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FORMULATION AND IN VITRO EVALUATION OF SUSTAINED RELEASE MATRIX TABLETS OF ROPINIROLE HCL

M. A. Rahman*, Mohammad Asif, K. Divya Laxmi and Vineela Sangu

Gyana Jyothi College of Pharmacy, Uppal Bus Depot., Hyderabad-500089, Telangana, India.

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***Corresponding Author**
M. A. Rahman
Gyana Jyothi College of Pharmacy, Uppal Bus Depot, Hyderabad-500089, Telangana, India.

ABSTRACT

The objective of this study was to develop matrix tablets of Ropinirole HCL for sustained release. Eudragit RSPO study the effect of various formulation factors such as polymer proportion on the *in vitro* release of the drug. Ropinirole HCL Matrix tablets were prepared by direct compression technique with average weight of drug 100mg. The prepared tablets were evaluated for Weight variation, Friability, Hardness, Thickness and *In vitro* dissolution studies. The Formulation F4 is selected as the optimized formulation by *in vitro* drug release for 12 hours it has released 99.26%.

KEYWORDS: Ropinirole HCL, Eudragit RSPO, Sustained Release Matrix Tablets.

INTRODUCTION

Oral drug delivery has been known for decades as the most widely utilized route of administration among all the routes that for the systemic delivery of drugs. The reasons that the oral route achieved such popularity may be in part attributed to its ease of administration belief that by oral administration of the drug is well absorbed. 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.

Sustained Drug Delivery System

Over the past 30 years, as the expense and complication involved in marketing new entities have increased with concomitant recognition of the therapeutic advantages of controlled drug delivery, greater attention has been focused on development of sustained or controlled drug delivery system. 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 adminisatration 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.

Recent trends in sustained drug delivery system

Sustained release dosage forms are categorized as:

➢ Single unit dosage form.

➢ Multiple unit dosage form.

➢ Mucoadhesive system.

Characteristics That Makes Drugs Suitable For Sustained Release Matrix DDS

Biological characteristics

1. Biological Half-Life
2. Absorption
3. Distribution
4. Metabolism
5. Physicochemical characteristics
6. Dose Size
7. Aqueous Solubility
8. Partition Coefficient
9. Stability
10. Protein Binding

Types of Srdds

1) Diffusion sustained system

a) Diffusion reservoir system

b) Diffusion Matrix type.

2) Dissolution sustained systems

a) Soluble reservoir system

b) Soluble matrix system.

3) Methods using Ion Exchange

a) Cation exchange resin:

b) Anion exchange resin:

4) pH– Independent formulations

Polymers used in matrix tablet

Hydrogels: Polyhydroxyethylemethylacrylate (PHEMA), Crosslinked polyvinyl alcohol (PVA), Cross-linked polyvinyl pyrrolidone(PVP), Polyethylene-oxide (PEO), Polyacrylamide (PA).

Soluble polymers: Poly ethylene glycol (PEG), Poly vinyl alcohol(PVA), Poly vinyl pyrrolidone (PVP), Hydroxy propyl methyl cellulose (HPMC).

Biodegradable polymers: Polylactic acid (PLA), Poly glycolic acid (PGA), Poly caprolactone (PCL), Poly anhydrides, Poly orthoesters.

Non-biodegradable polymers: Poly ethylene vinyl acetate (PVA), Poly dimethyl siloxane(PDS), Poly ether urethane (PEU), Poly vinyl chloride (PVC), Cellulose acetate (CA), Ethyl cellulose (EC).

Mucoadhesive polymers: Polycarbophil, Sodium carboxy methyl cellulose, Polyacrylic acid, Tragacanth, Methyl cellulose, Xanthan gum, Guar gum, Karaya gum, Locust bean gum.15,16,17,18

Methodology: All the formulations were prepared by direct compression. The compositions of different formulations are given in Table. The tablets were prepared as per the procedure given below and aim is to prolong the release of Ropinirole HCL. Total weight of the tablet was considered as 100mg.

Procedure

1) Ropinirole HCL and all other ingredients were individually passed through sieve no 60.

2) All the ingredients were mixed thoroughly by triturating up to 15 min.

3) The powder mixture was lubricated with talc.

4) The tablets were prepared by using direct compression method.

