International Journal of Pharmaceuticals and Health care Research (IJPHR)

ISSN: 2306-6091

IJPHR |Vol.13 | Issue 4 | Oct - Dec -2025

www.ijphr.com

DOI : https://doi.org/10.61096/ijphr.v13.iss4.2025.569 -580

Review

Development and in-*Vitro* Evaluation of Raltegravir Sustain Release Tablets

Durgasi Prembabu Reddy, Zareena, Dr. L. Harikiran.

[1]*Department of Pharmaceutics, Princeton College of Pharmacy in Narapally, Ghatkesar, Telangana.*

*Corresponding Author
DURGASI PREMBABU REDDY*
Department of Pharmaceutics, Princeton College of Pharmacy, Narapally, Ghatkesar, Telangana.
Email Id- princeton.pharmacy@gmail.com.

Published on: 24 Oct 2025

Published by:
Futuristic Publications

Abstract

The present study focuses on the development and in-vitro evaluation of sustained release tablets of Raltegravir, an antiretroviral drug used in the treatment of HIV. The aim was to enhance therapeutic efficacy and patient compliance by reducing the frequency of drug administration through sustained drug release. Various formulations were prepared using different polymers, among which Karya gum was selected as the natural polymer for sustained release.

A total of several batches was formulated, and formulation R4, containing 100 mg of Karya gum, was found to be the optimized batch based on evaluation parameters. All pre-compression and post-compression parameters, including hardness, friability, weight variation, and drug content, were within acceptable limits. In-vitro dissolution studies revealed that formulation R4 exhibited a sustained drug release of 99.57% over a period of 12 hours.

The drug release kinetics of the optimized formulation followed a sustained release pattern, indicating its potential in maintaining consistent plasma levels and improving therapeutic outcomes. Hence, R4 formulation using Karya gum can be considered a promising sustained release system for Raltegravir.

Keywords: Sustained Release Tablets of Raltegravir

1. INTRODUCTION

All the pharmaceutical products formulated for systemic delivery via the oral route of administration irrespective of the mode of delivery (immediate, sustained or controlled release) and the design of dosage forms (either solid dispersion or liquid), must be developed within the intrinsic characteristics of GI physiology, pharmacokinetics, pharmacodynamics and formulation design is essential to achieve a systemic approach to the successful development of an oral pharmaceutical dosage form[1,2] . Advantages of administering a single dose of a drug that is released over an extended period of time, instead of numerous doses, have been obvious to the Pharmaceutical industry for some time. The desire to maintain a near-constant or uniform blood level of a drug often translates into better patient compliance, as well as enhanced clinical efficacy of the drug for its intended use[3] . Because of increased complication and expense involved in marketing of new drug entities, has focused greater attention on development of sustained release or controlled release drug delivery systems[4]. Matrix system is widely used for the purpose of sustained 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[5]. One of the interesting results of pharmaceutical research is the fact that absorption rate of a drug can be decreased by reducing its rate of release from the dosage form.

The product so formulated are designated as sustained action, sustained release, delayed action, prolonged action, depot, respiratory, retarded release and timed release medication.[6,7] Over the past 30 years, as the expense and complication involved in marketing new entities have increased with concomitant recognition of the therapeutics advantages of controlled drug delivery, greater attention has been focused on development of sustained or controlled drug delivery system. Sustained release technology is relatively new field and as a consequence, research in the field has been extremely fertile and has produced many discoveries.

With many drugs, the basic goal is to achieve a steady state blood level that is therapeutically effective and non-toxic fir an extended period of time. The design of proper dosage form is an important element to accomplish this goal. Sustained release, sustained action, prolonged action, controlled release extended action, timed release and depot dosage form are term used to identify drug delivery system that are designed to achieve prolonged therapeutic effect by continuously releasing medication over an extended period of time after administration of a single dose. In the case of oral sustained released dosage form, an effect is for several hours depending upon residence time of formulation in the GIT. Conventional drug therapy requires periodic doses of therapeutic agents. These agents are formulated to produce maximum stability, activity and bioavailability. For most drugs, conventional methods of drug administration are effective, but some drugs are unstable or toxic and have narrow therapeutic ranges. Some drugs also possess solubility problems. In such cases, a method of continuous administration of therapeutic agent is desirable to maintain fixed plasma levels.[8]

Sustained release concept: - Sustained release, sustained action, prolong action, controlled release, extended action, depot are terms used to identify drug delivery systems that are designed to achieve prolong therapeutic effect by continuously releasing medication over an extended period of time after administration of single dose. In the case of orally administer this period is measured in hours while in the case of injectables this period varies from days to months.

Parameters for drug to be formulated in sustained release dosage form:

Physicochemical parameters for drug selection.

1. Molecular weight/size < 1000 Daltons.
2. Solubility > 0.1 mg/ml for pH 1 to pH 7.8.
3. Apparent partition coefficient High.
4. Absorption mechanism Diffusion.
5. General absorbability from all GI segments.
6. Release should not be influenced by pH and enzymes.

Pharmacokinetic parameters for drug selection

1. Elimination half-life preferably between 2 to 8 hrs
2. Total clearance should not be dose dependent
3. Elimination rate constant required for design
4. Apparent volume of distribution (Vd) The larger Vd and MEC, the larger will be the required dose size
5. Absolute bioavailability should be 75% or more
6. Intrinsic absorption rate must be greater than release rate
7. Therapeutic concentration Css The lower Css and smaller Vd, the loss among of drug required.
8. Toxic concentration Apart the values of MTC and MEC, safer the dosage form. Also suitable for drugs with very short half-life.

