IJPSR (2015), Vol. 6, Issue 9 (Research Article)

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 26 February, 2015; received in revised form, 16 April, 2015; accepted, 08 June, 2015; published 01 September, 2015

DEVELOPMENT AND *IN-VITRO* CHARACTERIZATION OF ABACAVIR AND ZIDOVUDINE TABLET IN COMBINATION

Srinivas Martha* and Satya Devi B.

Department of Pharmaceutics, Joginpally B.R. Pharmacy College, Yenkapally (V), Moinabad (M), Hyderabad- 500075, Telangana, India.

Keywords:

Abacavir, Zidovudine, Synergistic Activity, Forced Degradation, Accelerated Condition

Correspondence to Author:
Srinivas Martha

Joginpally B.R Pharmacy college
Yenkapally (v), Moinabad (M)
Hyderabad-500075, Telangana, India.

E-mail:srinivaaspharma@gmail.com

ABSTRACT: The present study outlines a systematic approach for Formulation and Evaluation of Immediate release Tablets of Abacavir and Zidovudine tablet. Combination of anti retiro-viral creates multiple obstacles to HIV replication to keep the number of off springs low, reduce the possibility of superior mutations, decrease viral load and potentiate synergistic activity with one another, combining two drugs into one tablet reduces the number of individual medications[1]. To achieve this goal various prototype formulation trials were taken with varying compositions of diluents and disintegrant and evaluated with respect to their various quality control tests such as Thickness, hardness, weight variation, dissolution, disintegration, hardness and assay. The formula was finalized by comparing the In-vitro dissolution profile of all formulations with the respective individual marketed products. The in vitro release study was performed in 0.1N Hcl upto 60 min. Among all the formulations, formulation F6 release profile was good as compared to the other formulations. Forced degradation studies at 550C & Stability studies at 40±2ºC/75±5%RH (accelerated condition) for 1& 3 months indicated that no characteristics changes in formulation. There was no chemical interaction between drugs and excipients.

INTRODUCTION: Acquired immunodeficiency syndrome (AIDS), which threatens to cause a great plague in the present generation HIV weakens the body's immune system and reduces the body's ability to fight infections [2]. Anti-HIV medicines do not kill the virus but they slow down or stop the HIV virus from making copies of it-self. This allows the body's immune system to keep working and gives the body a chance to fight other infections. Anti-HIV medicines are most effective when taken in combination with other anti-HIV-medicines. Combination therapy reduces the chances of the virus becoming resistant to a single medicine and also produces synergistic activity. Resistance to medicines makes HIV treatment more difficult [3].

QUICK RESPONSE CODE

DOI: 10.13040/IJPSR.0975-8232.6(9).4004-15

Article can be accessed online on: www.ijpsr.com

DOI link: http://dx.doi.org/10.13040/IJPSR.0975-8232.6(9).4004-15

Combination of antiretiroviral creates multiple obstacles to HIV replication to keep the number of off springs low, reduce the possibility of superior mutations, decrease viral load and potentiate synergistic activity with one another, combining two drugs into one tablet reduces the number of individual medications [4].

Abacavir & zidovudine are nucleoside reverse transcriptase inhibitors (NRTI's) with activity against human immunodeficiency virus type –I (HIV-I). They inhibit the HIV Reverse transcriptase enzyme and act as a chain terminator of DNA synthesis.

Abacavir and zidovudine are absorbed from the GIT & provide the oral bioavailability of 83% and 75% respectively. These were formulated in immediate release dosage forms due to their half lives 1.54±0.63hours & 0.5 to 3hours respectively and cannot retain for prolonged periods in stomach, thus providing drug to the absorption sites in a conventional manner and maintains the magnitude

of drug effect. In the present study immediate release tablets of abacavir & zidovudine were prepared with super disintegrant (Sodium Starch Glycolate) and a polymer (MCC) to provide immediate release within 60minutes.[5]

MATERIALS AND METHODS:

Materials:

Abacavir and zidovudine were obtained as a gift samples from Aurobindo pharma ltd., Hyderabad. Sodium starch glycolate, micro crystalline cellulose, talc were purchased from Signet Chemicals, Mumbai. Lactose and magnesium stearate from Aurolab, Madurai and SD Fine Chemicals limited, Mumbai respectively. All the ingredients used were of pharmaceutical grade.

Method:

Preparation of abacavir and zidovudine tablets:

Abacavir and Zidovudine tablets were prepared by direct compression method. All the ingredients were weighed accurately. The drug was mixed with the release rate enhancing disintegrants and other excipients, except magnesium stearate, in ascending order of their weight. The powder mix was blended for 20min to have uniform distribution of drug in the formulation. Then, magnesium stearate was added and mixed for not more than 1 min (to ensure good lubrication.) About 850 mg of the powder mix was weighed accurately and fed into the die of single punch machinery and compressed using 8 mm flat- surface punches [6]. Formulae is mentioned in **Table 1**.

Formulation design:

TABLE1: FORMULAE FOR ABACAVIR AND ZIDOVUDINE TABLETS

Ingredients (mg)	F1	F2	F3	F4	F5	F6
Abacavir	300	300	300	300	300	300
Zidovudine	300	300	300	300	300	300
Micro crystalline cellulose	95.25	86.75	91	82.5	99.5	103.75
Lactose	95.25	86.75	91	82.5	99.5	103.75
Sodium starch glycolate	42.5	59.5	51	68	34	25.5
Magnesium state	8.5	8.5	8.5	8.5	8.5	8.5
Talc	8.5	8.5	8.5	8.5	8.5	8.5
Total weight(mg)	850	850	850	850	850	850

Evaluation of abacavir & zidovudine immediate release tablets[7]:

These tablets were subjected to evaluation for the following parameters.

a) Physical appearance:

The general appearance of tablets, its visual identity and overall elegance is essential for consumer acceptance. The control of general appearance of tablet involves measurement of number of attributes such as tablet size, shape, color, presence or absence of odor, taste, surface texture and consistency of any identification marks.

b) Hardness test:

Hardness of the tablets was determined by using Monsanto hardness tester. The tablet to be tested is held in fixed and moving jaw and reading of the indicator adjusted to zero. Then force to the edge of the tablets was gradually increased by moving the screw knob forward until the tablet breaks. The reading was noted from the scale which indicates the pressure required in kg to break the tablet. The hardness of the tablets depends on the weight of the materials used, space between the upper and lower punches at the time of compression and pressure applied during compression.

c) Tablet size and Thickness:

Control of physical dimensions of the tablets such as size and thickness is essential for consumer acceptance and tablet-tablet uniformity. The diameter size and punch size of tablets depends on the die and punches selected for making the tablets. The thickness of tablet is measured by Vernier Calipers scale. The thickness of the tablet related to the tablet hardness and can be used as initial control parameter. Tablet thickness should be controlled within a ±5%. In addition thickness must be controlled to facilitate packaging.

d) Friability:

The Roche friability test apparatus was used to determine the friability of the tablets. Randomly selected twenty pre-weighed tablets were placed in the apparatus and operated for 100 revolutions and then the tablets were reweighed. The acceptable limits of the weight loss should not be more than 1%. The percentage friability was calculated according to the following formula.