Formulation composition for tablets

All the quantities were in mg

Ingredients Mg	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
Ropinirole HCL	4	4	4	4	4	4	4	4	4	4
Eudragit RSPO	10	20	30	40	50	-	-	-	-	-
Eudragit RLPO	-	-	-	-	-	10	20	30	40	50
Pvp K 30 in Iso propyl alcohol	QS	QS	QS	QS	QS	QS	QS	QS	QS	QS
Talc	1	1	1	1	1	1	1	1	1	1
Mg stearate	1	1	1	1	1	1	1	1	1	1
Spary dried Lactose	84	74	64	54	44	84	74	64	54	44
Total weight	100	100	100	100	100	100	100	100	100	100

RESULTS AND DISCUSSION

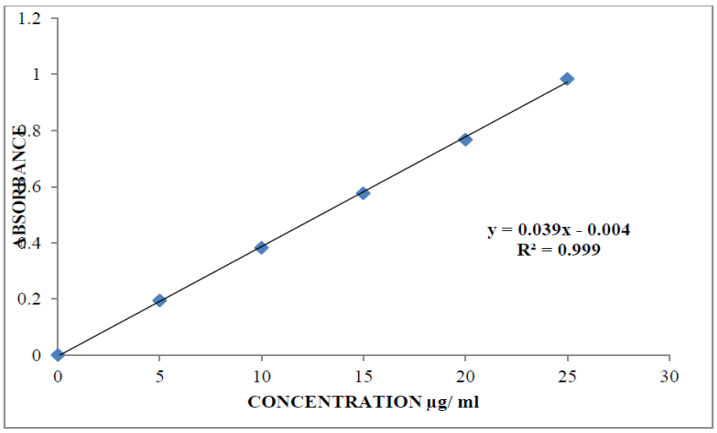
The present study was aimed to developing Sustained release tablets of Ropinirole HCL using various polymers. All the formulations were evaluated for physicochemical properties and *In-vitro* drug release studies.

Analytical Method

Graphs of Ropinirole HCL were taken in 0.1N HCl and in pH 6.8 phosphate buffer at 250 nm and 255 nm respectively.

Observations for graph of Ropinirole HCL in 0.1N HCl (250 nm)

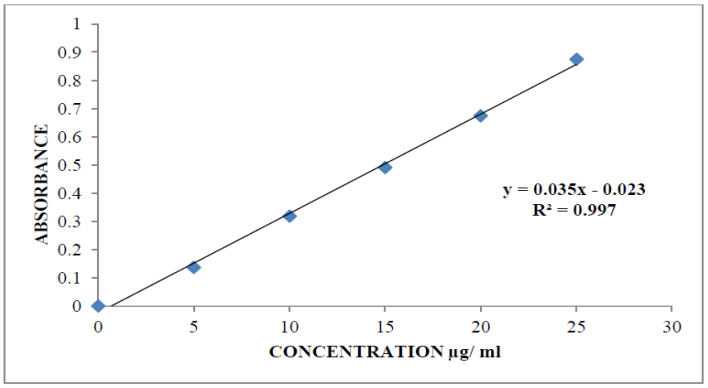
Conc [µg/ml]	Absorbance
0	0
5	0.194
10	0.382
15	0.577
20	0.767
25	0.984



Standard graph of Ropinirole HCL in 0.1N HCl

Observations for graph of Ropinirole HCL in pH 6.8 phosphate buffer (255nm)

Concentration [µg/ml]	Absorbance
0	0
5	0.137
10	0.319
15	0.492
20	0.675
25	0.875



Standard graph of Ropinirole HCL pH 6.8 phosphate buffer (255nm)

