include repeat action tablets and capsules and enteric-coated tablets where timed release is achieved by a barrier coating.

Controlled release:
During the last two decades there has been remarkable increase in interest in Controlled release drug delivery system. This has been due to various factor viz. the prohibitive cost of developing new drug entities, expiration of existing international patents, discovery of new polymeric materials suitable for prolonging the drug release, and the improvement in therapeutic efficiency and safety achieved by these delivery systems. Now-a-days the technology of Controlled release is also being applied to veterinary products. These systems also provide a slow release of drug over an extended period of time and also can provide some control, whet her this be of a temporal or spatial nature, or both, of drug release in the body, or in other words, the system is successful at maintaining constant drug levels in the target tissue or cells.

Controlled Release: These systems include any drug delivery system that achieves slow release of drug over an extended period of time.

Extended Release: Pharmaceutical dosage forms that release the drug slower than normal manner at pre determined rate& necessarily reduce the dosage frequency by two folds.

Site specific targeting: These systems refer to targeting of a drug directly to a certain biological location. In this case the target is adjacent to or in the diseased organ or tissue.

Receptor targeting: These systems refer to targeting of a drug directly to a certain biological location. In this case the target is the particular receptor for a drug within an organ or tissue. Site specific targeting and receptor targeting systems satisfy the spatial aspect of drug delivery and are also considered to be Controlled drug delivery systems.

METHODOLOGY:

2.1Analyticalmethoddevelopment:

Determination of absorption maxima: 100mg of Abacavir pure drug was dissolved in 100ml of Methanol (stock solution)10ml of above solutionwastakenandmakeupwith100mlbyusing 0.1 NHCL (100µg/ml).From this 10mlwastaken and make upwith100ml of 0.1NHCL (10µg/ml).andpH6.8PhosphatebufferUVspectrumsw astaken using DoublebeamUV/VISspectrophotometer.Thesolution wasscannedintherangeof 200–400nm.

Preparation calibration curve: 100mg of Abacavir pure drug was dissolved in 100ml of Methanol (stock solution)10ml of above solution was taken andmakeupwith100mlbyusing 0.1 NHCL (100µg/ml).From this 10mlwastaken and make up with 100 ml of 0.1 N HCL (10µg/ml). The above solution was sub sequently diluted with0.1N HCL to obtain series of dilutions Containing 5,10,15,20 and 25 µg/ml of Abacavir per ml of solution. The absorbance of the above dilutions was measured at 275 nm by using UV- Spectrophotometer taking 0.1N HCL as blank. Then a graph was plotted by taking C on centration on X- Axis and Absorbance on Y-Axis which gives a straight line Linearity of standard curve was assessed from the square of correlation coefficient (R^2) which determined by least-square linear regression analysis. The above procedure was repeatedbyusingpH6.8phosphate buffer solutions.

Pre formulation parameters: The quality of tablet, once formulated by rule, is generally dictated by the quality of physicochemical properties of blends. There are many formulations and process variables involved in mixing and all these can affect the characteristics of blends produced. The various characteristics of blends tested as per Pharmacopoeia.

Angle of repose: The frictional force in a loose powder can be measured by the angle of repose. It is defined as, the maximum angle possible between the surface of the pile of the powder and the horizontal plane. If more powder is added to the pile, it slides down the sides of the pile until the mutual friction of the particles producing a surface angle, is in equilibrium with the gravitational force. The fixed funnel method was employed to measure the angle of repose. A funnel was secured with its tip at a given height (h), above a graph paper that is placed on a flat horizontal surface. The blend carefully pored through the funnel until the apex of the conical pile just touches the tip of the funnel. The radius (r) of the base of the conical pile was measured. The angle of repose was calculated using the following formula:

Tan θ=h/r Tanθ=Angle of repose h =Height of the cone, r=Radius of the cone base

Table2.1: Angle of Repose values (as per USP)

Angle of Repose	Nature of Flow
<25	Excellent
25-30	Good
30-40	Passable
>40	Very poor

Bulk density: Density is defined as weight per unit volume. Bulk density, is defined as the mass of the powder divided by the bulk volume and is expressed as gm/cm^3. The bulk density of a powder primarily depends on particle size distribution, particle shape and the tendency of particles to adhere together. Bulk density is very important in the size of containers handling, shipping, and of raw material and blend. It is also important in size blending equipment. 10 gm powder blend was sieved and introduced into a dry 20 ml cylinder, without compacting. The powder was carefully leveled without compacting and the unsettled apparent 'volume, Vo, was read. The bulk density was calculated using the formula: Bulk Density=M /V_o

Where, M=weight of sample V_o= apparent volume of powder.

Tapped density: After carrying out the procedure as given in the measurement of bulk density the cylinder containing the sample was tapped using a suitable mechanical tapped density tester that provides 100 drops per minute and this was repeated until difference between succeeding measurement is less than 2% and then tapped volume, V measured ,to the nearest graduated unit. The tapped
Density was calculated,in gm per L, using the formula:

Tap=M/V
Where, Tap=Tapped Density

M=Weightof sample V=Tapped volume of powder

Measures of powder compressibility: The Compressibility Index (Carr's Index) is a measure of the propensity of a powder to be compressed. It is determined from the bulk and tapped densities. In theory, the less compressible a material the more flowable it is. As such, it is measures of the relative importance of inter particulate interactions. In a free-flowing powder, such interactions are generally less significant, and the bulk and tapped densities will be closerin value. For poorer flowing materials, there are frequently greater in therpartic leinteractions, and a greater difference between the bulk and tapped densities will be observed. These differences are reflected in the Compressibility Index which is calculated using the following formulas:
Carr's Index=[(tap-b)/tap]×100

Where, b=Bulk Density Tap=Tapped Density

Table2.2: Carr's index value (as per USP)

Carr'sindex	Properties
5–15	Excellent
12–16	Good
18–21	Fair to Passable
2–35	Poor
33–38	Very Poor
>40	Very very Poor

2.2.1formulation Development of Tablets: All the formulations were prepared by direct compression. The compositions of different formulations are given in Table 6.3. The tablets were prepared as per the procedure given below and aimistoprolongthereleaseofAbacavir.Totalweightoft hetabletwasconsideredas300mg.

Procedure:

1. Abacavir and all other ingredients were individually passed through sieve no 60.
2. Alltheingredientsweremixedthoroughlybytriturati ngupto15min.
3. The powder mixture was lubricated with talc.
4. The tablets wereprepared by using direct compression method.