% friability = (initial weight – final weight) / initial weight * 100

e) Average weight of Tablets:

It is desirable that all the tablets of a particular batch should be uniform in weight. If any weight variation is there, that should fall within the prescribed limits:

±10% for tablets weighing 300mg or less

±7.5% for tablets weighing 300mg to 315mg

±5% for tablets weighing more than 315mg

Twenty tablets were taken randomly and weighed accurately. The average weight is calculated by

$$\text{Average weight} = \frac{\text{weight of 20 tablets}}{20}$$

f) Disintegration test:

For most tablets the first important step toward solution is break down of tablet into smaller particles or granules, a process known as disintegration. This is one of the important quality control tests for disintegrating type tablets. Six tablets are tested for disintegration time using USP XXII apparatus in 0.1N Hcl the environment in stomach. Disintegration type conventional release tablets are tested for disintegrating time.

g) Drug Content uniformity:

Over ten tablets were selected randomly and average weight was calculated. Tablets were crushed in a mortar and accurately weighed amount of tablets triturate was taken for analysis, and it was diluted with the 0.1 N HCL. The content was shaken well and kept for 30 minutes for dissolving the drug and appropriate dilutions were made. The drug content was estimated by recording the absorbance at 277nm.

h) *In-vitro* Dissolution Studies of the tablets:

Dissolution studies were carried out for all the formulations combinations in triplicate, employing USP-II paddle method and 900ml of pH 0.1 N Hcl as the dissolution medium operated at 50RPM. The medium was allowed to equilibrate to temp of 37°c $\pm$ 0.5°c. The samples were collected after one hour at intervals 10, 20, 30, 40, 50, 60 minutes. The samples were analyzed spectrophotometrically at 277 nm using UV-spectrophotometer [8]. Dissolution parameters were mentioned in **Table 2**.

Dissolution parameters:

TABLE 2: *IN-VITRO* DISSOLUTION PARAMETERS

Drug Name	Dosage Form	Dissolution Apparatus	Speed (RPMs)	Medium	Medium Volume (ml)	Sampling intervals (minutes)
Abacavir & Zidovudine	Tablets	USP II Paddle type	50RPM	0.1N HCL	900	10, 20, 30, 40, 50, 60

i) Kinetics of drug release:

Data obtained from *in-vitro* drug release studies was fitted to various kinetic equations to find out the mechanism of drug release from immediate release tablets. The kinetic models were zero-order equation, first- order equation, higuchi's equation, Peppas and Korsemeyer equation (Power Law) to further characterize the type of release.[9]

j) Stability studies:

Accelerated stability testing: These are the studies designed to increase the rate of chemical degradation and physical change of a drug by using exaggerated storage conditions as part of the formal stability testing program. The data thus obtained, is by preserving the samples for the particular time period at $40^0C \pm 2^0C$/75% RH ± 5% RH.[10]

Forced degradation:

A series of tests designed to obtain information on the stability of a pharmaceutical product in order to define its shelf-life and utilization period under specified packaging and storage conditions (ICH, 1995).[11]

A stability indicating method accurately measures the Active ingredients, without interference from degradation products, process impurities, excepients, (or stress testing) typically involves exposure of drug substances to heat, heat and humidity, sunlight, acid, base, peroxide, (or) water.

RESULTS AND DISCUSSION:

Abacavir & zidovudine tablets were formulated with varying compositions of excepients (F1-F6) out of all the formulations F6 showed good release

character by the end of 1hour and stood as optimized formulation. Among the all six formulations F6 was selected as the best formulation by comparing with the marketed products. The formulation F6 contains 2-4% of Sodium starch glycolate (composition at which it acts as a super disintegrant) as disintegrating agent.

The powder blend containing equal ratios of talc and Magnesium stearate offered good flow properties. Powder satisfied all Pharmacopoeial requirements and it showed excellent tableting properties and immediate drug release drug within 1hr. This could be advantageous and the combination drugs were released before their respective half-life.

Pre compression parameters:

The Pre compression parameters were the primary requirements to determine whether the specific material was suitable for the targeted formulation or not. The aim was to formulate the tablet formulation with direct compression method, so it was mandatory to know the bulk density, tapped density, Carr's index, Hausner's ratio and angle of repose as those were the official requirement while choosing any material for its dosage form formulation. **Table 3** shows the results evaluated parameters of Bulk Density, Tapped Density, Carr's index, Hausner's ratio, Angle of Repose for various tablet formulations. The result of evaluation parameters clearly indicates its suitability to be the material of choice for formulation.

TABLE 3: PRE-COMPRESSION PARAMETER OF ABACAVIR AND ZIDOVUDINE IMMEDIATE RELEASE TABLETS PREPARED BY DIRECT COMPRESSION METHOD

S. No	Formulations	Bulk Density (gms/ml)	Tapped Density (gms/ml)	Angle of Repose	C.Index	Hausner's Ratio
1	F1	0.5443	0.6766	25.74	19.5652	1.2432
2	F2	0.5795	0.6710	26.28	13.6363	1.1579
3	F3	0.5669	0.6714	26.06	15.5555	1.1842
4	F4	0.5802	0.6718	27.40	13.6363	1.1579
5	F5	0.5797	0.6712	28.72	13.6363	1.1579
6	F6	0.5668	0.6712	28.65	15.5555	1.1842

Post compression parameters:

All the prepared batches were evaluated systematically. Finally the comparison parameters were keenly observed to finalize for selection of the optimized batch and formula. Hardness of tablets was found to be in the range of 4.18 to 5 kg/cm^2 given in **Table 4**. The friability of all tablets was found to be in the range of 0.23 to 0.32 which is less than 1% that showed good mechanical strength. Thus finally formulation F6 i.e. shows disintegration time 11.52 minutes and drug release 98% which is higher than other tablets formulations.

