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R E S E A R C H A R T I C L E

Development and *In-Vitro* Evaluation of Raltegravir Sustain Release Tablets Using Solid Compaction Method

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A B S T R A C T

The present study was to establish Ratlegravir SR tablets by liquid solid compaction method using Propylene glycol and Tween 80. Sustained layer was prepared by using Guargum and Xanthan gum as polymers. The tablets were evaluated for Bulk density, Tapped density, Compressibility index, Hausner ratio, and Angle of repose. All the values were found within limits of standard. In vitro release studies were carried out by USP type 2 paddle apparatus. The results showed that Xanthan gum in sustained can control the release of drug. The formulation (F2) having sustained effect 100.00% within 12 hours. The present study concluded Raltegravir Sustained release tablets can be a better alternative to conventional dosage form.

Keywords: Raltegravir, Sustained release, Liqui solid compaction method.

A R T I C L E I N F O

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C O N T E N T S

1. Introduction

With many drugs, the basic goal of therapy is to achieve a steady-state blood or tissue level that is therapeutically effective and non-toxic for an extended period of time. The design of proper dosage regimens is an important element in accomplishing this goal[1].The idealized objective points to the two aspects most important to drug delivery, namely, spatial placement and temporal delivery of a drug. Spatial placement relates to targeting a drug to a specific organ of tissue, while temporal delivery refers to controlling the rate of drug delivery to the target tissue. An appropriately designed sustained release drug delivery system can be a major advance toward solving these two problems. The bulk of research has been directed at oral dosage forms that satisfy the temporal aspect of drug delivery, but many of

the newer approaches under investigation may allow for spatial placement as well.

Conventional drug therapy

Sustained Release Drug Therapy

Drug Properties Relevant to Sustained–release Formulation

Discovery, testing and marketing of new chemical entities, the so – called medicinal agents, is what differentiates the pharmaceutical industry from many other enterprises. The primary objective is to determine the impact of various factors that have forced the drug industry to direct efforts towards development of modified – release or so – called specialized drug delivery systems.

Physicochemical Properties

A more is an important tool in the development[5] of the best formulation, in the understanding of the drug's biopharmaceutical characteristics, and in interpretation of possible risks, such as potential food effect on bioavailability or interaction with other drugs.

Table 1

Physical Properties	Biological Properties
Aqueous solubility& pKa	Absorption
Partition coefficient	Distribution
Drug Stability	Metabolism
Protein Binding	Elimination and Biological Half-life
Molecular Size and Diffusivity	Side effects and Safety Considerations
----------	Dose Size

After ingestion, the tablet is wetted by gastric fluid and the polymer begins to hydrate. A gel layer forms around surface of the tablet and an initial quantity of drug is exposed and released. As water penetrates further into the tablet the thickness of the gel layer is increased and soluble drug diffuses through the gel layer. As the outer layer becomes fully hydrated it erodes from the tablet core. If the drug is insoluble, it is released as such with the eroding gel layer. Thus, the rate of drug release is controlled by the processes of diffusion and tablet erosion.

2. Materials and Methods

Analytical Method Development

Preparation of 6.8 phosphate buffer

Determination of λ_{max} of Raltegravir6.8 phosphate buffer: This solutions was scanned at range of 200-400nm wavelength light corresponding scan spectrum curve was noted. The corresponding wavelength having highest absorbance is noted as $\lambda_{max..}$

- Construction of calibration curve of Raltegravir6.8 phosphate buffer:
- Formulation of Raltegravir SR tablets by liquid solid compact method
- Processing steps involved in liquid solid compact method

Evaluation of Tablets

Pre Compression studies:

- ❖ Angle of Repose.
- ❖ Density.
- ❖ Carr's Index.
- ❖ Hausner's Ratio

Post compression studies:

- General appearance:
- Average weight/Weight Variation:
- Thickness:
- Hardness test:
- Friability test:
- Assay Procedure.

***In-vitro* Dissolution Study**

In vitro Release Kinetics Studies:

- Zero Order Release Kinetics:
- First Order Release Kinetics:
- Peppa's-Korsemeyer equation (Power Law).