Table2.3: Formulation composition for tablets

INGREDIENTS	FORMULATIONCODE											
	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
Abacavir	100	100	100	100	100	100	100	100	100	100	100	100
Carbopol974P	20	40	60	80	-	-	-	-	-	-	-	-
Xanthan Gum	-	-	-	-	20	40	60	80	-	-	-	-
HPMCK 15M	-	-	-	-	-	-	-	-	20	40	60	80
MCC	171	151	131	111	171	151	131	111	171	151	131	111
Magnesium Stearate	4	4	4	4	4	4	4	4	4	4	4	4
Talc	5	5	5	5	5	5	5	5	5	5	5	5
Total Weight(mg)	300	300	300	300	300	300	300	300	300	300	300	300

All the quantities were in mg Total Tablet Weight=300mg

2.2Evaluation of post compression parameters for prepared Tablets: The designed formulation tablets were studied for their physicochemical properties like weight variation, hardness, thickness, friability and drug content.

Weight variation test: To study the weight variation, twenty tablets were taken, and their weight was determined individually and collectively on a digital weighing balance. The average weight of one tablet was determined from the collective weight.

The weight variation test would be a satisfactory method of deter mining the drug content uniformity. Not more than two of the individual weights deviate from the average weight by more than the percentage shown in the following table and none deviate by more than twice the percentage. The mean and deviation were determined. The percent deviation was calculated using the following formula.
%Deviation = (Individual weight –Average weight/Average weight) ×100

Table 2.4: Pharmacopoeial specifications for tablet weight variation

rageweightoftablet (mg)(I.P)	rageweightoftablet (mg)(U.S.P)	Maximumpercentage differenceallowed
Lessthan80	Lessthan130	10
80-250	130-324	7.5
Morethan	Morethan324	5

Hardness: Hardness of tablet is defined as the force applied across the diameter of the tablet in order to break the tablet. The resistance of the tablet to chipping, abrasion or breakage under condition of storage Transformation and handling before usage depends on its hardness. For each formulation, the hardness of three tablets was determined using Monsanto hardness tester and the average is calcula ted and presented with deviation.

Thickness: Tablet thickness is an important characteristic in reproducing appearance. Tablet thickness is an important characteristic in reproducing appearance. Average thickness for core and coated tablets is calculated and presented with deviation.

Friability:

It is measured of mechanical strength of tablets. Roche friabilator was used to determine the friability by following procedure. Pre weighed tablets were placed in the friabilator. The tablets were rotated at 25 rpm for 4 minutes (100 rotations). At the end of test, the tablets were re weighed, loss in the weight of tablet is the measure of friability is expressed in percentage as

%Friability=[(W1-W2)/W]×100

Where, W1=Initial weight of three tablets W2=Weight of the three tablets after testing

Determination of drug content: Tablets were tested for their drug content. Ten tablets were finely powdered quantities of the powder equivalent to one tablet weight of drug were accurately weighed, transferred to a 100 ml volumetric flask containing 50 ml water and were allowed to stand to ensure complete solubility of the drug. The mixture was made up to volume with media. The solution was suitably diluted and the absorption was determined by UV –Visible spectrophotometer. The drug concentration was calculated from the calibration curve.

***In vitro* drug release studies Dissolution parameters:**

Apparatus	--	USP-II, Paddle Method
Dissolution Medium	--	0.1NHCL,pH6.8Phophatebuffer
RPM	--	50
Samplingintervals(hrs)	--	0.5,1,2,3,4,5,6,7,8,10,11,12
Temperature	--	37°c±0.5°c

Procedure: 900ml 0f 0.1 HCL was placed in vessel and the USP apparatus –II (Paddle Method) was assembled. The medium was allowed to equilibrate to temp of 37°c ± 0.5°c. Tablet was placed in the vessel and apparatus was operated for 2 hours and then the media 0.1 N HCL was removed and pH 6.8 phosphatebuffer was added process was continued from upto 12 hrs at 50 rpm. At defi nite time intervals withdrawn 5 ml of sample, filtered and again 5ml media was replaced. Suitable dilutions were done with media and analyzed by spectrophotometrically at 275 and 282 nm using UV-spectrophotometer.

Application of Release Rate Kinetics to Dissolution Data: Various models were tested for explaining the kinetics of drug release. To analyze the mechanism of the drug release rate kinetics of the dosage form, the obtained data were fitted into zero-order, first order , Higuchi, and Korsmeyer Peppas release model.

Zero order release rate kinetics: To study the zero–order release kinetics there lease rated at a are fitted to the following equation. $F=K_o$ t Where, 'F' is the drug release at time 't', and 'K_o' is the zero order release rate constant. The plot of %drug release versus time is linear.

First order release rate kinetics: The release rate data are fitted to the following equation

Log(100-F)=kt
A plotoflogcumulativepercentofdrug remaining to be released vs .time is plotted then it gives first order release.

Higuchi release model: To study the Higuchi release kinetics, the release rate data were fitted to the following equation.

F=kt1/2 Where, 'k' is the Higuchi constant. In higuchi model, a plot of %drug release versus square root of time is linear.

Korsmeyer and Peppas release model: The mechanism of drug release was evaluated by plotting the log percentage of drug released versus log time according to Korsmeyer-

Hixson-Crowell release model:

$(100-Q_t)^{1/3}=100^{1/3}–K_{HC}.t$

Where, k is the Hixson-Crowell rate constant.

Hixson-Crowell model describes the release of drugs from an insoluble matrix through mainly erosion. (Where the thereisa change in surface area and diameter of particles or tablets).

2.4. Drug–Excipient compatibility studies Fourier Transform Infra-red(FTIR) spectroscopy: The physical properties of the physical mixture were compared with those of plain drug. Samples was mixed thoroughly with 100mg potassium bromide IR powder and compacted under vacuum at a pressure of about 12 psi for 3 minutes. The resultant disc was mounted in a suitable holder in IR spectrophotometer and the IR spectrum was recorded from 4000 cm to 550 cm^{-1}. The result any spectrum was compared for any spectrum changes.

Peppas equation. The exponent 'n' indicates the mechanism of drug release calculated through the slope of the straight Line.

$M_t/M_\infty = K\ t^n$

Where, M_t/M_∞ is fraction of drug released at time 't', k represents a constant, and 'n' is the diffusional exponent, which characterizes the type of release mechanism during the dissolution process. For non-Fickian release, the value of n falls between 0.5 and 1.0; while in case of Fickian diffusion, n = 0.5; for zero-order release (case II transport), n=1; and for super case II transport, n > 1. In this model, a plot of log (M_t/M_∞) versus log(time) is linear.

RESULTS AND DISCUSSION:

The present study was aimed to developing Controlled release tablets of Abacavir using various polymers. All the formulations were evaluated for physicochemical propertie sand *in vitro* drug release studies.