TABLE 4: POST COMPRESSION PARAMETERS OF ABACAVIR AND ZIDOVUDINE TABLETS

S. No	Formulations	Weight Variation (mg)	Hardness (kg/cm^2)	Drug Content Uniformity (%)	Friability (%)	Disintegration Time(min)
1	F1	849.6	4.18	100	0.32	12.50
2	F2	850.3	4.28	99	0.26	10.03
3	F3	850.9	4.35	100	0.25	11.11
4	F4	849.1	4.42	100	0.26	13.55
5	F5	850.5	4.90	99	0.23	12.85
6	F6	849.7	5.00	99	0.26	11.52

Compatibility studies between abacavir & zidovudine:

Abacavir and zidovudine are said to be compatible by comparing these results with their respective individual marketed products (ziagen, retrovir) irrespective with the branded drug Trizivir (combination of abacavir, zidovudine and lamivudine). These were performed by physical parameters and chemical parameters.

a) Physical parameter:

The compatibility studies provide the frame work for the drugs combination with the excipients in the fabrication of the dosage form. The study was carried out to establish that the therapeutically active drugs have not undergone any changes, after it has been subjected to processing steps during formulation. Compatibility studies are carried out by mixing definite properties of drugs and excipient and kept in glass vials, which is stored at 55°C for one month.

b) Chemical parameters:

Drug excipient compatibility studies were performed by FTIR (Fourier transform infrared spectroscopy). The IR Spectrum of pure Abacavir & zidovudine was compared with each other and also the IR spectrum of drug-polymer mixture such as lactose and sodium starch glycolate. There was no appearance or disappearance of any characteristics peaks. This showed that there was no significant interaction between drugs and polymer which is used in the tablets.[12] Finally drug and polymer compatibility studies were performed by FTIR. FTIR absorption spectra of abacavir, zidovudine and combination with that of excepients shows no significant interaction between drugs and Polymer (**Fig. 1, 2, 3, 4, 5.**).