Approaches To Sustain Release Drug Delivery System

1. Dissolution controlled release systems.
2. Diffusion controlled release systems.
3. Dissolution and diffusion-controlled release systems.
4. Ion exchange resin- drug complexes.
5. pH dependent formulation.
6. Osmotic pressure-controlled systems.

1. Dissolution controlled release systems

These systems are easy to formulate. Drug which are formulated using system have slow dissolution rate, produce slow dissolving forms with gastric intestinal fluids and the drugs which are having high aqueous solubility and dissolution rate. Dissolution controlled release system can be classified into two techniques

A. Matrix dissolution controlled release system

Matrix dissolution system is known as monolithic because the drug present in the matrix is completely dissolved in the medium which controls the drug release. They are mostly made of waxes like beeswax, carnauba wax, hydrogenated castor oil, etc. and play important role to control the drug release rate by controlling the rate of dissolution fluid penetration into the matrix by altering the porosity of tablet, decreasing its wettability or by itself getting dissolved at a slower rate The drug release generally follows first order kinetics from such matrices system.

B. Reservoir dissolution controlled release system

In reservoir system, the drug particles are coated or encapsulated with one of the several microencapsulation techniques using slowly dissolving materials like cellulose, polyethylene glycol and waxes. This unit can be encapsulated in capsules or may be compressed into tablets Solubility and thickness of the coating play important role in dissolution rate of drug.

2. Diffusion controlled release systems

In diffusion release models, the diffusion of dissolved drug through a polymeric membrane is a rate limiting step. In this system, the drug release rate never follows zero-order kinetics, because the diffusion path length increases with time as the insoluble matrix is drug depleted. The mechanism of diffusion process shows the movement of drug molecules from a region of a higher concentration to region of lower concentration. The flux of the drug J (in amount / area -time), across a membrane in the direction of decreasing concentration is given by Fick's law.J = -D dc/dx where, J = flux of the drug across a membrane in the direction of decreasing conc.,D = Diffusion coefficient of the drug, and dc /dx = Change in the concentration of the drug in the membranewhereas when drug present in a water insoluble membrane, it must diffuse through the membrane.The drug release rate dm/ dt is given by dm = ADK∆ C/dt L where, A = Area. K = Partition coefficient of drug between the membrane and drug core. L = Diffusion path length (i.e. thickness of coat). ∆C=Concentration difference across the membrane.

3. Dissolution and diffusion controlled release systems

In this kind of system, the drug is enclosed in a membrane which is partially water soluble. The dissolution of the membrane take place due to which pores are formed and these pores allows aqueous medium to enter in the membrane. This results in the dissolution of the drug in membrane followed by the diffusion of the dissolved drug from the system. Example of such coating is combination of ethyl cellulose with PVP or methyl cellulose.

4. Ion exchange resin- drug complexes:

Resins are the materials which are insoluble in water. Resin contains anionic groups such as amino or quaternary ammonium groups and cationic groups such as carboxylic groups, or sulfonic groups in repeating positions on the chain. A drug–resin complex is formed by prolonged exposure of drug to the resin. The drug from these complexes gets exchanged in gastrointestinal tract and later they are released with excess of Na+ and Cl- present in gastrointestinal tract.

7. METHODOLOGY

7.1. Analytical method development:

a) Determination of absorption maxima:

100mg of Raltegravir pure drug was dissolved in 15 ml of Methanol and make up to 1000ml with 0.1N HCL (stock solution-1). 10ml of above solution was taken and make up with 100ml by using 0.1N HCL (stock solution -2 i.e. 100µg/ml). From this 10 ml was taken and make up with 100 ml of 0.1 N HCL (10µg/ml). Scan the 10µg/ml using Double beam UV/VIS spectrophotometer in the range of 200-400nm.

b) Preparation calibration curve:

100mg of Raltegravir pure drug was dissolved in 15ml of Methanol and volume make up to 100ml with 0.1N HCL (Stock solution-1). 10ml of above solution was taken and male up with 100ml by using 0.1N HCL (Stock solution-2 i.e. 100µ/ml). From this take 0.5,1.0,1.5,2.0 and 2.5ml of solution and make up to 10 ml 0.1N HCL to obtain 5, 10, 15, 20, and 25 µg/ml of Raltegravir per ml of solution. The absorbance of the above dilutions was measured at 246 nm by using UV- Spectrophotometer taking 0.1N HCL as blank. Then a graph was plotted by taking Concentration on X-Axis and Absorbance on Y-Axis Which gives a straightline Linearity of standard curve was assessed from the square of correlation coefficient (R^2) Which determined by least-square linear regression analysis. The above was procedure was repeated by using pH 6.8 phosphate buffer solutions.

7.2. Formulation development of Sustained release Tablets:

All the formulations were prepared by wet granulation Method. The compositions of different formulations are given in the Table 7.1. The tablets were prepared as per the procedure given below and aim is to prolong the release of Raltegravir.

Procedure:

1) Raltegravir and all other ingredients except Mg Streate and Talc were individually passed through sieve no ≠ 40.
2) Raltegravir polymer mix thoroughly than add the binder solution mix properly up to 15 min.
3) Dry the above mixture at 65-70ºC by using dryer
4) After completion of drying the mixture is passed through sieve no ≠ 22.
5) The powder mixture was lubricated with Mg Streate and Talc.
6) Finally go for compression.