Preformulation parameters of powder blend

Pre-formulation parameters of Core blend

Formulation Code	Angle of Repose	Bulk density (gm/ml)	Tapped density (gm/ml)	Carr's index (%)	Hausner's Ratio
F1	27.68±0.57	0.36±0.35	0.42±0.62	14.29±0.80	1.321±0.08
F2	27.00±0.5	0.38±0.71	0.48±0.34	20.63±0.77	1.266±0.17
F3	28.41±0.32	0.39±0.12	0.45±0.93	15.22±0.42	1.193±0.99
F4	27.41±0.66	0.37±0.20	0.41±0.32	12.06±0.71	1.206±0.12
F5	27.00±0.5	0.37±0.43	0.46±0.74	19.3±0.49	1.276±0.16
F6	28.41±0.32	0.38±0.02	0.45±0.02	14.42±0.5	1.303±0.08
F7	27.41±0.66	0.37±0.20	0.41±0.32	12.06±0.71	1.299±0.04
F8	28.21±0.90	0.37±0.43	0.46±0.74	19.3±0.49	1.313±0.16
F9	27.68±0.57	0.38±0.02	0.45±0.02	14.42±0.5	1.276±0.12
F10	25.73±0.45	0.38±0.71	0.48±0.34	20.63±0.77	1.298±0.44

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 0.36±0.35 to 0.39±0.12 (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 0.41±0.32 to 0.48±0.34 showing the powder has good flow properties. The compressibility index of all the formulations was found to be below 20 which

show that the powder has good flow properties. All the formulations has shown the hausner ratio below 1.321 indicating the powder has good flow properties.

Quality Control Parameters for tablets

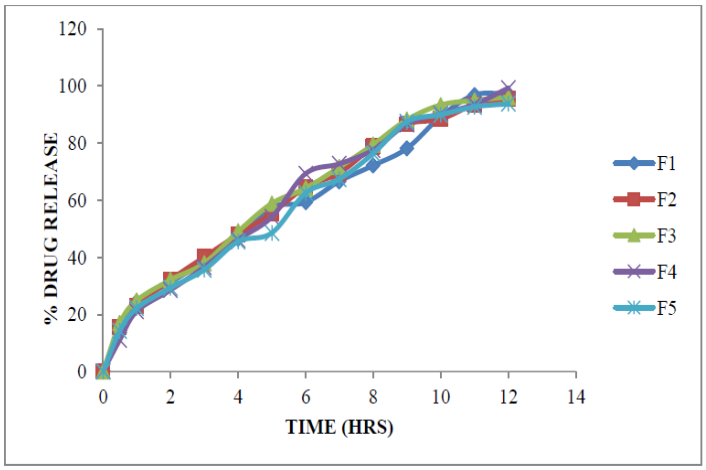
***In-vitro* quality control parameters for tablets**

Formulation codes	Average Weight (mg)	Hardness(kg/cm2)	Friability (%loss)	Thickness (mm)	Drug content (%)
F1	99.56±0.41	3.34 ± 0.28	0.25±0.65	1.12±0.85	99.36±0.62
F2	98.22±0.98	2.94 ± 0.62	0.65±0.24	1.24±0.64	98.25±0.74
F3	99.28±0.37	2.63±0.40	0.29±0.94	1.19±0.27	97.34±0.39
F4	100.13±0.65	2.48 ±0.97	0.34±0.29	2.01±0.35	99.48±0.86
F5	104.68±0.92	3.02 ±o.14	0.44±0.33	2.24±0.65	99.64±0.12
F6	99.76±0.76	3.12 ±0.95	0.56±0.42	1.54±0.31	98.96±0.85
F7	98.44±0.59	2.87 ±0.36	0.49±0.22	1.96±0.87	97.72±0.32
F8	99.56±0.27	2.65 ±0.32	0.58±0.18	2.24±0.34	98.55±0.87
F9	100.71±0.35	2.84 ±0.48	0.41±0.45	2.23±0.41	99.75±0.95
F10	102.33±0.49	3.11 ±0.36	0.29±0.39	1.95±0.68	99.35±0.28

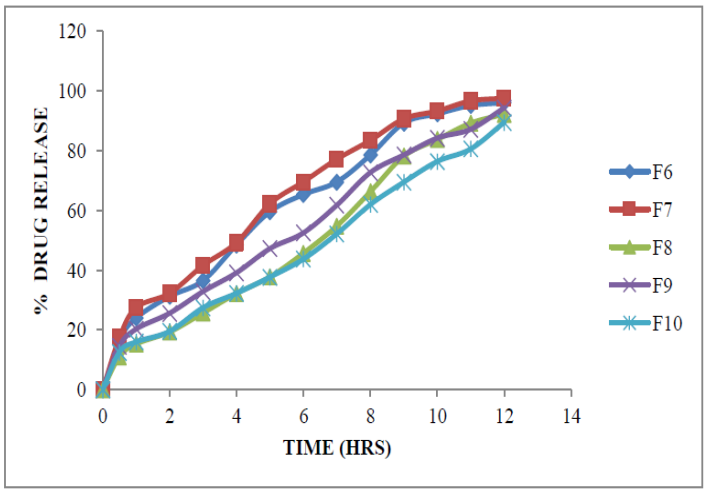
All the parameters such as weight variation, friability, hardness, thickness and drug content were found to be within limits.