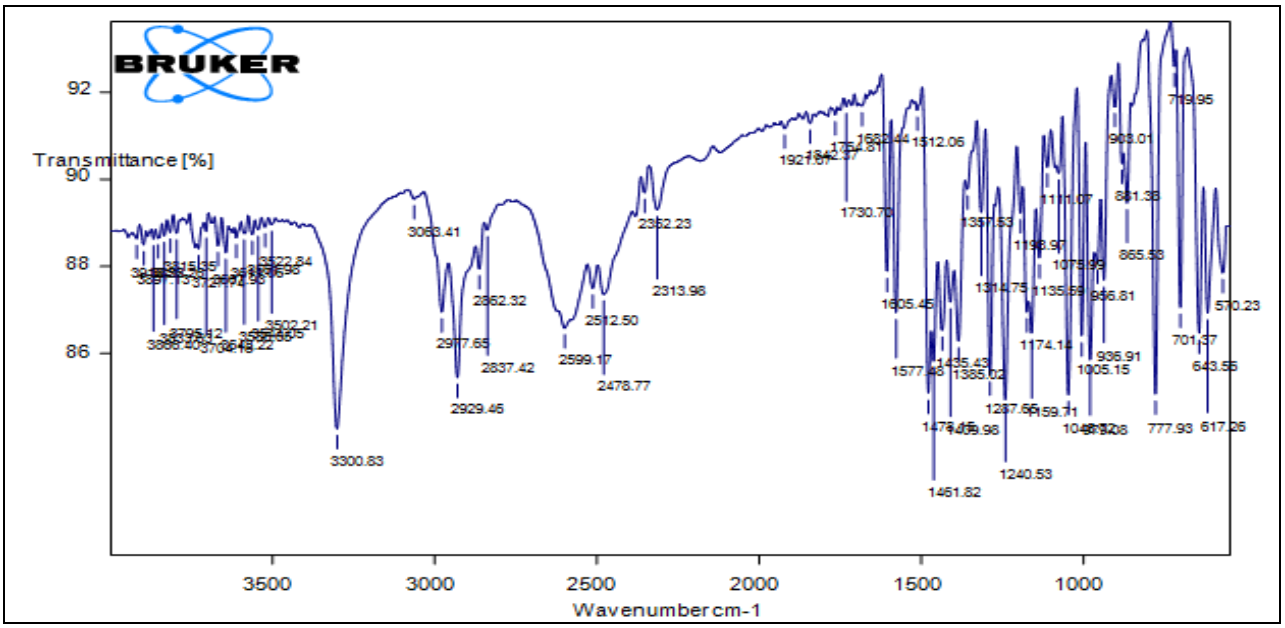

FIG.1: FTIR SPECTRA OF ABACVIR + ZIDOVUDINE

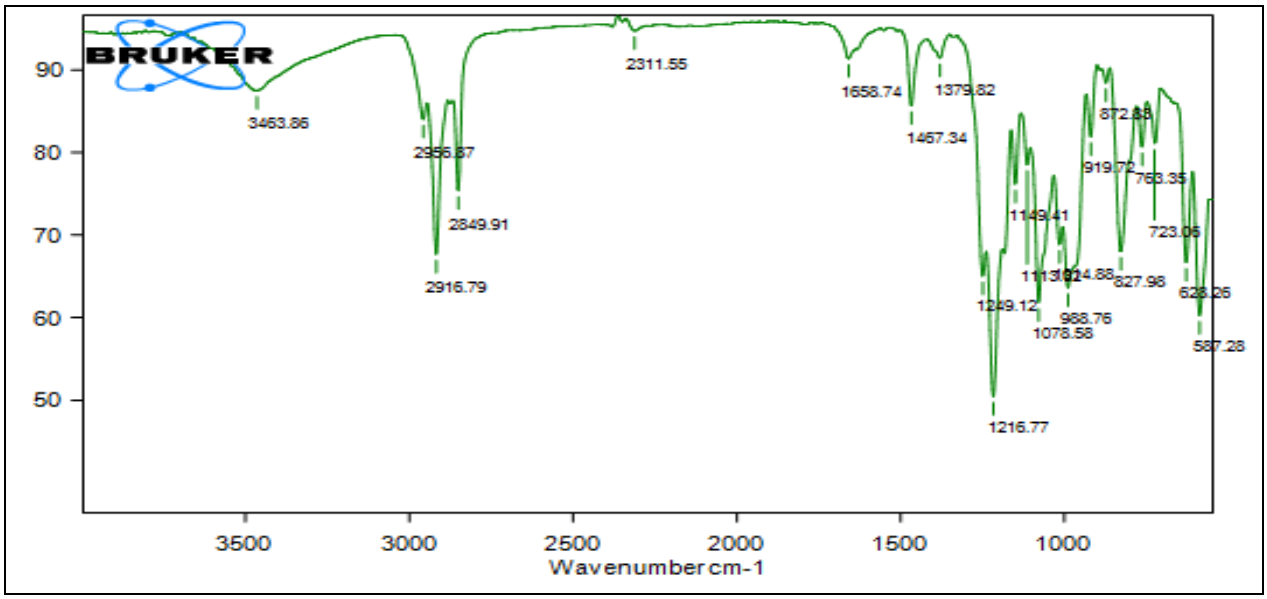

FIG.2: FTIR SPECTRA OF ABACAVIR + LACTOSE

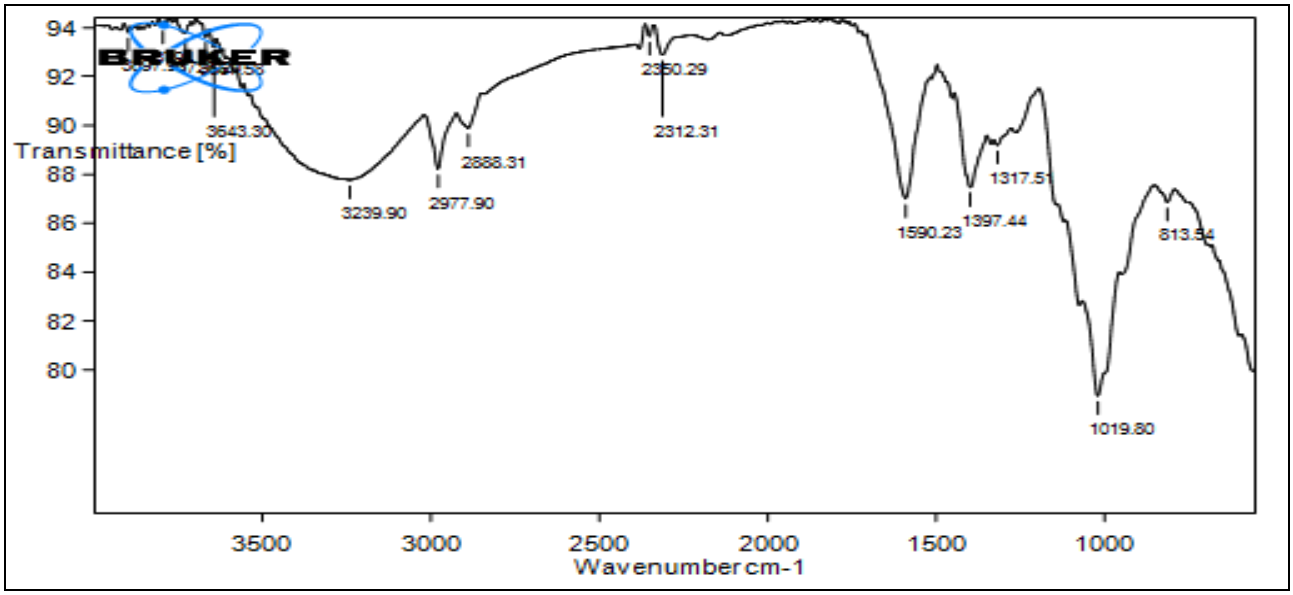

FIG. 3: FTIR SPECTRA OF ZIDOVUDINE + LACTOSE

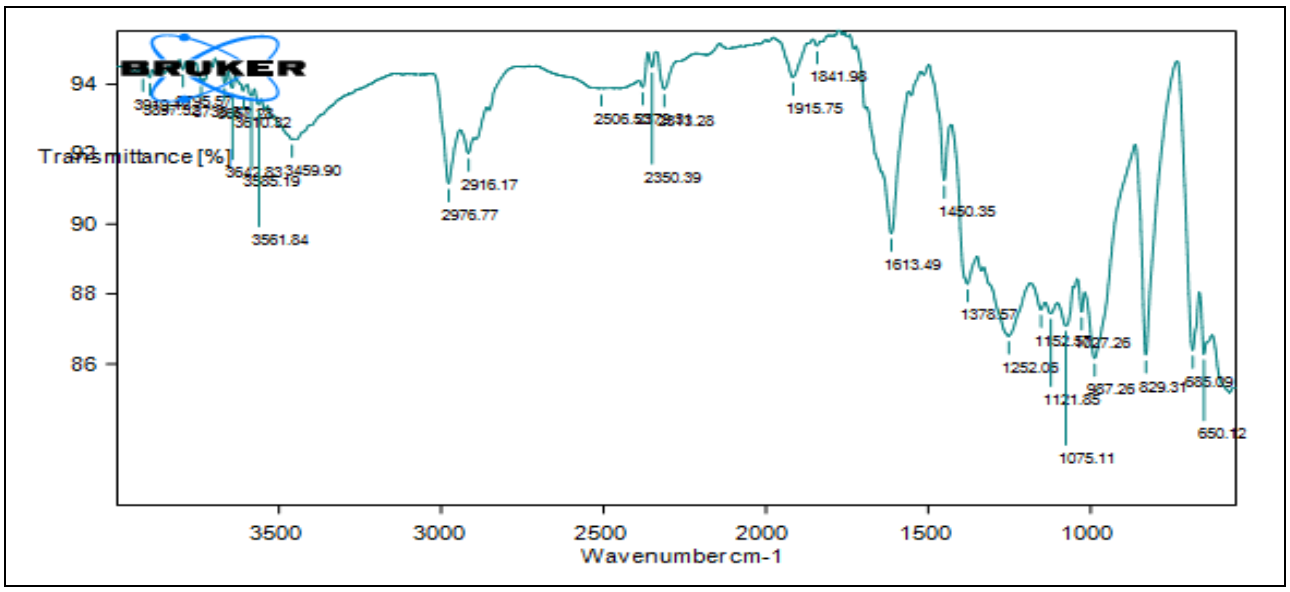

FIG.4: FTIR SPECTRA OF ABACAVIR + SODIUM STARCH GLYCOLATE

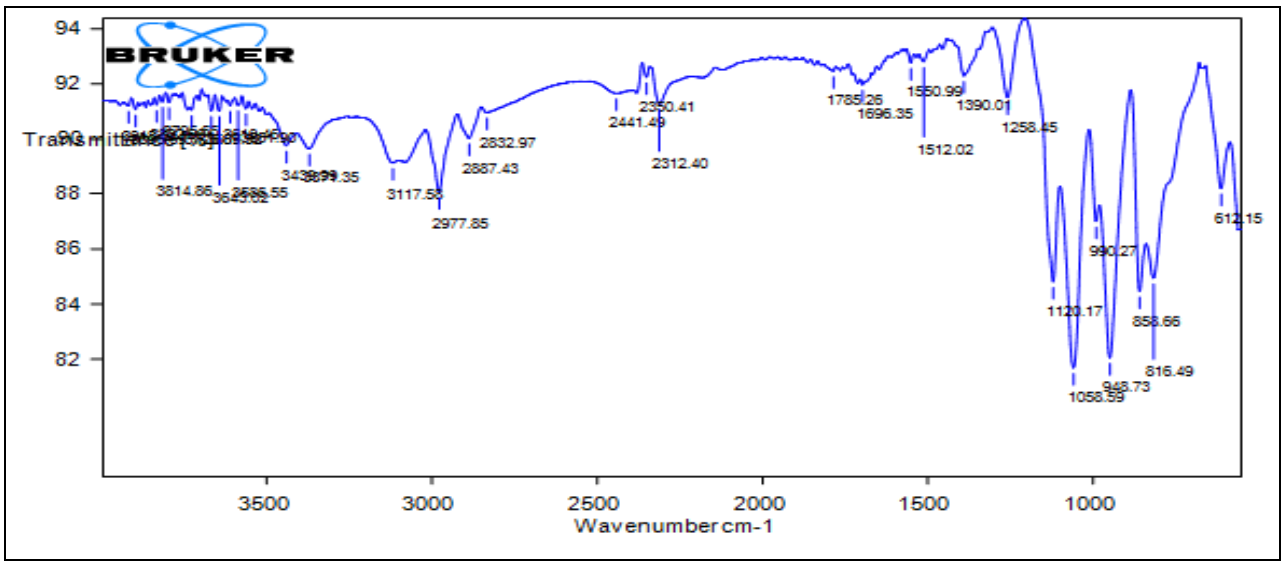

FIG.5: FTIR SPECTRA OF ZIDOVUDINE + SODIUM STARCH GLYCOLATE

In the FTIR graphs, optimized formulation containing the pure drug, the excipients interaction and different functional groups stretching was mentioned. The FTIR analysis was carried out to find possible drug-polymer interactions. The FTIR studies were performed to standard drugs Abacavir, Zidovudine and polymers. As a pure drug the FTIR curves shows the options of the strong interactions between the components and suggested drug. From the observations it was concluded that all the formulations containing drug and different excipients does not have any interactions.

***In-vitro* drug release:**

Compared to conventional tablets of individual marketed products of abacavir (ziagen) & zidovudine (retrovir), all formulations showed immediate release by the end of 1hour showed in **Table 5**. The *in-vitro* drug release profile of tablets from each batch (F1-F6) was carried in 0.1N HCl, for an hour by using USP II paddle type. The F1 - F6 formulations were done with varying compositions of MCC, Lactose, SSG (Sodium starch glycolate) which is showing immediate release and the total drug was released at the end of 1 hr. In the formulations (F1-F6) MCC and lactose were used as major and minor diluents and hence used in same compositions in each formulation where as SSG varies from formulation to formulation and plays a vital role in release mechanics. Talc and Magnesium stearate were used in same compositions in all the formulations which are only helpful in keeping the tablet intact during compression process. The formulations F1-F4 were done with decreasing amounts of diluents & increasing amounts of disintegrant (SSG) which is showing the release comparatively very less at the end of 60 minutes.