3. Results and Discussions

Construction of Standard calibration curve of Raltegravir in 6.8 phosphate buffer: The absorbance of the solution was measured at 328nm, using UV spectrometer with 6.8 phosphate bufferas blank. The values are shown in table no 20. A graph of absorbance Vs Concentration was plotted which indicated in compliance to Beer's law in the concentration range 2 to 10 µg/ml

Inference:

- The Raltegravir SR tablets were evaluated for their flow properties; the results for the blends of compression tablets.
- The bulk density and the tapped density for all formulations were found to be almost similar.
- The Carr's index and Hausner's ratio were found to be in the range of ≤ 18 and 1.0 to 1.56 respectively, indicating good flow and compressibility of the blends.
- The angle of repose for all the formulations was found to be in the range of 11.03-18.23˚ which indicating passable flow (i.e. incorporation of glidant will enhance its flow).

Formulation Code	Bulk density (Kg/cm²)	Tapped density (Kg/cm²)	Cars index	Hausners ratio	Angle of repose (°)
F1	0.43	0.52	17.3	1.41	12.62
F2	0.40	0.46	13.0	1.5	12.29
F3	0.50	0.58	13	1.16	11.58
F4	0.44	0.51	13.7	1.25	9.29
F5	0.39	0.47	17.0	1.56	18.23
F6	0.42	0.52	19.2	1.45	13.24
F7	0.36	0.39	7.6	1.0	11.03
F8	0.41	0.50	18	1.5	17.4
F9	0.39	0.48	18	1.23	11.96
F10	0.41	0.51	19.6	1.53	12.26
F11	0.44	0.52	15.3	1.40	13.62
F12	0.41	0.45	8.8	1.0	11.85

Pre compression studies of Raltegravir SR tablets

Post compression studies of Raltegravir SR tablets

Inference:

- The variation in weight was within the limit

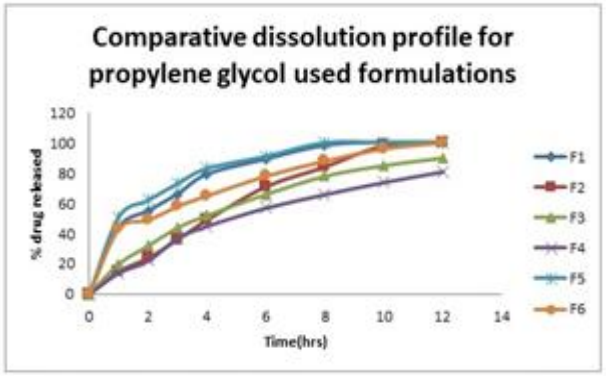
- The thickness of tablets was found to be between 3.03 -5.26 mm.
- The hardness for different formulations was found to be between 4.39 to 5.98 kg/cm^2, indicating satisfactory mechanical strength.
- The friability was < 1.0% W/W for all the formulations, which is an indication of good mechanical resistance of the tablet.
- The drug content was found to be within limits 98 to 102 %.

Formulation Code	% weight vaiation	Thickness	% Friability	%Drug Content	Hardness (Kg/cm^2)
F1	pass	3.16±0.11	0.22	102.0 ±1.1	4.68 ±0.17
F2	pass	3.53±0.15	0.15	101.3 ±1.5	5.13 ±0.15
F3	pass	4.06±0.057	0.12	99.8±1.3	5.58 ±0.13
F4	pass	5.1±0.1	0.43	101.7 ±0.8	5.98 ±0.04
F5	pass	3.03±0.05	0.32	100.6±1.2	4.63 ±0.05
F6	pass	3.83±0.15	0.14	98.9 ±2.1	5.2 ±0.02
F7	pass	4.93±0.05	0.20	99.2± 1.7	5.7 ±0.10
F8	pass	5.26±0.1	0.33	99.5± 1.4	5.93 ±0.05
F9	pass	3.02±0.2	0.18	99.2±1.3	4.39 ±0.02
F10	pass	3.48±0.14	0.21	100.3 ±1.4	4.86 ±0.03
F11	pass	4.91±0.18	0.32	101.2± 1.6	5.72 ±0.12
F12	pass	5.14±0.12	0.16	100.3 ±1.8	5.89 ±0.13

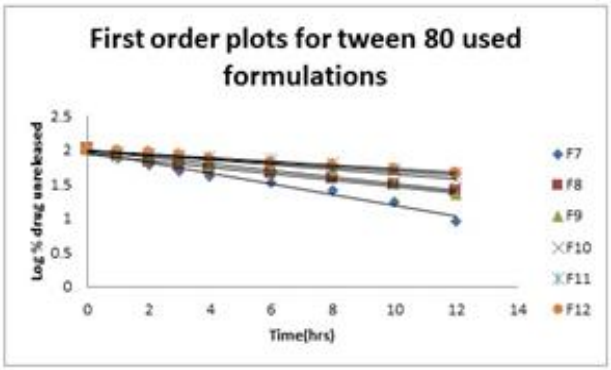
Post compression studies of Raltegravir SR tablets