Table 7.1: Formulation of Sustained release tablets

Ingredients	R1	R2	R3	R4	R5	R6	R7	R8	R9
Raltegravir	100	100	100	100	100	100	100	100	100
Xanthan gum	50	100	150	-	-	-	-	-	-
Karaya gum	-	-	-	50	100	150	-	-	-
HPMC K100M	-	-	-	-	-	-	50	100	150
Talc	20	20	20	20	20	20	20	20	20
Mg Streate	15	15	15	15	15	15	15	15	15
Lactose	215	165	115	215	165	115	215	165	115
Total weight	400	400	400	400	400	400	400	400	400

RESULTS AND DISCUSSION

The present work was designed to develop sustained tablets of Raltegravir using various polymers. All the formulations were evaluated for physicochemical properties and *in vitro* drug release studies.

8.1 Analytical Method

8.1.1 Standard graph of Raltegravir in 0.1N HCL:

The scanning of the 10µg/ml solution of Raltegravir the ultraviolet range (200–400 nm) against 0.1 N HCL the maximum peak observed at λ_{max} as 246 nm. The standard concentration of Raltegravir (5–25 µg/ml) was prepared in 0.1N HCL showed good linearity with R^2 value of 0.998, which suggests that it obeys the Beer-Lamberts law.

Table 8.1: Standard curve of Raltegravir0.1N HCL

Concentration (µg/ mL)	Absorbance
0	0
5	0.114
10	0.213
15	0.325
20	0.431
25	0.537

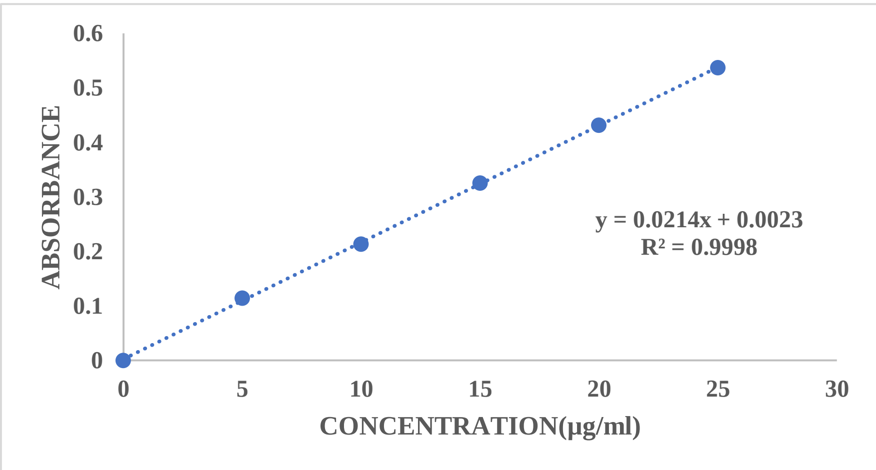

Figure 8.1: Calibration curve of Raltegravir0.1N HC1 at 246 nm

8.1.2 Standard Curve of Raltegravir Phosphate buffer pH 6.8

The scanning of the 10 µg/ml solution of Raltegravir the ultraviolet range (200-400nm) against 6.8 pH phosphate the maximum peak observed at the λ_{max} as 246 nm. The standard concentrations of Raltegravir

(5-25µg/ml) prepared in 6.8 pH phosphate buffer showed good linearity with R^2 value of 0.998, which suggests that it obeys the Beer-Lamberts law**.**

Table 8.2: Standard curve of Raltegravir Phosphate buffer pH 6.8

Concentration (µg/ml)	Absorbance
0	0
5	0.165
10	0.292
15	0.418
20	0.549
25	0.677

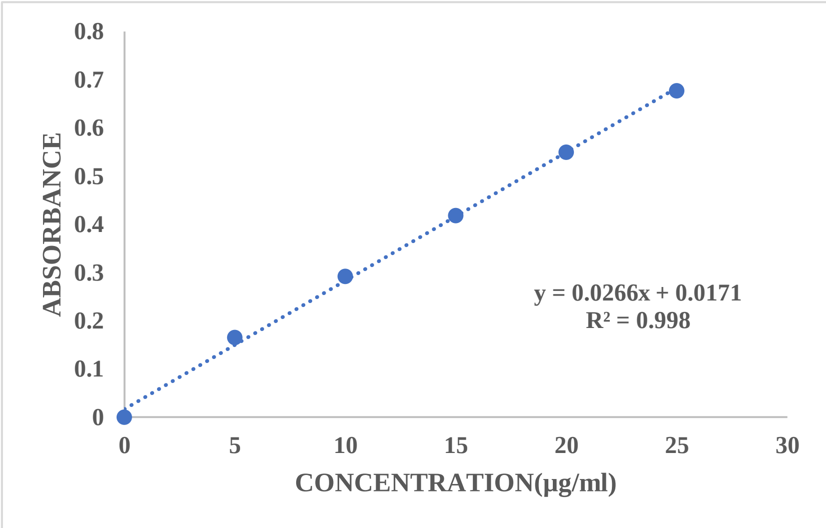

Figure.8.2: Calibration of RaltegravirPhosphate buffer pH 6.8

8.2 EVALUATION PARAMETERS

8.2.1 Pre-compression parameters

Table 8.3: Pre-compression parameters of powder blend

Formulation Code	Angle of Repose	Bulk density (gm/ml)	Tapped density (gm/ml)	Carr's index (%)	Hausner's Ratio
R1	25.01	0. 59	0.57	14.03	1.16
R2	26.8	0. 46	0.67	16.41	1.19
R3	27.7	0. 32	0. 54	18.75	1.23
R4	25.33	0.54	0.64	15.62	1.18
R5	25.24	0.52	0.65	18.46	1.22
R6	28.12	0. 46	0. 56	15.15	1.17
R7	27.08	0.58	0.69	15.94	1.18
R8	25.12	0.48	0.67	15.78	1.18
R9	26.45	0.54	0.65	16.92	1.25