***In-Vitro* Drug Release Studies**

Time (hrs)	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
0	0	0	0	0	0	0	0	0	0	0
0.5	14.19	15.64	16.96	11.13	14.32	16.42	17.42	10.99	14.54	12.54
1	24.46	22.96	24.89	21.11	22.21	23.96	27.44	15.25	20.25	15.96
2	31.25	32.16	32.12	28.58	29.36	31.19	32.24	19.29	25.56	19.48
3	38.58	40.14	37.96	36.64	35.65	36.46	41.54	25.65	32.84	27.41
4	46.42	47.98	49.03	46.12	45.51	48.47	49.25	32.18	39.11	32.24
5	57.48	55.46	58.86	54.14	48.57	59.54	62.21	37.72	47.21	37.67
6	59.26	64.54	64.21	69.28	62.49	65.31	69.56	45.66	52.47	43.68
7	66.62	69.54	71.58	72.74	67.42	69.54	77.15	54.79	61.75	52.16
8	72.16	78.76	79.46	77.59	76.34	78.54	83.45	66.24	72.69	61.94
9	78.14	86.56	88.14	86.64	87.47	89.26	90.65	78.15	78.58	69.46
10	89.26	88.38	93.34	90.29	89.95	92.32	93.28	83.74	84.22	76.37
11	96.84	93.45	94.97	93.54	92.69	95.12	96.65	89.19	87.17	80.58
12	97.22	95.57	96.14	99.26	93.73	96.06	97.56	92.25	94.35	89.46



Dissolution profile of Ropinirole HCL (F1, F2, F3, F4, F5 formulations).



Dissolution profile of Ropinirole HCL (F6, F7, F8 , F9 , F10 formulations)

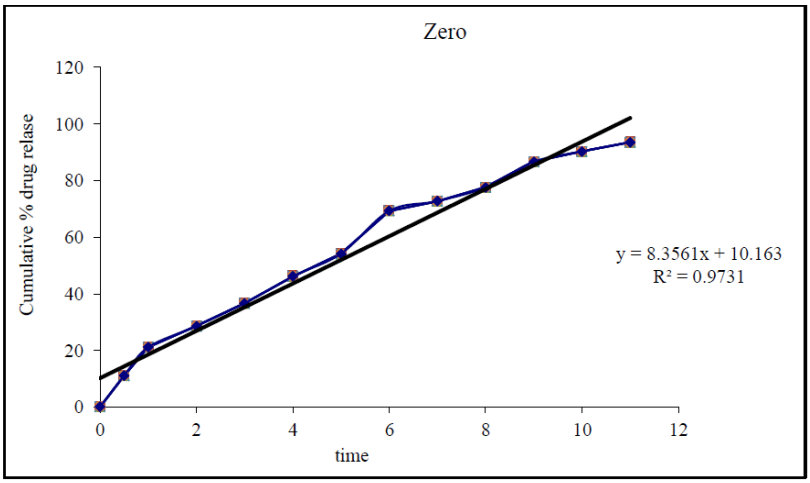
Formulations prepared with Eudragit RSPO retarded the drug release in the concentration of 40 mg (F4 Formulation) showed required release pattern i.e., retarded the drug release up to 12 hours and showed maximum of 99.26% in 12 hours with good retardation.