TIME (hrs)	% DRUG RELEASED											
	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
0	0	0	0	0	0	0	0	0	0	0	0	0
1	11	15	20	14	51	43	23	22	18	11	10	5
2	55	24	32	22	62	49	38	34	23	19	15	11
3	66	36	44	37	73	58	52	41	29	23	19	18
4	79	49	52	45	83	65	59	49	38	33	22	28
6	89	71	66	57	91	78	67	56	45	41	28	36
8	98	84	78	66	100	88	75	62	54	49	36	42
10	100	98	85	74	100	96	83	69	68	51	46	49
12	100	100	90	81	100	100	91	76	78	63	55	56

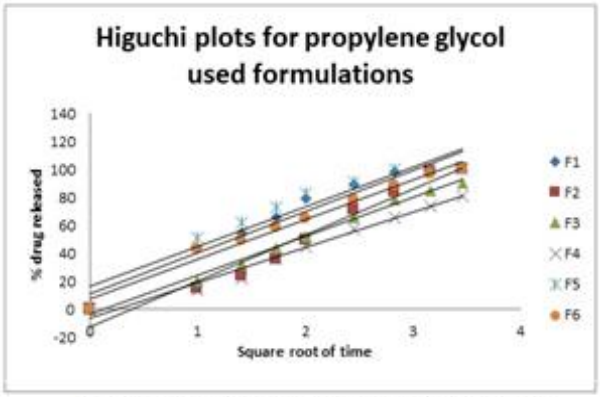
In-vitro Dissolution results of Formulation trails



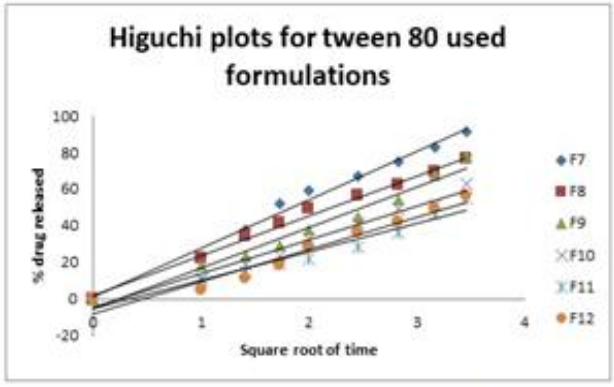
Comparative dissolution profile for F1-F6 formulations



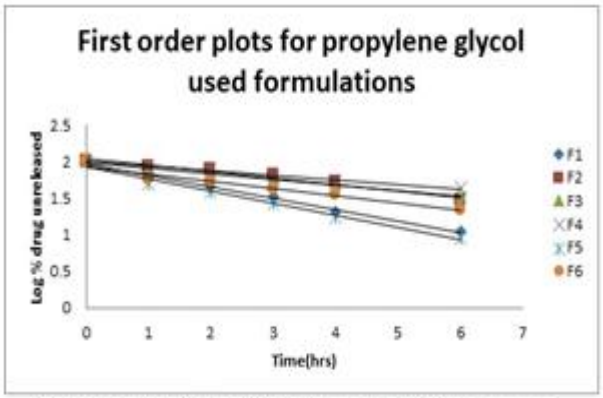
First order plot for best formulations F7-F12 formulations



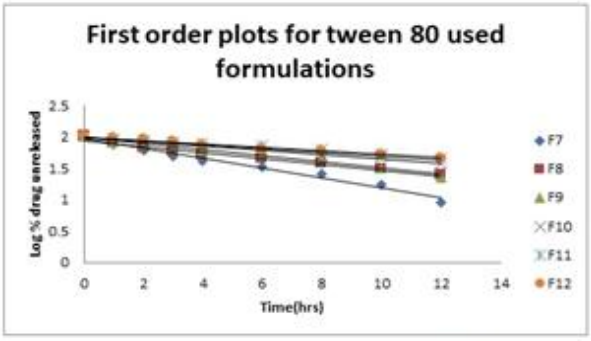
Higuchi plot for best formulations F1-F6 formulations