In the formulations F5, F6 increased amounts of diluents and decreased amounts of disintegrant were used which markly showing good release characteristics. Formulation F6 was selected as an optimized formulation due to its suitable release profile as compared to other formulations.

TABLE 5: % CUMMULATIVE DRUG RELEASE OF ABACAVIR & ZIDOVUDINE TABLETS

Time (min)	% Cumulative Drug release					
	F1	F2	F3	F4	F5	F6
0	0	0	0	0	0	0
10	21	27	30	33	29	31
20	39	41	44	49	44	46
30	45	55	54	54	52	59
40	48	61	62	64	71	73
50	61	68	85	88	87	89
60	67	72	87	92	94	98

TABLE 6: *IN-VITRO* DRUG RELEASE PROFILE OF ABACAVIR AND ZIDOVUDINE OPTIMIZED FORMULATION (F6) AND MARKETED PRODUCT (A) -ZIAGEN

Time(min)	Optimized Formulation (F6) (% CDR)	Marketed Product (A) ZIAGEN	Marketed Product (B) RETROVIR
0	0	0	0
10	31	28	25
20	46	42	41
30	59	53	56
40	73	67	70
50	89	85	86
60	98	96	95

Kinetics of drug release:

All the above- described models for selecting the release profile were applied for formulations F1-F6. The best fit model in case of all the formulations was determined by considering the higher corelation coefficient value (r). The release rate kinetic data for the F6 was best explained by First order equation, as the plots showed the highest linearity (R^2 = 0.979), followed by Higuchi's equation (R^2= 0.981) hence, the drug release was best fitted in First order kinetics, indicating that the rate of drug release is concentration dependent. The corresponding plot (log cumulative percent drug release vs log time)

for the Korsmeyer-Peppas equation indicated a good linearity (R^2= 0.972). The diffusion exponent "n" was between 0.45-0.89, which appears as diffusion mechanism is non-fickian diffusion. Thus, indicates that the drug release was controlled by more than one process (both diffusion and dissolution).[13]