Tablet powder blend was subjected to various pre-compression parameters. The angle of repose values was showed from 25.01 to 28.12; it 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. 32 to 0.59 (gm/cm^3) showing that the powder has goof flow properties. The tapped density of all the formulations was found to be in the range of 0.54 to 0.69 showing The powder has good flow properties. The compressibility index of all the formulations was found to ranging from 14.03 to 18.75 which showed that the powder has good flow properties. All the formulations were showed the Hausner ratio ranging from 1.16 to 1.25 indicating the powder has good flow properties.

8.2.2 Post Compression Parameters for tablets

Table.8.4: Post Compression Parameters of tablets

Formulation codes	Average Weight (mg)	Hardness (kg/cm2)	Friability (% loss)	Thickness (mm)	Drug content (%)
R1	398.37	5.67±0.84	0.37	3.25±0.22	98.72
R2	399.91	5.51±0.47	0.56	3.68±0.18	97.88
R3	397.88	5.62±0.55	0.48	3.75±0.47	99.62
R4	400.05	5.48±0.38	0.44	3.98±0.71	100.02
R5	396.53	5.66±0.22	0.58	3.55±0.38	98.96
R6	399.78	5.58±0.49	0.42	3.62±0.26	99.57
R7	397.62	5.45±0.96	0.61	3.48±0.55	97.34
R8	398.58	5.61±0.44	0.54	3.71±0.48	98.87
R9	396.86	5.58±0.82	0.39	3.48±0.66	99.66

Weight variation and thickness: all the formulations were evaluated for uniformity of weight using electronic weighing balance and the results are shown in table 9.5. The average tablet weight of all the formulations was found to be between 396.53 to4100.05. The maximum allowed percentage weight variation for tablets weighing >400 mg is 5% and no formulations are not exceeding this limit. Thus, all the formulations were found to comply with the standards given in I.P and thickness of all the formulations was also complying with the standards that were found to be between 3.25±0.22 to 3.98±0.71.

Hardness and friability: all the formulations were evaluated for their hardness, using Monsanto hardness tester and the results are shown in table. The average hardness for all the formulations was found to be between (5.45±0.96 to 5.67±0.84) kg/cm^2 which was found to be acceptable.

Friability was determined to estimate the ability of the tablets to withstand the abrasion during packing, handling and transporting. All the formulations were evaluated for their percentage friability using Roche friabilator and the results were shown in table. The average percentage friability for all the formulations was between 0.37 and 0.61, which was found to be within the limit.

Drug content: All the formulations were evaluated for drug content according to the procedure described in the methodology section and the results were shown in table. The drug content values for all the formulations were found to in range of (97.88 to 100.02). According to IP standards the tablets must contain not less than 95% and not more than 105% of the stated amount of the drug. Thus, all the FDT formulations comply with the standards given in IP.

***In vitro* drug release studies:**

The formulations prepared with different polymers by direct compression method. The tablets dissolution study was carried out in paddle dissolution apparatus using 0.1 N HCL for 2 hr and 6.8 pH phosphate buffer for remaining hours as a dissolution medium

Table 8.5: Dissolution Data of Raltegravir Tablets

TIME (hr)	CUMULATIVE PERCENTAGE DRUG RELEASED								
	R1	**R2**	**R3**	**R4**	**R5**	**R6**	**R7**	**R8**	**R9**
0	0	0	0	0	0	0	0	J0	0
1	8.62	9.71	8.23	11.81	9.51	10.25	9.62	11.62	9.89
2	15.11	18.02	17.21	19.96	16.73	18.01	15.11	16.22	21.66
3	22.37	26.11	24.53	26.87	28.88	28.19	26.37	21.57	25.53
4	32.74	33.25	31.45	39.19	35.52	34.35	39.74	34.51	38.52
5	38.06	44.75	39.27	43.72	47.17	42.85	45.06	47.37	42.36
6	49.52	51.13	46.55	49.31	57.91	52.11	56.52	55.96	46.61
7	57.09	54.26	56.05	57.69	64.74	59.32	65.09	63.05	57.69

8	62.92	59.53	62.78	66.33	73.95	69.88	72.92	68.23	61.91
9	69.33	64.01	68.59	73.76	76.82	74.34	79.63	75.77	69.42
10	73.82	72.91	75.81	78.98	77.67	83.75	82.82	85.67	76.85
11	81.74	77.36	88.22	87.71	88.08	88.27	89.74	87.56	85.44
12	89.69	89.29	93.25	99.57	91.93	92.22	98.12	95.31	93.79