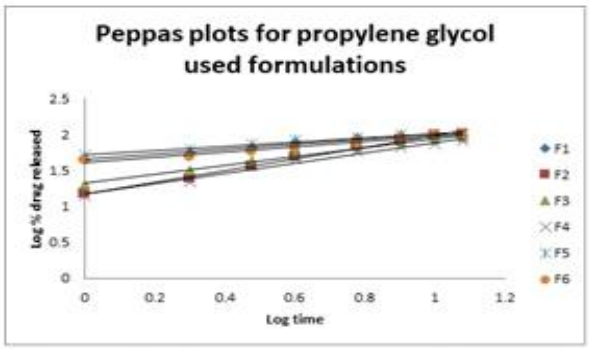
Higuchi plot for best formulations F7-F12 formulations



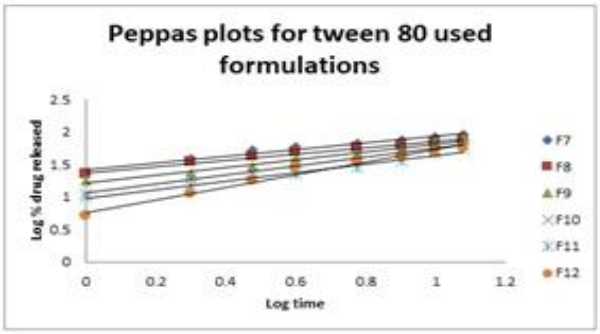
First order plot for best formulations F1-F6 formulations



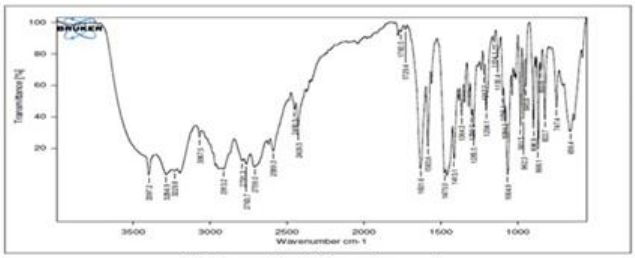
First order plot for best formulations F7-F12 formulations



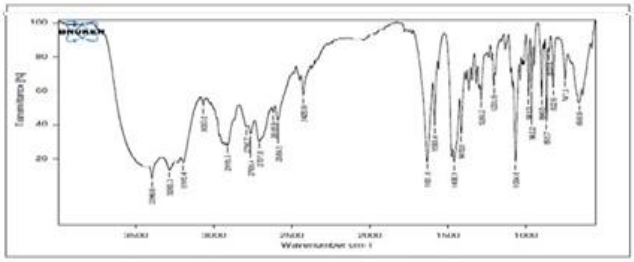
Korsmayerspepas plot for F1-F6 formulations



Korsmayerspepas plot for F7-F12 formulations



FTIR graph for Raltegravir pure drug



FTIR graph for formulation F2

FT-IR spectroscopy

The FTIR spectra's, observed that the characteristic absorption peaks of pure Raltegravir were obtained at 3087.56, 2994.16, 1707.56, 1460.7, 13620.10 and 705.5cm-1 corresponding to O-H, C-H, C=O C-C, C-O stretching and OH- bending (Figure1). The spectral data suggests that the major peaks for drugs are obtained as nearer value and there were no considerable changes in IR peaks in all physical mixtures of drug and polymers. This indicates that the drugs were molecularly dispersed in the polymers or in drug loaded formulations thus thereby indicating the absence of any interactions.

Discussion

The approach of the present study was to make a comparative evaluation among these polymers (Guargum and Xanthan gum) and to assess the effect of physico-chemical nature of the active ingredients on the drug release profile by liquid solid compact method using Propylene glycol and Tween 80. The angle of repose, compressibility index and sieve analysis results shown that the formulation is suitable for wet granulation. This study have been showed that Raltegravir could be used in extended release drug delivery system by formulating it has extended drug delivery system, provides extend duration of action in therapeutic range without reaching toxic levels as in the case of conventional dosage forms. These dosage forms have the ability to reduce the dosing frequency and increasing.

4. Conclusion

By the results we can confirm that order of drug release first order and the mechanism of drug release from sustained release matrix tablets is Higuchi model. Success of the *In vitro* drug release studies recommends the product for further *In vivo* studies, it may improve patient compliance.

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