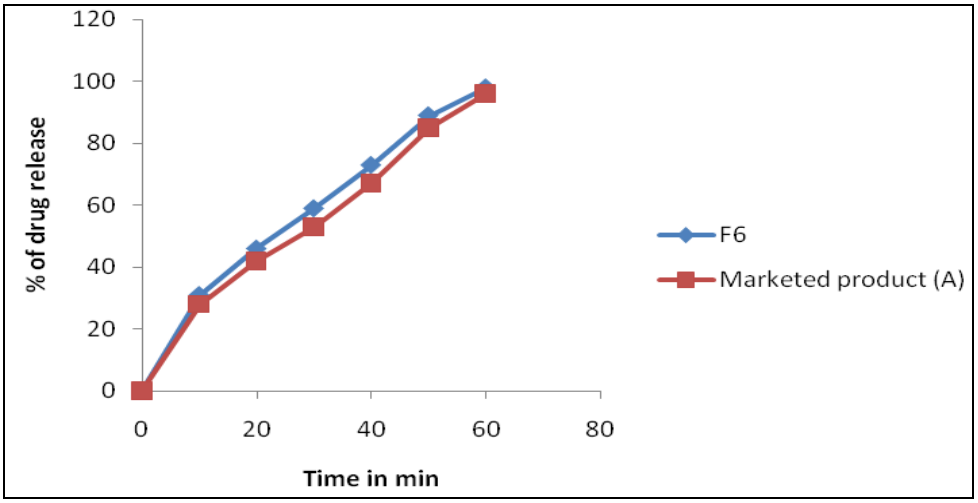

FIG.6: COMPARISON OF *IN VITRO* DISSOLUTION OF OPTIMIZED FORMULATION (F6) AND MARKETED PRODUCT (A) ZIAGEN

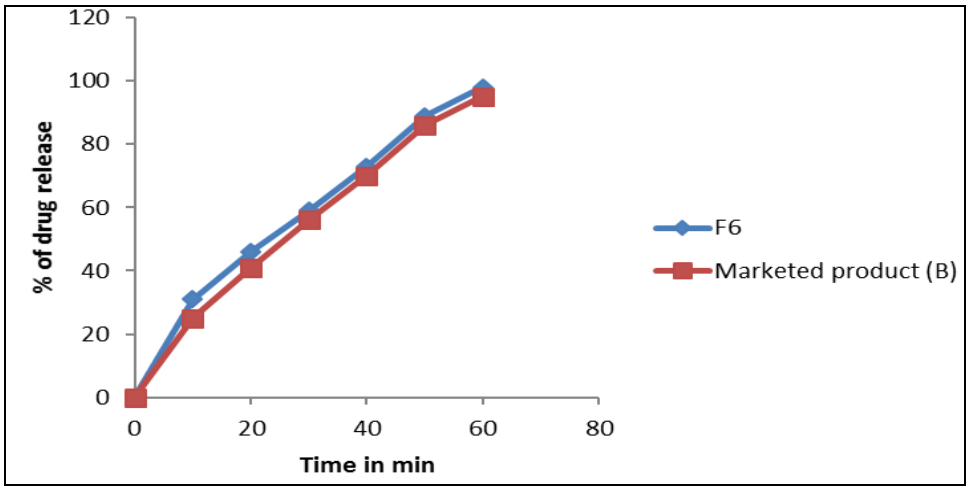

FIG. 7: COMPARISON OF *IN VITRO* DISSOLUTION OF OPTIMIZED FORMULATION (F6) AND MARKETED PRODUCT (B) RETROVIR

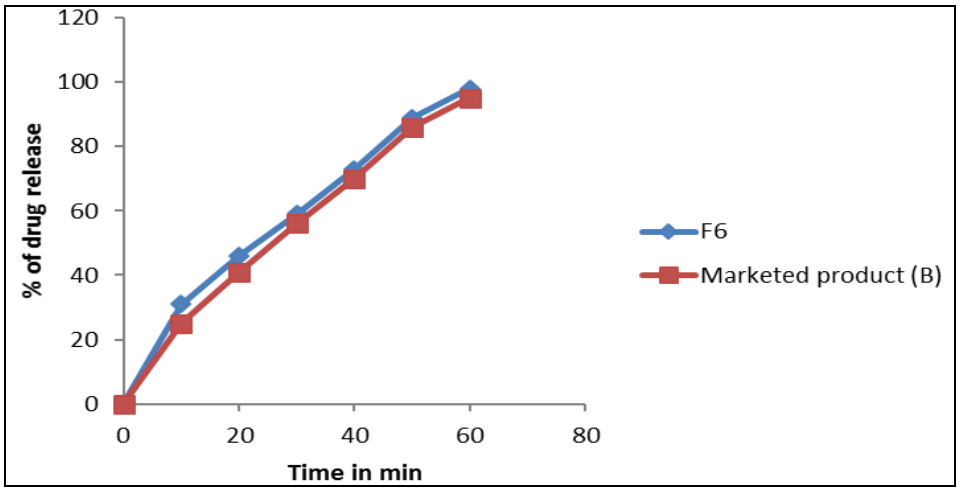

FIG.8: COMPARISON OF *IN VITRO* DISSOLUTION OF OPTIMIZED FORMULATION (F6) AND MARKETED PRODUCTS (A, B)

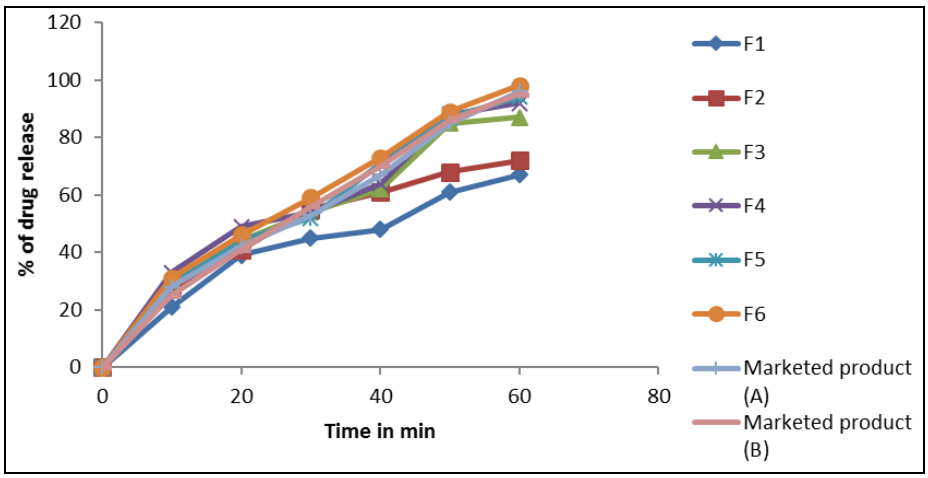

FIG. 9: COMPARISON OF *IN VITRO* DISSOLUTION OF FORMULATIONS (F1- F6) WITH MARKETED PRODUCTS (A, B)

TABLE 7: *IN VITRO* DRUG RELEASE KINETIC DATA OF ABACAVIR AND ZIDOVUDINE TABLETS FORMULATED WITH DIFFERENT CONCENTRATION

Formulation Code	Zero Order	First Order	Higuchi's	Peppas's
F1	0.9037	0.9704	0.9809	0.9769
F2	0.9541	0.9581	0.9679	0.9885
F3	0.9888	0.9751	0.9695	0.9882
F4	0.9689	0.8169	0.9834	0.9913
F5	0.9277	0.9955	0.9797	0.9568
F6	0.9370	0.9790	0.9812	0.9720