Application of Release Rate Kinetics to Dissolution Data

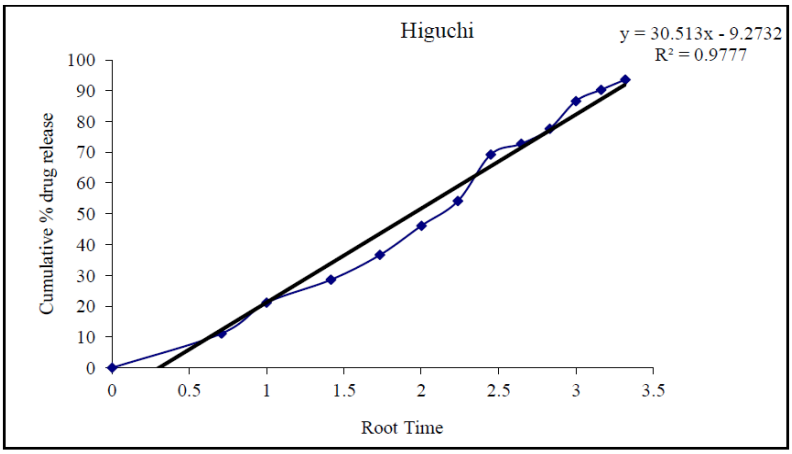
Various models were tested for explaining the kinetics of drug release. To analyze the mechanism of the drug release rate kinetics of the dosage form, the obtained data were fitted into zero-order, first order, Higuchi, and Korsmeyer-Peppas release model.

Release kinetics data for optimised formulation

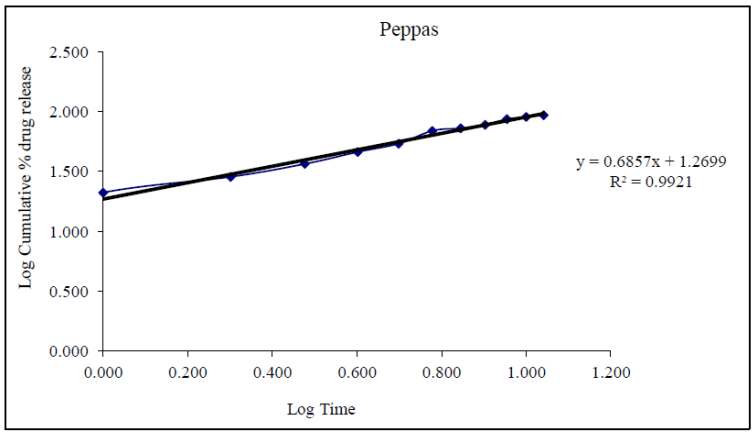
CUMULATIVE (%) RELEASE Q	TIME (T)	ROOT (T)	LOG(%) RELEASE	LOG (T)	LOG (%) REMAIN	RELEASE RATE (CUMULATIVE % RELEASE / t)	1/CUM% RELEASE	PEPPAS log Q/100	% Drug Remaining	Q01/3	Qt1/3	Q01/3-Qt1/3
0	0	0			2.000				100	4.642	4.642	0.000
11.13	0.5	0.707	1.046	-0.301	1.949	22.260	0.0898	-0.954	88.87	4.642	4.463	0.179
21.11	1	1.000	1.324	0.000	1.897	21.110	0.0474	-0.676	78.89	4.642	4.289	0.353
28.58	2	1.414	1.456	0.301	1.854	14.290	0.0350	-0.544	71.42	4.642	4.149	0.493
36.64	3	1.732	1.564	0.477	1.802	12.213	0.0273	-0.436	63.36	4.642	3.987	0.655
46.12	4	2.000	1.664	0.602	1.731	11.530	0.0217	-0.336	53.88	4.642	3.777	0.865
54.14	5	2.236	1.734	0.699	1.661	10.828	0.0185	-0.266	45.86	4.642	3.579	1.062
69.28	6	2.449	1.841	0.778	1.487	11.547	0.0144	-0.159	30.72	4.642	3.132	1.510
72.74	7	2.646	1.862	0.845	1.436	10.391	0.0137	-0.138	27.26	4.642	3.010	1.632
77.59	8	2.828	1.890	0.903	1.350	9.699	0.0129	-0.110	22.41	4.642	2.819	1.822
86.64	9	3.000	1.938	0.954	1.126	9.627	0.0115	-0.062	13.36	4.642	2.373	2.269
90.29	10	3.162	1.956	1.000	0.987	9.029	0.0111	-0.044	9.71	4.642	2.133	2.508
93.54	11	3.317	1.971	1.041	0.810	8.504	0.0107	-0.029	6.46	4.642	1.862	2.779
99.26	12	3.464	1.997	1.079	-0.131	8.272	0.0101	-0.003	0.74	4.642	0.905	3.737