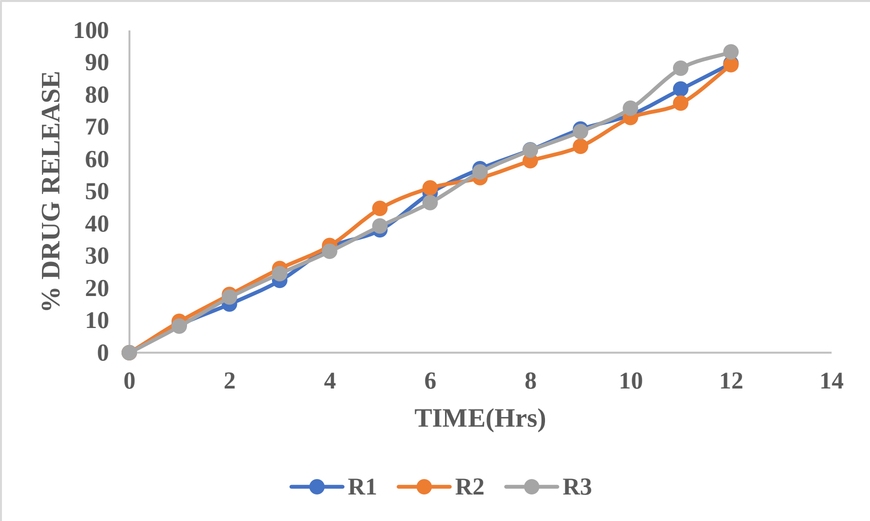

Figure 8.3: Dissolution study of RaltegravirSustained Release tablets (R1 to R3)

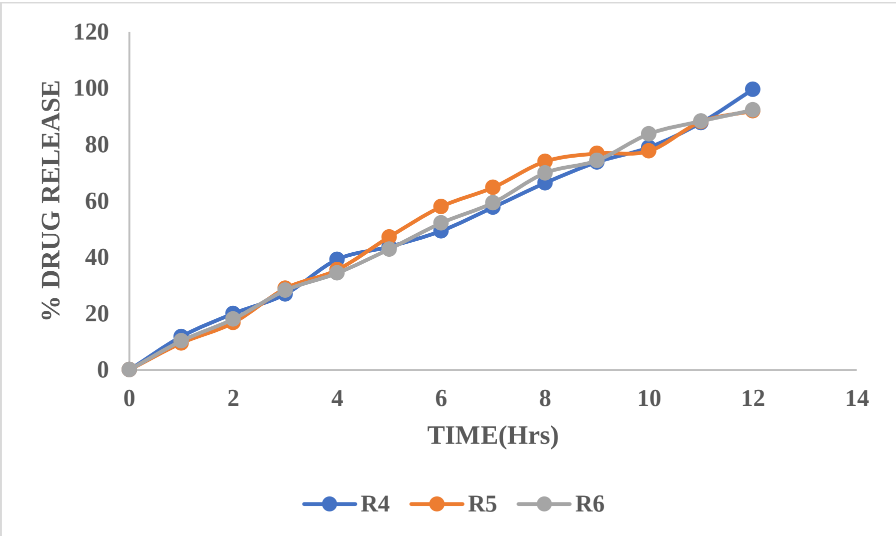

Figure 8.4: Dissolution study of Raltegravirtablets (R4 to R6)

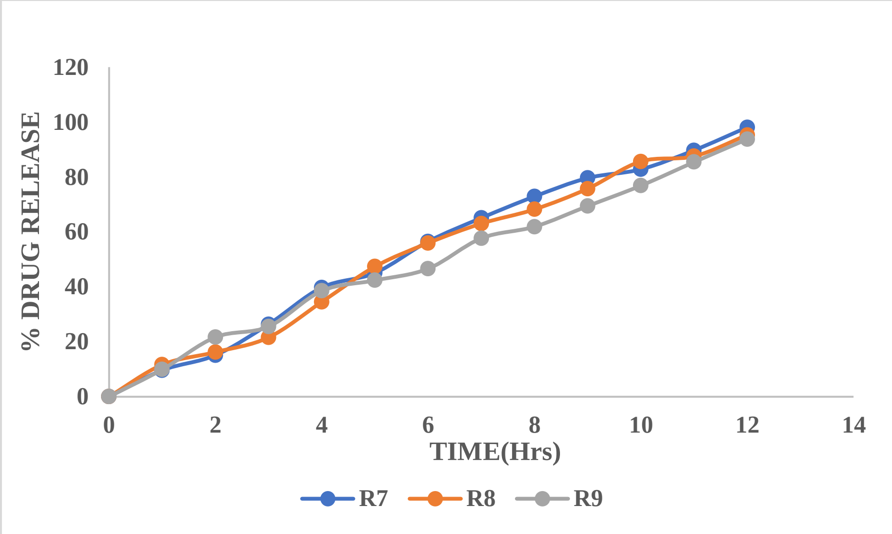

Figure 8.5: Dissolution study of Raltegravir tablets (R7 – R9)

From the dissolution data it was evident that the formulations prepared with Xanthan gum as polymer were able to retard the drug release up to desired time period i.e., 12 hours.

Formulations prepared with Karaya gum retarded the drug release in the concentration of 100mg (R4 Formulation) showed required release pattern i.e., retarded the drug release up to 12 hours and showed maximum of 99.57 % in 12 hours with good retardation.

The formulations prepared with HPMC K100M were able to retard up to 12 hours.

Among all the formulations R4 formulation containing (Drug: Karaya gum) 1:1 ratio showed maximum % drug release i.e. 99.57 % at 12 hr.

Hence based on dissolution data of 9 formulations, R4 formulation showed better release up to 12 hours. So R4 formulation is optimized formulation,

8.3 Application of Release Rate Kinetics to Dissolution Data

Data of *in vitro* release studies of formulations which were showing better drug release were fit into different equations to explain the release kinetics of Raltegravir release from sustained tablets. The data was fitted into various kinetic models such as zero, first order kinetics, Higuchi and Korsmeyer peppas mechanisms and the results were shown in the below table.