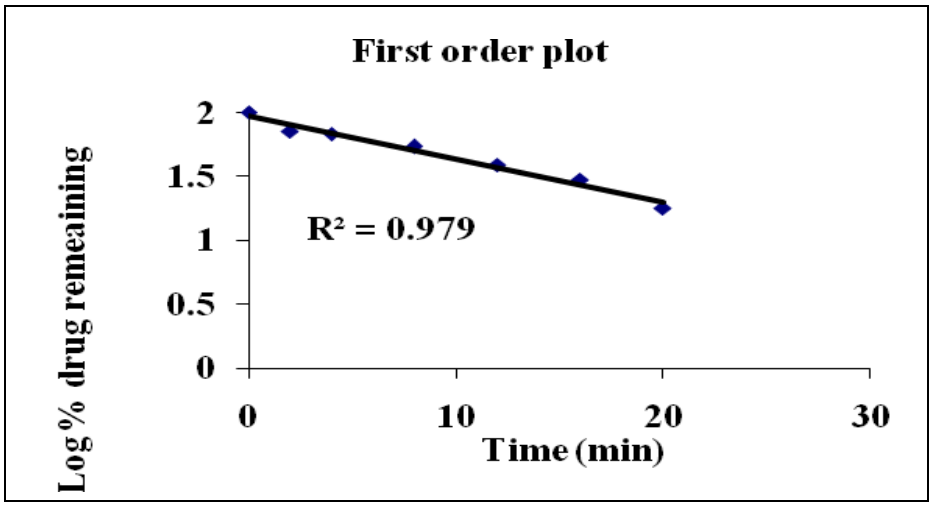

FIG.10: FIRST ORDER PLOT OF ABACAVIR AND ZIDOVUDINE FORMULATION (F6)

Stability Studies:

The stability studies were conducted by comparing the initial results with that of the stability samples obtained after one month and three months. Forced degradation studies at 55^0C & Stability studies at 40±2ºC/75±5%RH (accelerated condition) for 1& 3 months indicated that no characteristics changes in formulation. There was no chemical interaction between drugs and excipients. Showed in **Table 8, 9, 10,** and **11.**

After 1 Month:

TABLE 8: PERCENTAGE CUMULATIVE RELEASE FOR STABILITY SAMPLES OF OPTIMIZED FORMULATION (F6) AT 40^0C / 75% RH AND 55^0C FOR 1 MONTH

Time (Min)	% Cumulative Drug Release		
	Initial	55^0C (Forced Degradation)	40^0C / 75% RH (Acclerated)
0	0	0	0
10	31±5.0	30±4.5	30±4.1

20	46±4.9	45±4.1	44±3.5
30	59±4.0	59±3.2	59±2.9
40	73±3.2	72±4.1	71±1.8
50	89±2.1	89±4.0	88±1.1
60	98±2.0	97±2.1	96±1.0

TABLE 9: EVALUATION FOR STABILITY STUDIES OF OPTIMIZED FORMULATION (F6) AFTER 1 MONTH STABILITY TESTING

Parameter	Initial	55^0C	40^0C / 75% RH
Color	White	White	White
Surface	Smooth	Smooth	Smooth
Thickness (mm)	6.40 mm	6.40 mm	6.41 mm
Hardness (kg/cm^2)	4.0-5.0	4.0-5.0	4.0-5.0
Weight (mg)	850 ± 0.11	850 ± 0.76	850 ± 1.89
Assay	99.12%	98.45%	97.99%

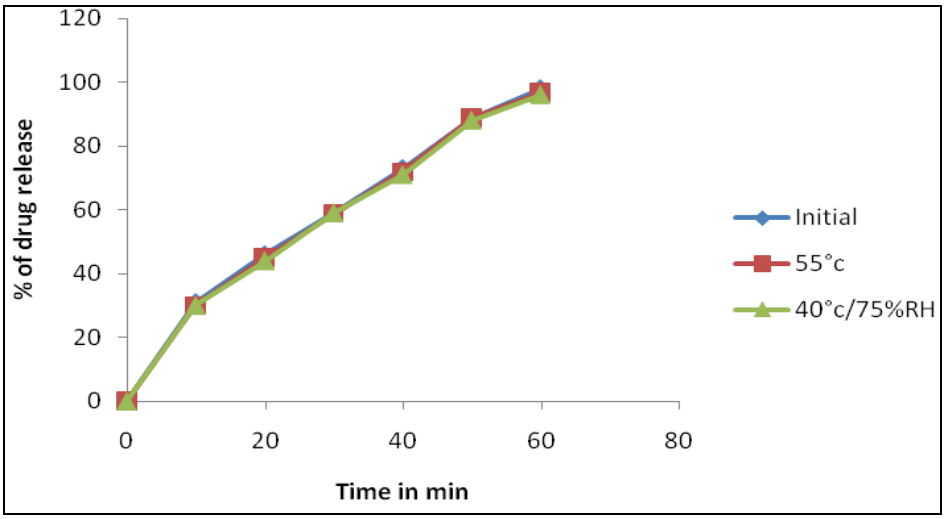

FIG. 11: DISSOLUTION PROFILES OF 1 MONTH STABILITY SAMPLES AT DIFFERENT CONDITIONS INITIAL, 40^0C / 75% RH AND 55^0C (FORCED DEGRADATION)

After 3 Months:

TABLE 10: PERCENTAGE CUMULATIVE RELEASE FOR STABILITY STUDIES OF OPTIMIZED FORMULATION (F6) AT 40^0C / 75% RH AND 55^0C FOR THREE MONTHS

	% Cumulative Drug Release		
Time (min)	Initial	55^0C (Forced Degradation)	40^0C / 75% RH (Acclerated)
0	0	0	0
10	31±5.0	30±4.8	29±5.1
20	46±4.9	45±4.1	44±5.2
30	59±4.0	57±3.5	57±2.6
40	73±3.2	72±2.1	71±4.2
50	89±2.1	88±2.0	87±2.9
60	98±2.0	97±1.8	96±1.2