3.1. Analytical Method: Graphs of Abacavir was taken in Simulated Gastric fluid (pH 1.2) and in pH 6.8 phosphate buffer at 275 nm and 282 nm respectively.

Table3.1: Observations for graph of Abacavir in0.1NHCl(275)

Concentration [µg/mL]	Absorbance
0	0
5	0.132
10	0.241
15	0.369
20	0.478
25	0.582

It was found that the estimation of Abacavir by UV spectrophotometric method at λ_{max}275.0nm in 0.1N Hydrochloric acid had good reproducibility and this method was used in the study. The correlation coefficient for the standard curve was found to be closer to 1, at the concentration range, 5- 25µg/ml. The regression equation generated was y=0.023x+0.009

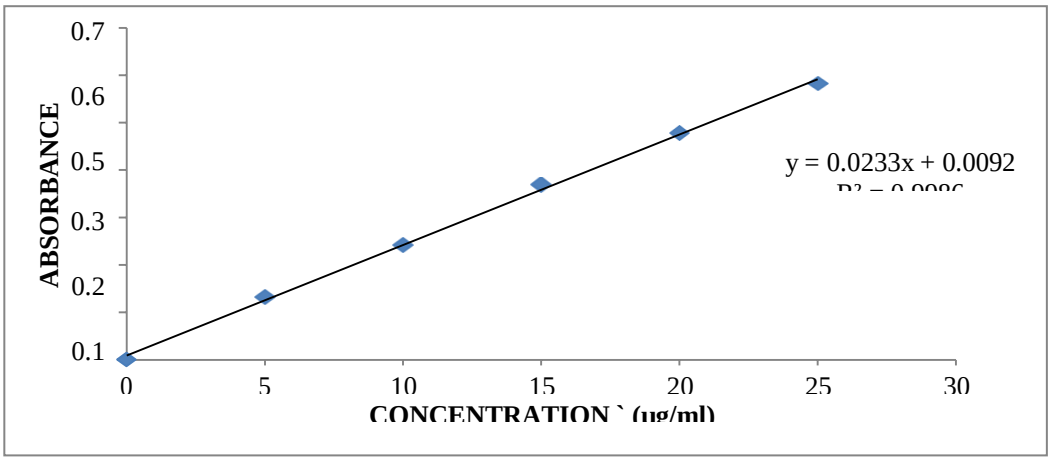

Figure3.1: Standard graph of Abacavir in 0.1NHCl

Table3.2: ObservationsforgraphofAbacavirinpH6.8phosphatebuffer(282nm)

Conc [µg/ml]	Abs
0	**0**
5	**0.117**
10	**0.248**
15	**0.359**
20	**0.471**
25	**0.594**

It was found that the estimation of Abacavir by UV spectrophotometric method at λ_{max} 282 nm in pH 6.8 Phosphate buffer. had good reproducibility and this method was used in the study. The correlation coefficient for the standard curve was found to be closer to 1, at the concentration range, 5-25µg/ml. The regression equation generated was y=0.023x+0.002.

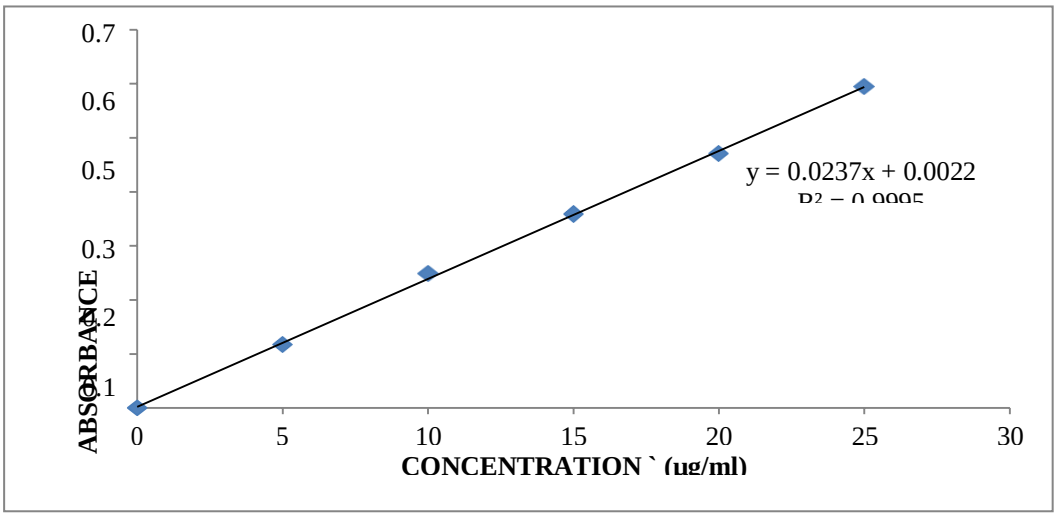

Figure3.2: StandardgraphofAbacavirpH6.8 phosphate buffer(282nm) 3.2. Pre formulation parameter so powder blend

Table3.3: Pre-formulation parameters of Core blend

Formulation Code	Angle of Repose	Bulk density (gm/ml)	peddensity (gm/ml)	Carr's index (%)	lausner's Ratio
F1	24.2	0.419	0.486	13.95	1.162
F2	24.5	0.409	0.485	15.68	1.186
F3	25.2	0.409	0.480	14.77	1.173
F4	27.8	0.429	0.488	12.14	1.138
F5	27.2	0.450	0.501	10.25	1.114
F6	26.4	0.462	0.522	11.54	1.130
F7	30.2	0.450	0.507	11.25	1.127
F8	29.3	0.439	0.504	12.93	1.148
F9	28.5	0.462	0.526	12.31	1.140
F10	28.0	0.450	0.500	10.00	1.111
F11	27.5	0.439	0.496	11.46	1.129
F12	28.3	0.429	0.493	13.10	1.151

Tablet powder blend was subjected to various pre-formulation parameters. The angle of repose values indicates that the powder blend has good flow properties. The bulk density of all the formulations was found to be in the range of 0.409 to 0.450 (gm/cm3) showing that the powder has good flow properties. The tapped density of all the formulations was found to be in the range of 0.480 to 0.526 showing the powder has good flow properties. The compressibility index of all the formulations was found to be ranging between 12.14 to 15.68 which shows that the powder has good flow properties. All the formulations has shown the hausner ratio ranging between 1.111 to 1.173 indicating the powder has good flow properties.

3.3. Quality Control Parameters For tablets: Tablet quality control tests such as weight variation, hardness, and friability, thickness, and drug release studies in different media were performed on the compression coated tablet.