Table 8.6: Release Kinetics data for optimized formulation (R4)

CUMULAT IVE (%) RELEASE Q	TIME (T)	ROOT (T)	%) REL	LOG (T	LOG (%) REM AIN	RELEASE RATE (CUMUL ATIVE % RELEASE/t)	1/CU M% RELE ASE	PEPP AS log Q/100	% Drug Remaining	Q01/3	Qt1/3	Q01/3- Qt1/3
0	0	0	0	0	0	0	0	0	0	0	0	0
11.81	1	1.000	1.072	0.000	1.945	11.810	0.0847	-0.928	88.19	4.642	4.451	0.190
19.96	2	1.414	1.300	0.301	1.903	9.980	0.0501	-0.700	80.04	4.642	4.310	0.332
26.87	3	1.732	1.429	0.477	1.864	8.957	0.0372	-0.571	73.13	4.642	4.182	0.460
39.19	4	2.000	1.593	0.602	1.784	9.798	0.0255	-0.407	60.81	4.642	3.932	0.709
43.72	5	2.236	1.641	0.699	1.750	8.744	0.0229	-0.359	56.28	4.642	3.832	0.809
49.31	6	2.449	1.693	0.778	1.705	8.218	0.0203	-0.307	50.69	4.642	3.701	0.941
57.69	7	2.646	1.761	0.845	1.626	8.241	0.0173	-0.239	42.31	4.642	3.485	1.157
66.33	8	2.828	1.822	0.903	1.527	8.291	0.0151	-0.178	33.67	4.642	3.229	1.412
73.76	9	3.000	1.868	0.954	1.419	8.196	0.0136	-0.132	26.24	4.642	2.972	1.670
78.98	10	3.162	1.898	1.000	1.323	7.898	0.0127	-0.102	21.02	4.642	2.760	1.882
87.71	11	3.317	1.943	1.041	1.090	7.974	0.0114	-0.057	12.29	4.642	2.308	2.334
99.57	12	3.464	1.998	1.079	0.540	8.298	0.0100	-0.002	0.43	4.642	0.755	3.887