TABLE11: EVALUATION FOR STABILITY STUDIES OF OPTIMIZED FORMULATION (F6) AFTER 3 MONTHS OF STABILITY TESTING

Parameter	Initial	55^0C	40^0C / 75% RH
Color	White	White	White
Surface	Smooth	Smooth	Smooth
Thickness (mm)	6.40 mm	6.42 mm	6.41 mm
Hardness (kg/cm^2)	4.0-5.0	4.0-5.0	4.0-5.0
Weight (mg)	850± 0.11	850 ± 0.76	850 ± 1.89
Assay	99.12%	98.90%	97.98%

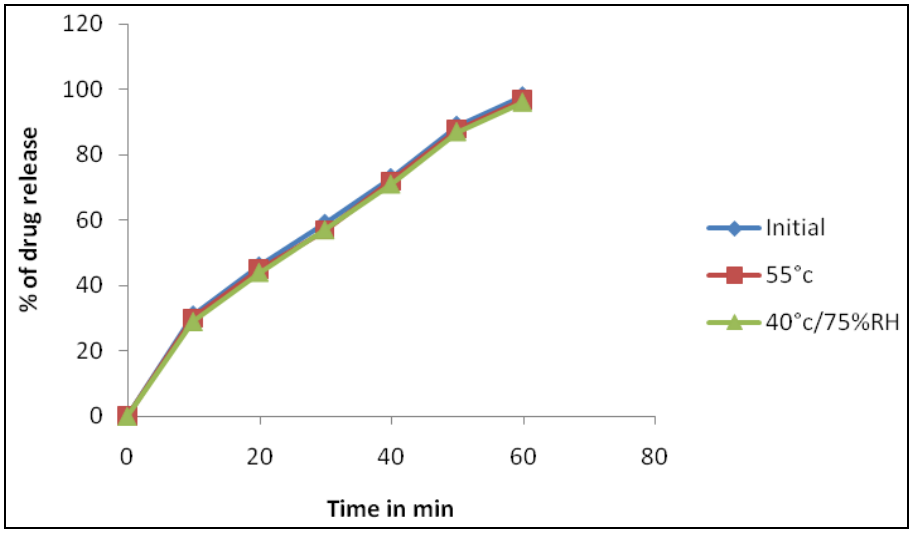

FIG.12: DISSOLUTION PROFILES OF 3 MONTHS STABILITY SAMPLES AT DIFFERENT CONDITIONS INITIAL, 40^0C / 75% RH AND 55^0C (FORCED DEGRADATION)

CONCLUSION: Abacavir and zidovudine tablets were successfully formulated using good proportions of ingredients and appropriate method i.e, direct compression method. The stable robust quality of Abacavir and Zidovudine conventional tablets is formulated. The formulated tablets are evaluated for the tests like weight variation, friability, disintegration, hardness, drug content and the optimised formulation complies with the specifications. The disintegrant used in the formulation is sodium starch glycolate which is different from that of the innovator and even the binder differs from the innovator even though the specifications of the evaluation are compiled as per the specifications. The optimised formulation is kept for stability studies and the results are good In **Fig. 11, 12**.

ACKNOWLEDGMENT: The authors sincerely express thanks to the Management, Department of pharmaceutics of joginpally B R Pharmacy College and Jawaharlal Nehru Technological University, Hyderabad for providing facilities to carry out this research work. Authors are thankful to Rainbow Labs, Hyderabad, India for providing Drug and other Excipients.

REFERENCES:

1. Thompson MA, Aberg JA, Cahn P, et al. Antiretroviral treatment of adult HIV infection: 2010 recommendations of the International AIDS Society-USA panel. JAMA 2010; 304:321-33.
2. Pathak Jagriti, Sudhakar C.K., Dr. Jain Sanjay. Pharmacokinetic Boosting of Zidovudine for HIV Treatment. International Journal of Pharmaceutical and Clinical Research 2012; 4:31-36.
3. Kayitare E, Vervaet C, Ntawukulilyayo J, Seminega B, Bortel V, Remon J. Development of fixed dose combination tablets containing zidovudine and lamivudine for paediatric applications. Int J Pharm. 2009; 370:41–46.
4. Maserati R, De Silvestri A, Uglietti A, et al. Emerging mutations at virological failure of HAART combinations containing tenofovir and lamivudine or emtricitabine. AIDS 2010; 24:1008-13.
5. Kar RK, Mohapatra S, Barik BB. Design and characterization of controlled release matrix tablets of Zidovudine. Asian J Pharm Cli Res 2009; 2:54-61.
6. Srikanth Thota, A.k. Radhalakshmi, .lamivudine, zidovudine and nevirapine. Thota et al., IJPSR, 2011; 2: 1772-1776.
7. Ravi P, Ganga S, Saha R. Design and *in vitro* evaluation of zidovudine oral controlled release tablets prepared using Hydroxypropyl methylcellulose. Chem Pharm Bull. 2008; 56:518-524.
8. Nagulwar Vaishali P, Bhusari Kishor P. Simultanious estimation of abacavir, lamivudine and zidovudine in combined tablet unit dosage form by uv spectroscopic method. IJRAP 2011; 2: 610-614.
9. D. Varun, B.V.P. Deepthi, P.V. Ayodhya Neelima, G. Suma Latha, M. Srikar, B. Anuhya and V. Siva Lalitha. Formulation and In Vitro Assessment of Controlled Release Matrix Tablets of Abacavir.RJPDFT 2011; 3: 298-303.
10. Vikramjit Singh, Nawazish Alam, Monika Sharma, Md. Sarfaraz Alam, Md. Sajid Ali, Md. Intakhab Alam. Development, Evaluation and Stability Studies of Zidovudine and Lamivudine (ZILA) Tablet Dosage Form. Singh *et al.* / Journal of Applied Pharmaceutical Science 2012; 2: 149-154.
11. Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents. Department of Health and Human Services; 2011; 1:174-178.

12. Smith KY, Patel P, Fine D, et al. Randomized, double-blind, placebo-matched, multicenter trial of abacavir/lamivudine or tenofovir/emtricitabine with lopinavir/ritonavir for initial HIV treatment. AIDS 2009; 23:1546-1547.

13. Punna Rao Ravi, Udaya Kanth Kotreka, Ranendra Narayan Saha. Controlled Release Matrix Tablets of Zidovudine: Effect of Formulation Variables on the *in vitro* Drug Release Kinetics. AAPS Pharmscitech March 2008; 9:302-313.

How to cite this article:
Martha S and Devi BS: Development and *in-vitro* Characterization of Abacavir and Zidovudine Tablet in Combination. Int J Pharm Sci Res 2015; 6(9): 4004-15.doi: 10.13040/IJPSR.0975-8232.6(9).4004-15.