TABLE: 3.4. *In vitro* quality control parameters fo r tablets

Formulation codes	Average Weight (mg)	Hardness(kg/cm2)	Friability (%loss)	Thickness (mm)	Drug` content (%)
F1	298.15	5.1	0.25	4.31	98.68
F2	299.65	5.3	0.41	4.68	97.35
F3	295.79	5	0.63	4.39	99.25
F4	300.02	5.9	0.58	4.82	96.9
F5	297.32	5.6	0.49	4.93	97.58
F6	298.54	5.7	0.11	4.52	99.12
F7	299.78	5.8	0.57	4.33	98.45
F8	300	5.1	0.62	4.27	97.65
F9	297.28	5.9	0.75	4.12	99.1
F10	299.82	5.4	0.61	4.96	100
F11	299.1	5.6	0.38	4.86	97.52
F12	300.1	5.9	0.27	4.33	99.44

All the parameters such as weight variation, friability, hardness, thickness and drug content were found To be within limits.

3. 3 In Vitro Drug Release Studies

Table3.5: Dissolution Data of Abacavir Tablets Prepared With Carbopo l974P Different Concentrations

TIME	CUMULATIVEPERCENTDRUGDISSOLVED			
(hr)	F1	F2	F3	F4
0	**0**	**0**	**0**	**0**
0.5	16.4	13.2	9.6	9.28
1	23.7	15.8	12.3	13.4
2	31.6	17.2	14.8	19.75
3	40.4	22.8	18.9	26.05
4	53.4	33.3	22.3	30.58
5	59.4	39.2	33.9	40.04
6	65.4	47.8	38.7	47.96
7	71.5	56.4	44.8	52.45
8	87.3	59.9	53.6	56.11
9	97.45	62.2	66.6	63.74
10	99.2	72.8	72.8	68.91
11		83.8	79.5	70.04
12		89.2	81.2	78.74

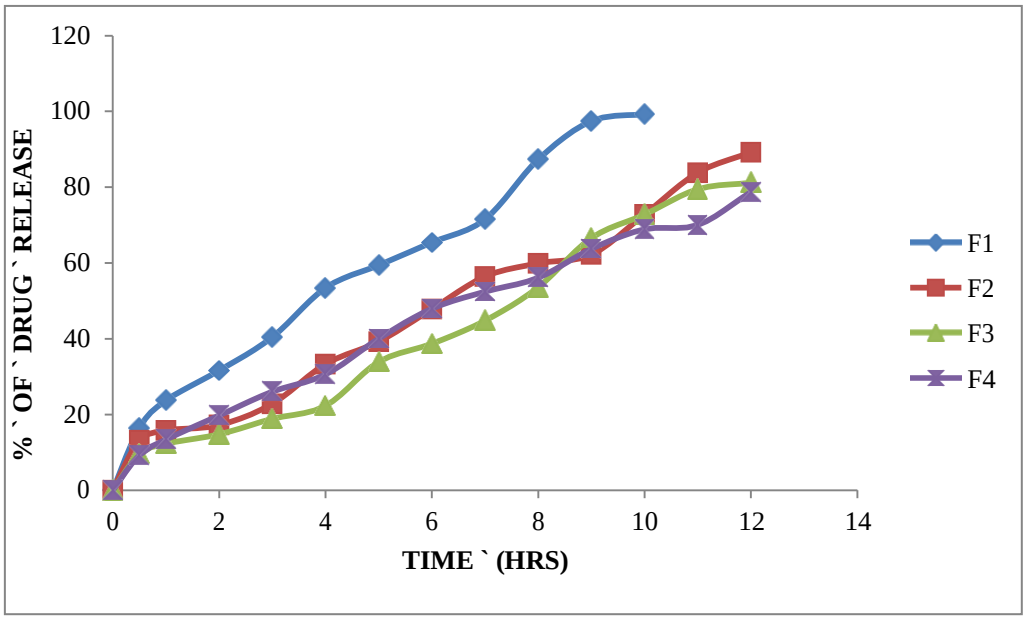

Fig 3.3: Dissolution profile of Abacavir (F1, F2, F3 and F4 formulations).

Table3.6: Dissolution Data of Abacavir Tablets Prepared With Xanthan Gum In Different Concentrations

TIME	CUMULATIVEPERCENTDRUGDISSOLVED			
(hr)	F5	F6	F7	F8
0	0	0	0	0
0.5	09.61	8.59	9.28	10.22
1	18.06	17.56	13.40	17.97
2	24.35	25.70	19.75	28.22
3	34.59	39.05	26.05	37.35
4	41.78	44.9	30.58	41.10
5	48.35	58.54	40.04	45.34
6	56.50	63.54	47.96	52.23
7	64.52	65.47	58.45	58.76
8	70.90	70.17	66.11	63.38
9	75.53	74.36	72.74	69.45
10	81.27	79.67	78..91	74.56
11	89.19	85.75	80.04	76.12
12	99.16	90.48	84.74	79.27

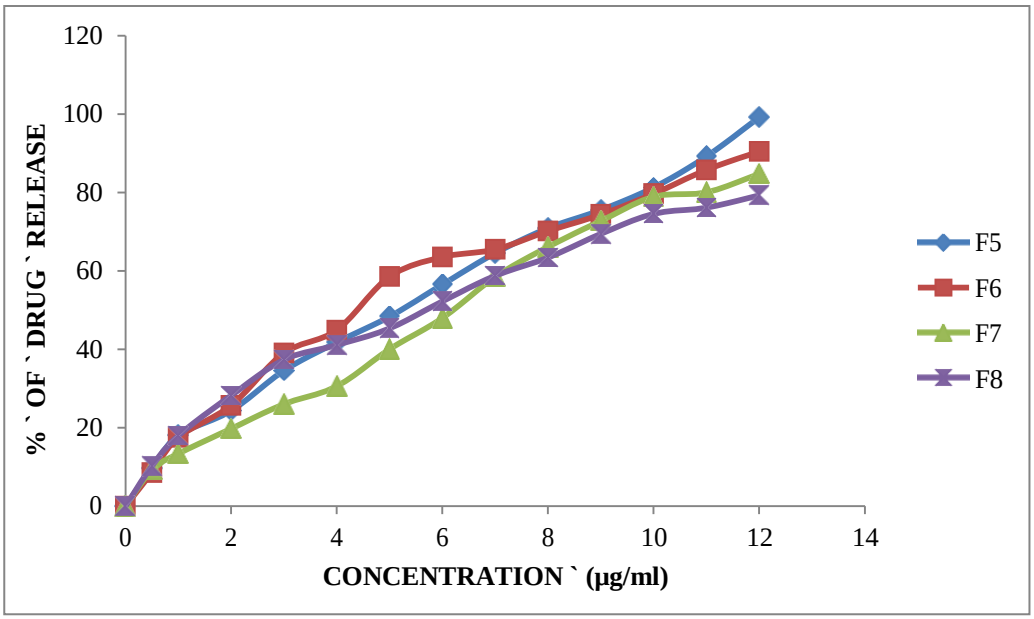

Fig 3.4: Dissolution profile of Abacavir (F5, F6, F7 and F8 formulations)