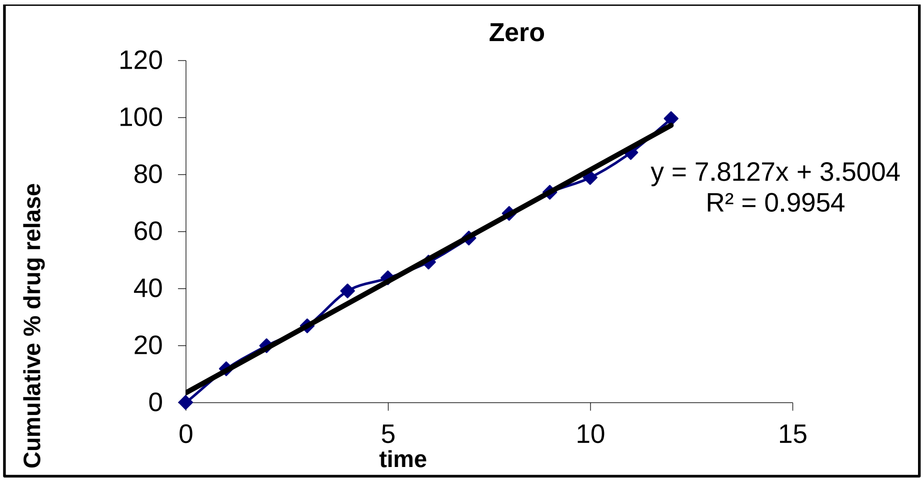

Figure 8.6: Graph of zero order kinetics

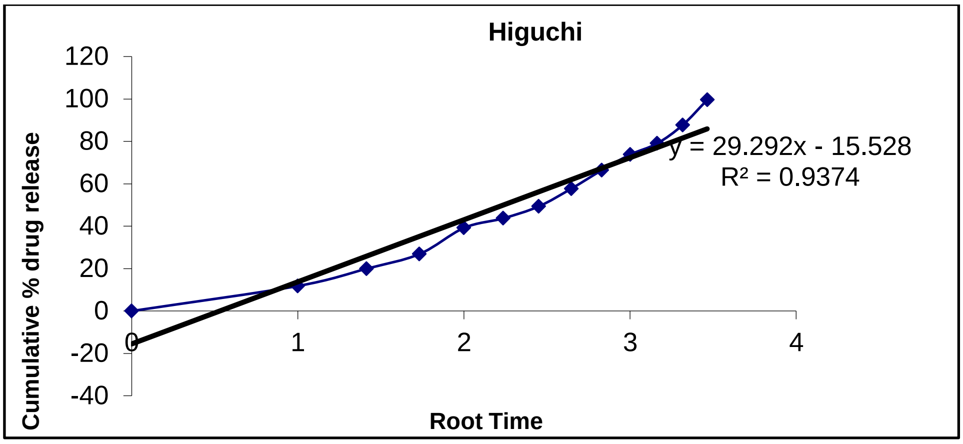

Figure 8.7: Graph of Higuchi release kinetics

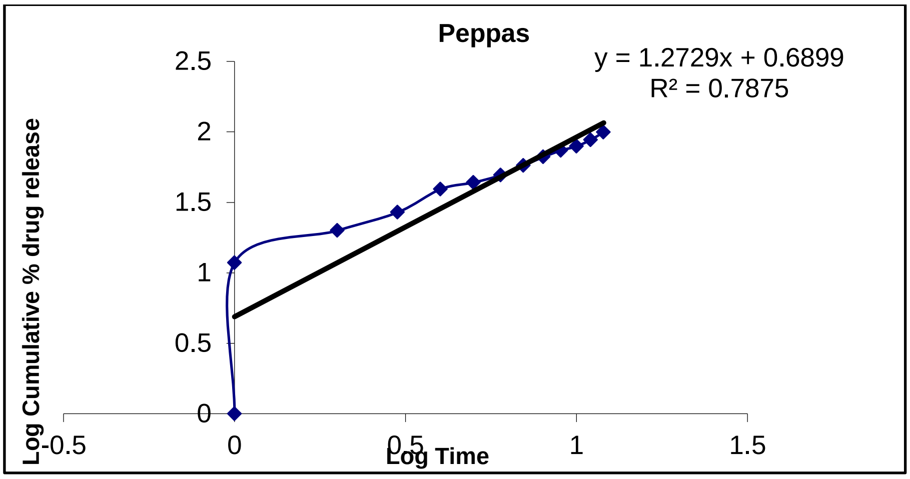

Figure 8.8: Graph of peppas release kinetics

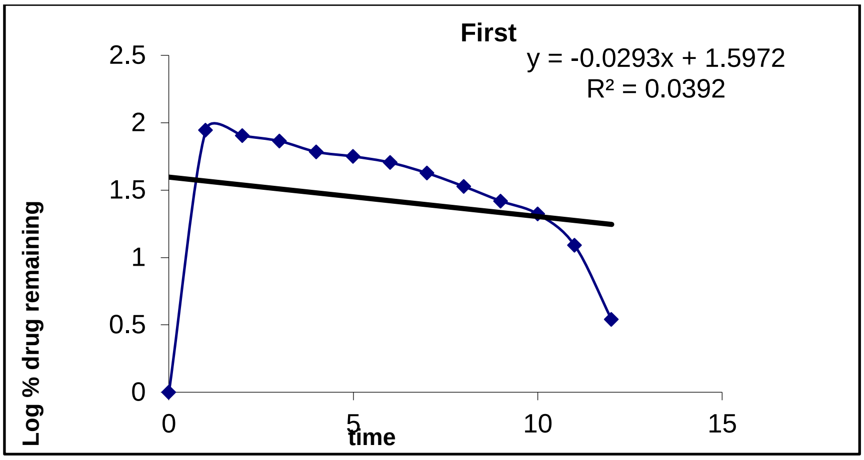

Figure 8.9: Graph of first order release kinetics

Based on the data above results the optimized formulation followed Kors mayer Peppas Release Kinetics.

9.4 Drug and Excipient Compatibility Studies

9.4.1 FTIR study

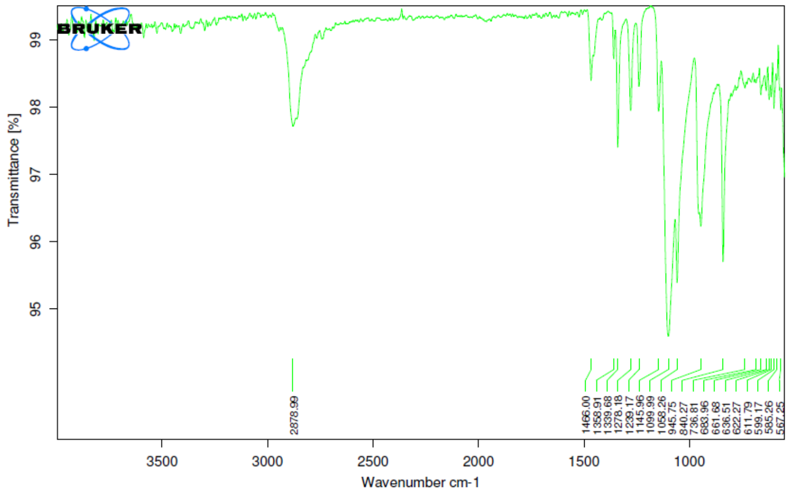

Figure. 8.10: Ftir Graph Of Pure Drug

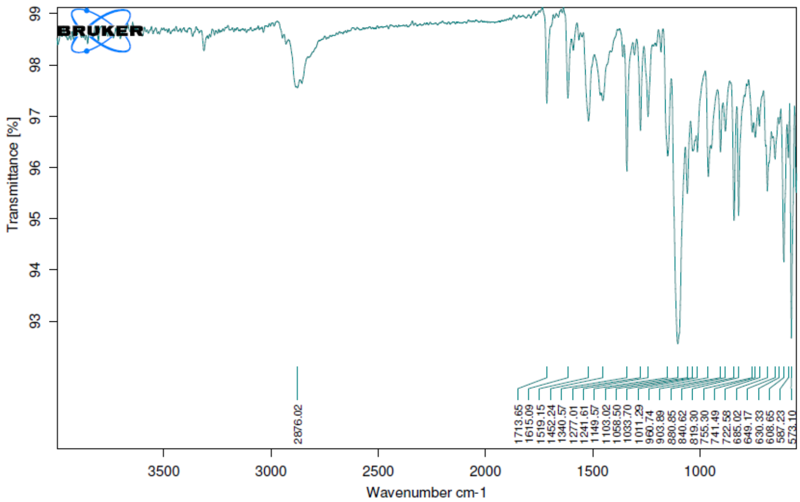

Figure. 8.11: Ftir graph of optimized Formulation

From the FTIR data is was evident that the drug and excipient does not have any interactions. Hence they were compatible.