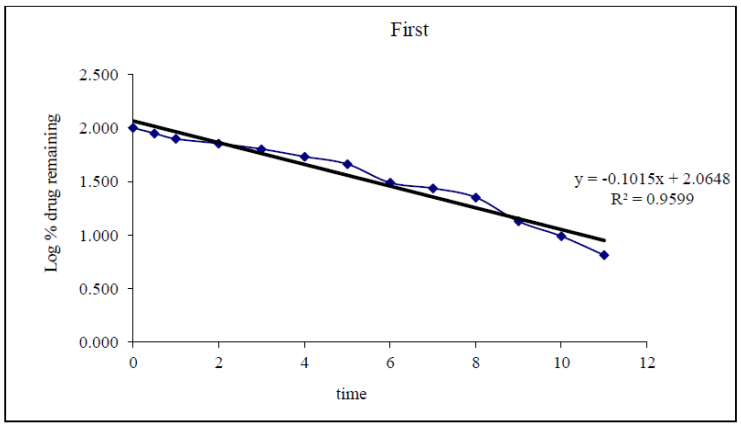
Zero order release kinetics graph



Higuchi release kinetics graph



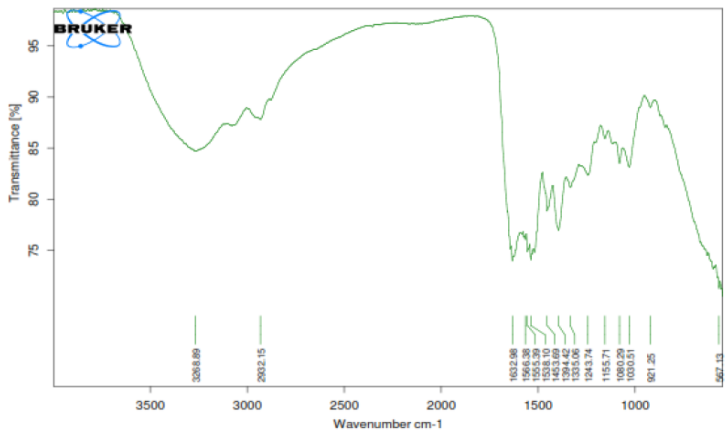
Kars mayer peppas graph



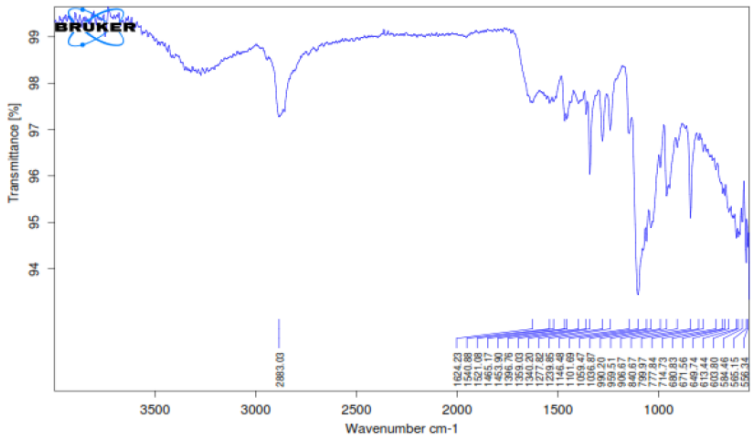
First order release kinetics graph

From the above graphs it was evident that the formulation F4 was followed Higuchi release kinetics.

Drug – Excipient compatability studies



FT-TR Spectrum of Ropinirole HCL pure drug.



FT-IR Spectrum of Optimised Formulation

CONCLUSION

The study was under taken with the aim to Formulation and evaluation of Ropinirole HCL Sustained release tablet using Eudragit polymer as retarding agent. From the above results and discussion it is concluded that the formulation of sustained release tablets of Ropinirole HCL containing Eudragit shows improved sustained release. Among all the formulations F4 shows better sustained release 99.26% drug release for 12 hours as it fulfills all the requirements. The formulation F4 was followed Higuchi release kinetics.

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