Table 3.7: Dissolution Data of Abacavir Tablets Prepared With HPMCK15InDifferent Concentrations

TIME (hr)	CUMULATIVEPERCENTDRUGDISSOLVED			
	F9	F10	F11	F12
0	0	0	**0**	**0**
0.5	12.63	9.14	7.23	13.28
1	24.87	26.05	13.24	15.87
2	33.41	33.52	29.06	17.29
3	40.54	48.45	37.25	22.85
4	46	56.74	49.98	33.32
5	54.1	64.86	54.57	39.21
6	66.06	69.52	69.67	47.86
7	75.28	73.29	72.5	56.47
8	88.95	77.19	81.6	59.93
9	95.72	81.87	87.34	62.24
10		90.78	90.17	72.88
11		98.31	93.23	83.42
12			98.64	89.12

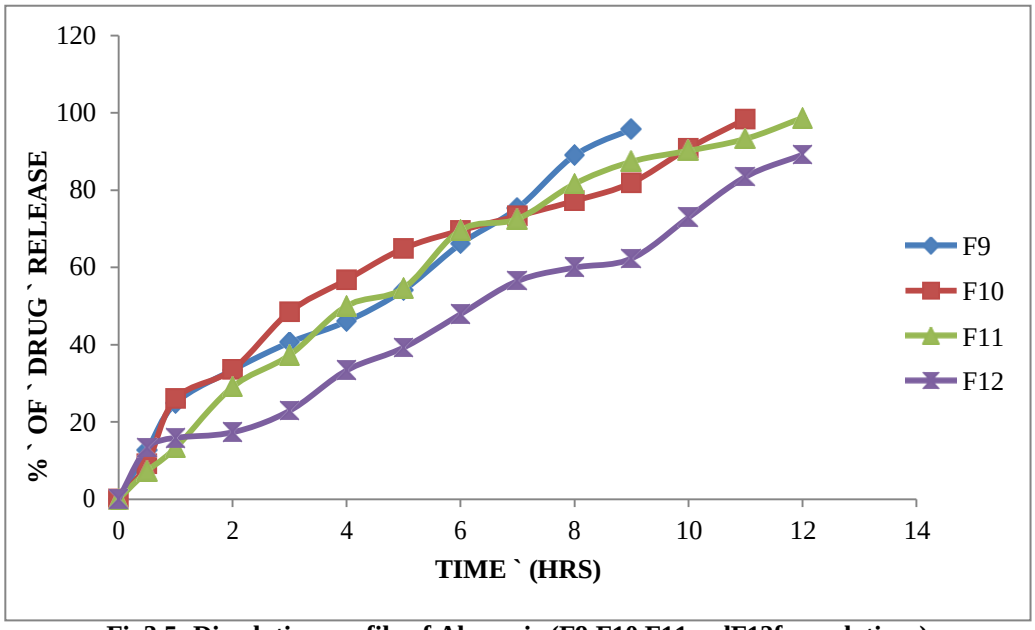

Fig3.5: Dissolution profile of Abacavir (F9,F10,F11andF12formulations)

From the dissolution data it was evident that the formulations prepared with Carbopol974P as polymer were able to retard the drug release euptodesiredtimeperiodi.e.,12hours.

The formulations prepared with Xanthan Gum were able retarded the drug release. they were shown total drug release.
Whereas the formulations prepared with HPMC K 15M were retarded the drug release in the concentration of 60 mg (F11 Formulation) showed required release pattern i.e., retarded the drug releaseupto12hours and showed maximum of 98.64%in 12hourswithgoodretardation.

From the above results it was evident that the formulationF5 is best formulation with desired drug release pattern extended upto12hours.

Application of Release Rate Kinetics to Dissolution Data: Various models were tested for explaining the kinetics of drug release. To analyze

the mechanism of the drug release rate kinetics of the dosage form, the obtained data were fitted into zero-order, first order, Higuchi,and Korsmeyer - Peppas releasemodel.

Table3.8: Release kinetics data for optimized formulation

CUMULATIVE (%) RELEASE Q	TIME (T)	ROOT (T)	LOG(%) RELEASE	LOG (T)	LOG (%) REMAIN	RELEASE RATE (CUMULATIVE % RELEASE / t)	1/CUM% RELEASE	PEPPAS log Q/100	% Drug Remaining	Q01/3	Qt1/3	Q01/3-Qt1/3
0	**0**	0			2.000				100	4.642	4.642	0.000
9.61	**0.5**	0.707	0.983	-0.301	1.956	19.220	0.1041	-1.017	90.39	4.642	4.488	0.154
18.06	**1**	1.000	1.257	0.000	1.913	18.060	0.0554	-0.743	81.94	4.642	4.343	0.298
24.35	**2**	1.414	1.386	0.301	1.879	12.175	0.0411	-0.614	75.65	4.642	4.229	0.412
34.59	**3**	1.732	1.539	0.477	1.816	11.530	0.0289	-0.461	65.41	4.642	4.029	0.612
41.78	**4**	2.000	1.621	0.602	1.765	10.445	0.0239	-0.379	58.22	4.642	3.876	0.766
48.35	**5**	2.236	1.684	0.699	1.713	9.670	0.0207	-0.316	51.65	4.642	3.724	0.917
56.5	**6**	2.449	1.752	0.778	1.638	9.417	0.0177	-0.248	43.5	4.642	3.517	1.125
64.52	**7**	2.646	1.810	0.845	1.550	9.217	0.0155	-0.190	35.48	4.642	3.286	1.356
70.9	**8**	2.828	1.851	0.903	1.464	8.863	0.0141	-0.149	29.1	4.642	3.076	1.566
75.53	**9**	3.000	1.878	0.954	1.389	8.392	0.0132	-0.122	24.47	4.642	2.903	1.738
81.27	**10**	3.162	1.910	1.000	1.273	8.127	0.0123	-0.090	18.73	4.642	2.656	1.986
89.19	**11**	3.317	1.950	1.041	1.034	8.108	0.0112	-0.050	10.81	4.642	2.211	2.430
99.16	**12**	3.464	1.996	1.079	-0.076	8.263	0.0101	-0.004	0.84	4.642	0.944	3.698