CONCLUSION

The present study successfully demonstrated the development and in-vitro evaluation of sustained release tablets of Raltegravir. Various formulations were prepared using different concentrations and combinations of polymers to achieve the desired sustained release profile. Among the prepared batches, the optimized formulation exhibited acceptable physicochemical properties including hardness, friability, weight variation, and uniform drug content, all within pharmacopeial limits.

The in-vitro dissolution studies confirmed that the optimized batch provided a prolonged and controlled release of Raltegravir over an extended period, thereby potentially reducing dosing frequency and improving patient compliance. Drug release kinetics analysis revealed that the release followed a Higuchi or Korsmeyer-Peppas model, indicating a diffusion-controlled or polymer erosion mechanism.

Overall, the study concludes that sustained release tablets of Raltegravir can be effectively formulated using appropriate polymers, and the developed formulation holds promise for improved therapeutic efficacy in the management of HIV by maintaining consistent plasma drug levels.

ACKNOWLEDGEMENT

The Authors are thankful to the Management and Principal, Princeton College of Pharmacy, Narapally, Ghatkesar, Telangana, for extending support to carry out the research work. Finally, the authors express their gratitude to the Sura Pharma Labs, Dilsukhnagar, Hyderabad, for providing research equipment and facilities.

REFERENCES

1. M.m. Gupta, ray brijesh. A Review On: Sustained Release Technology. International Journal of Therapeutic Applications, Volume 8, 2012, 18–23.
2. Chien Y. W. Novel Drug Delivery System 1992; 2: 139–140.
3. Altaf AS, Friend DR, MASRx and COSRx Sustained-Release Technology in Rathbone MJ, Hadgraft J, Robert MS, Modified Release Drug Delivery Technology, Marcell Dekker Inc., New York, 2003.
4. Gwen MJ and Joseph RR, In Banker GS and Rhodes CT, Eds., Modern Pharmaceutics, 3rd Edn , Vol. 72, Marcel Dekker Inc. New York, 1996, 575.
5. Salsa T, Veiga F and Pina M.E, Drug Develop. Ind. Pharm., 1997, 23, 931.
6. Jantez GM, Robinson JR. Sustained and controlled release drug delivery systems. In: Banker GS, Rhodes CT, editors. Modern pharmaceutics. 3rd edition. New York: marcel dekker inc; 1996.
7. Popli H, shrma SN. Trends in oral sustained release formulations-I The eastern pharmacist 1989; 32: p. 99–103.
8. Remington. The Science and Practice of pharmacy, 20th Edition, vol. I: 903–913.
9. Abhijeet Welankiwar. Review: Sustained Release Dosage Forms.
10. Piyush Mandhar, Gayitri Joshi. Development of Sustained Release Drug Delivery System: A Review. Asian Pac. J. Health Sci., 2015; 2(1): 179–185.

11. Bechgaard H, Nielson GH. Controlled release multiple units and single unit dosage. Drug Dev & Ind Pharm 1978; 4(1): 53–67.
12. Qiu Y, Zhang G, Wise DL. Handbook of pharmaceutical controlled release technology. New York: Marcell Dekke, 3rd edition 2000.
13. Chugh I, Seth N, Rana AC, Gupta S. Oral sustained release drug delivery system: anoverview. International research journal of pharmacy 2012; 3(5): 57–62.
14. Chauhan MJ, Patel SA. A Concise Review on Sustained Drug Delivery System and Its Opportunities. Am. J. PharmTech Res 2012; 2(2): 227–238.
15. Remington. The Science and Practice of pharmacy. Lippincott Williams & Wilkins, 20th Edition 2006.
16. Davis SS, Hardy JG, Taylor MJ, Whalley DR, Wilson CG. Comparative study of gastrointestinal.
17. Rakesh Roshan Mali, Vaishali Goel, Sparsh Gupta. Novel Study in Sustained Release Drug Delivery System: A Review. Int. J. Pharm. Med. Res. 2015; 3(2):204–215.
18. Patel Chirag J., Satyanand T., Novel Sustained Release Drug Delivery: A Modern Review, International Journal of Applied Pharmaceutics 2014; 1: 115–119.
19. Pogula M., Nazeer S., Extended Release Formulation, International Journal of Pharmacy & Technology 2010;2: 625– 684.
20. Parashar T., Soniya S., Singh V., Novel oral sustained release technology: A Concise Review, International Journal of Research and Development in Pharmacy and Life Sciences 2013;262–269.
21. Patel Kundan K., Patel Mehul S., Bhatt Nayana M., An Overview: Extended Release Matrix Technology, International Journal of Pharmaceutical and Chemical Sciences 2012; 112–115.
22. Rao Raghavendra NG., Raj Prasanna Richard K., Nayak S., Review on Matrix Tablet as Sustained Release, International Journal of Pharmaceutical Research & Allied Sciences 2013;2:1700–1717.
23. Wadher G., Satish B., Tukaram MK., Recent (Aspects) trend on Sustained drug delivery system, International Journal of Chemical and Pharmaceutical Sciences 2013; 4:1–7.
24. Kumar Sampath KP., Bhowmik D., Srivastava S., Sustained release drug delivery system potentials, International Journal of Pharmaceutics 2010; 2:751–754.
25. Deore KR., Kuncha K and Theetha GT., Preparation and evaluation of sustained release matrix tablets of Tramadol hydrochloride using Glycerol Palmitostearate, Tropical Journal of Pharmaceutical Research 2010; 275–281.