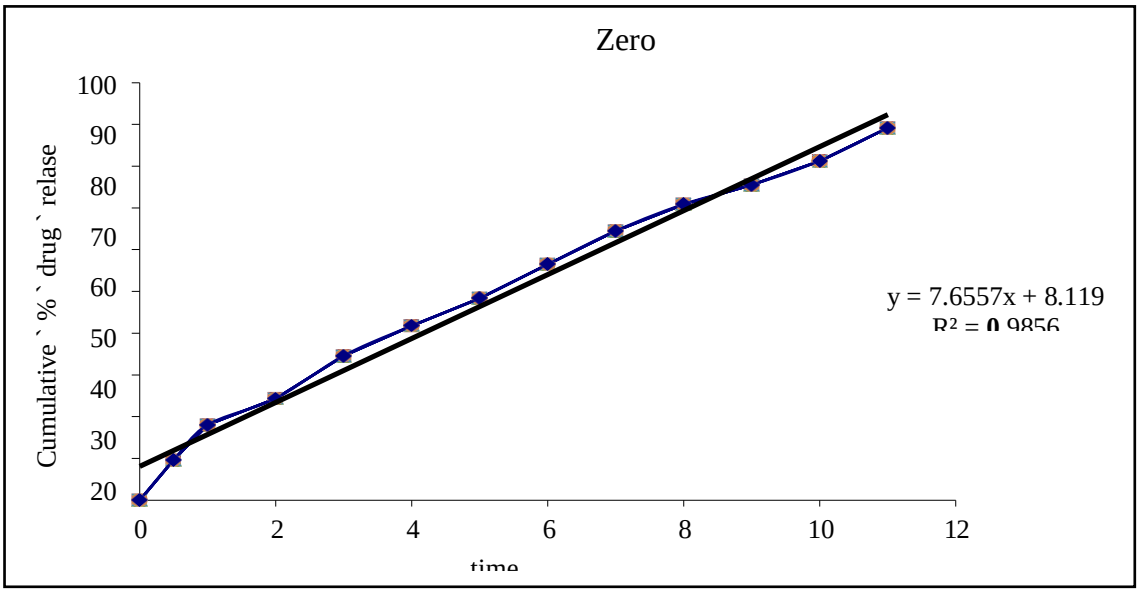

Fig3.6:Zero order release kinetics graph

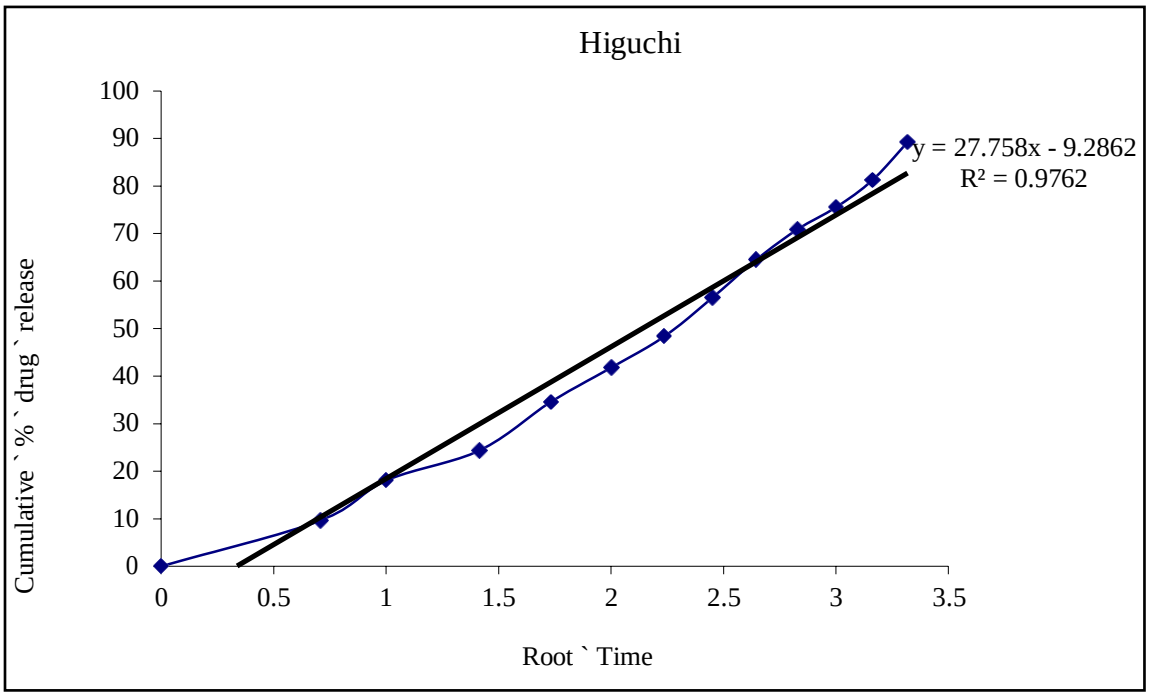

Fig 3.7:Higuchi release kinetics graph

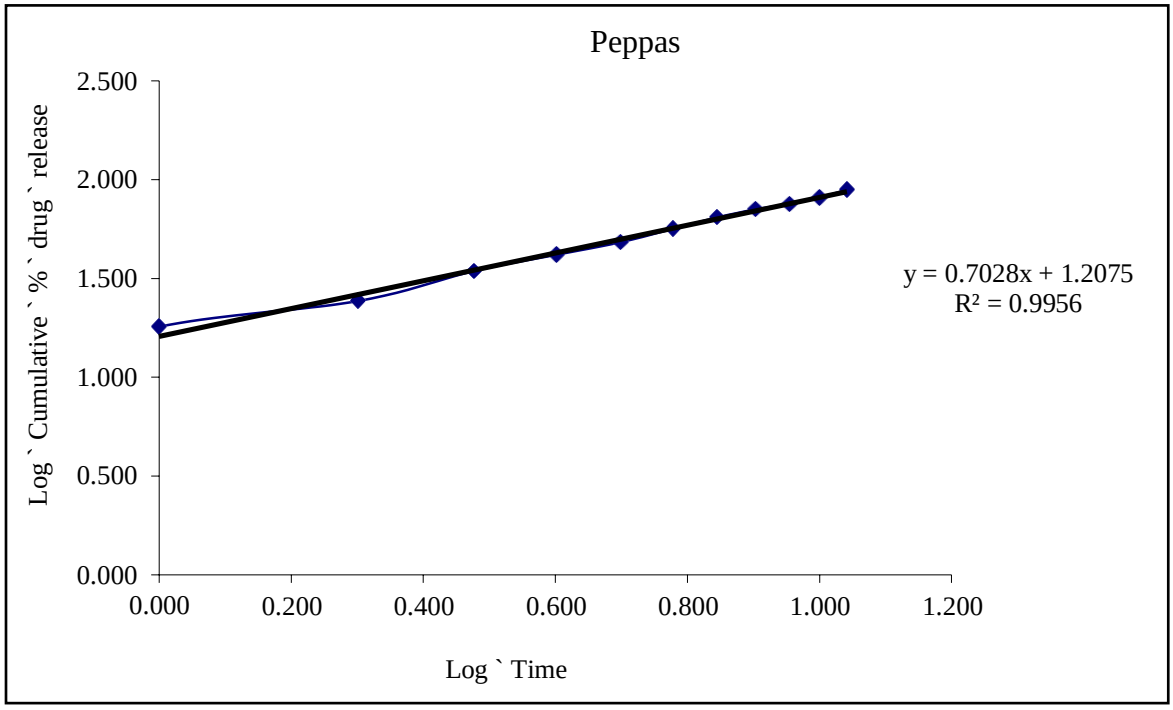

Fig 3.8: Kars mayer peppas graph

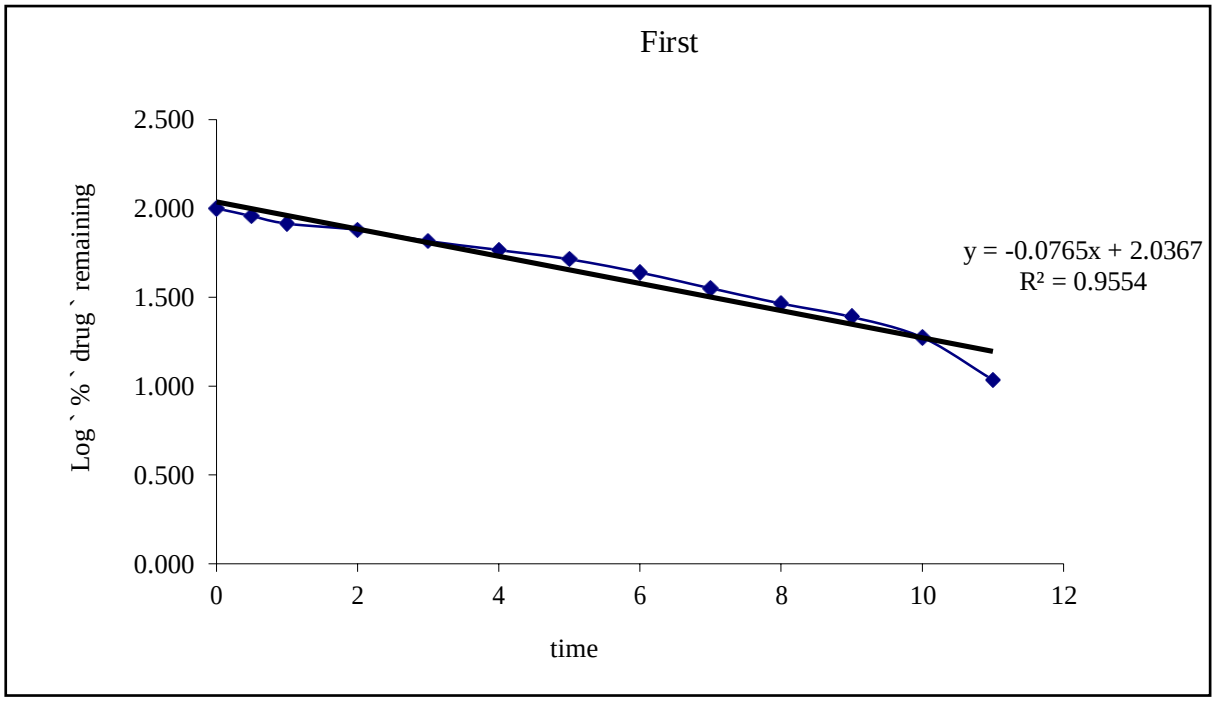

Fig 3.9: First order release kinetics graph

From the above graphs it was evident that theformulationF5wasfollowed peppas order release kinetics.

3.3.Drug–Excipient compatibility studies Fourier Transform-Infrared Spectroscopy:

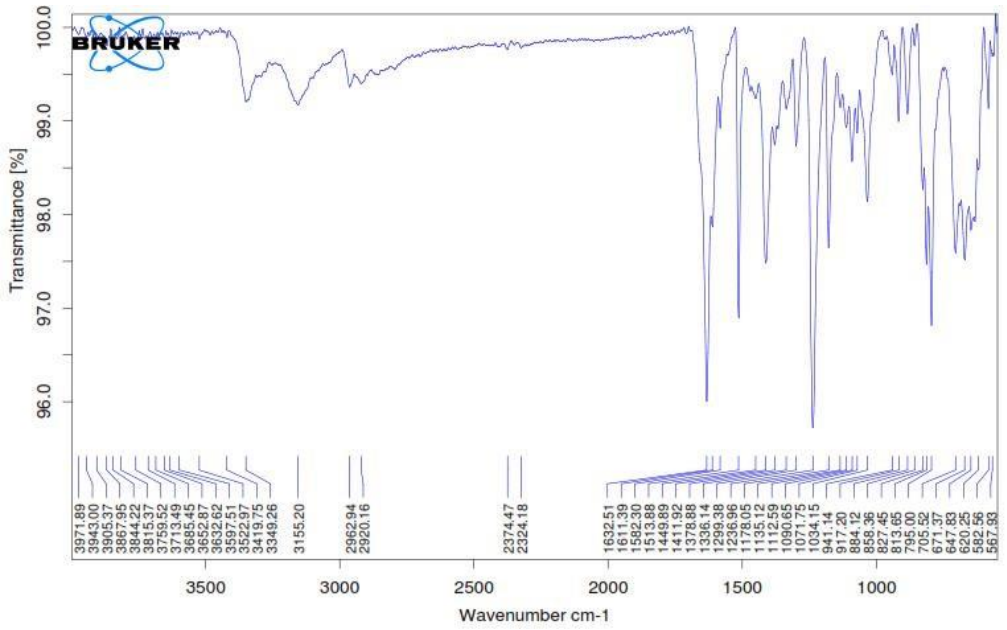

Figure8.10:FT-IRSpectrumofAbacavirpure drug:

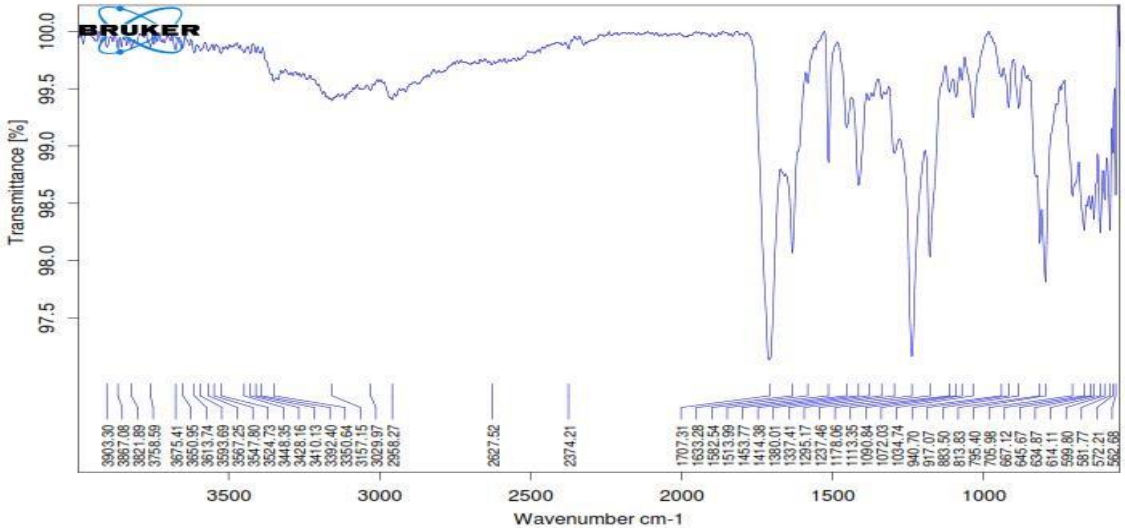

Figure3.11:FT-IRSpectrumof OptimisedFormulation

From the FTIR data it was evident that the drug and excipients doses not have any interactions. Hence they were compatible.

CONCLUSION[18-19]:

In the present work, an attempt has been made to develop Controlled release tablets of Abacavir by selecting different Types of polymers Carbopol974P, Xanthan Gum and HPMCK 15M as retarding. All the formulations were prepared by direct compression method. The blend of all the formulations showed good flow properties such as angle of repose, bulk density, tapped density. The prepared tablets were shown good post compression parameters and they passed all the quality control evaluation parameters as per I.P limits. Among all the formulations F5 formulation showed maximum % drug release i.e., 99.16 % in 12 hours hence it is considered as optimized formulation F5 which contains Xanthan Gum (20mg) . Whereas the formulations with HPMC K 15M showed high retarding with increasing concentration of polymer. The formulations with

Carbopol974P were did not produce the desired drug release pattern.

REFERENCES:

1. Altaf AS, Friend DR, MAS Rx and COS Rx. Sustained-Release Technology in Rathbone MJ, Hadgraft J, Robert MS, Modified Release Drug Delivery Technology, Marcell Dekker Inc., New York,2003;1:102-117.
2. Reddy KR., Mutalik S, Reddy S. AAPS Pharm. Sci. Tech.2003; 4: 19. 12 1-125.
3. Mohammed AD et al. Release of propranolol hydrochloride from matrix tablets containing sodium carboxymethylcellulose and Hydroxypropyl methyl cellulose. Pharm Dev Tech.1999; 4: 313- 324.
4. SalsaT, VeigaF. Drug Develop. IndPharm.1997;23:931.
5. Jantzen GM, Robinson JR, Sustained and controlled-release drug delivery systems, in Banker GS, Rhodes CT (Eds.) Modern Pharmaceutics, 3rd Ed, Revised and Expanded, Drugs and the Pharmaceutical Sciences., Marcell Dekker,Inc. NewYork.1995;72:575-609.
6. Jantzen GM, Robinson JR. Sustained and Controlled- Release Drug Delivery systems Modern Pharmaceutics,4thed;2003;121:501-502.
7. Lee BJ, Ryu SG, Cui JH, Drug Dev. Ind.Pharm.1999; 25: 493-501.
8. Gwen MJ, Joseph RR, In Banker GS and Rhodes CT, Ed. Modern Pharmaceutics, 3rdEd Marcel DekkerInc.NewYork.1996;72:575.
9. Vidyadhara S,Rao PR,Prasad JA.Indian J Pharm Sci.2004;66:188-192.
10. Bogner RH. Bioavailability and bioequivalence of extended-release oral dosage forms. US Pharmacist.1997;22:3–12.
11. Rogers JD, Kwan KC. Pharmacokinetic requirements for controlled-release dosage forms. In: John Urquhart, ed. Controlled-release Pharmaceuticals. Academy of Pharmaceutical Sciences. AmericanPharmaceuticalAssociation.1979:95–119.
12. Madan PL. Sustained-release drug delivery systems, part II: Preformulation considerations. Pharm Manu fact. 1985; 2: 41–45.
13. Wani MS, Controlled Release System-AReview,2008;61:56-62.
14. Banker GS, Anderson NR. The Theory and Practice of Industrial Pharmacy: Tablet, Lachman, (3rded)VarghesePublishingHouse,Bombay.1990 ;3:293-303.
15. Lee VHL, Controlled Drug Delivery Fundamentals and Applications: Influence of drug properties ondesign,MarcelDekker,INC,andNewYork.198 7;2:16-29.
16. Ghulam Razaque, Gul M. Khan, Muhammad Z. Danish, Shafi Muhammad, Nisar A. Shahwani, Kamran A. Khan4, Nayab B. Rizvi, Muhammad Younis. Formulation and In-Vitro Evaluationof Controlled Release Matrix Tabletsof Diltiazem Hydrochloride Using Different Rate Controlling Polymers.Volume10,2019.
17. Al-Hanbali OA, Hamed R, Arafat M, Bakkour Y, Al-Matubsi H, Mansour R, Al-Bataineh Y6, Aldhoun M, Sarfraz M, Dardas AKY. Formulation and evaluation of diclofenac-controlled release matrix tablets made of HPMC and Poloxamer 188 polymer: An assessment on mechanism of drug release. Pak J PharmSci.2018.
18. Dr. Khaja Pasha, Dr. Shahana Banu. Formulation and Evaluation of Controlled Release Osmotic Tablet of Glipizide. International Journal of Research in Pharmacy and Biosciences Volume 4, Issue 5, 2017, PP 12-16.
19. Moumita Das, Bijaya Ghosh, Swapnoleena Sen, L. K. Ghosh. Formulation and Optimization of Controlled 5-Fluorouracil Tablets for Colonic Delivery. J Young Pharm, 2017; 9(2): 192-196.