Formulation, Development and Evaluation of Sustained Release Matrix tablets of Ropinirole HSCl.

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ABSTRACT

The objective of this research work is to develop sustained release tablets of Ropinirole HCl using different hydrophilic polymers like Polyox WSR303 and HPMC K100M by direct compression technique. The granules were evaluated for angle of repose, bulk density, tapped density, compressibility index and Hausner ratio. The tablets were subjected to thickness, hardness, friability, weight variations, and *in vitro* dissolution studies. The drug release from Ropinirole HCl sustained release tablets was carried out in 1.2 N HCl, and 6.8 pH phosphate buffer for 24hrs.F12 batch showed expected result and considered as optimized batch. The study clears that when Polyox WSR303 & HPMC K100M used separately sustained drug release upto 20 Hrs. but, when used in combination it retards drug release upto24 Hrs. So, it can be concluded that when both Polyox WSR303 & HPMC K100M are used in combination increases sustained action than using separately.

1. INTRODUCTION[1,13,14]

Oral drug delivery is the most widely utilized route of administration among all the routes nasal, ophthalmic, rectal, transdermal and Parental routes that have been explored for systemic delivery of drugs via pharmaceutical products of different dosage form. Oral route is considered most natural, uncomplicated, convenient and safe in respect to parenteral route due to its ease of administration, patient acceptance and cost effective manufacturing process. [1]

1.1 MODIFIED RELEASE ORAL DRUG DELIVERY SYSTEM [2]

MODIFIED RELEASE ORAL DRUG DELIVERY SYSTEM

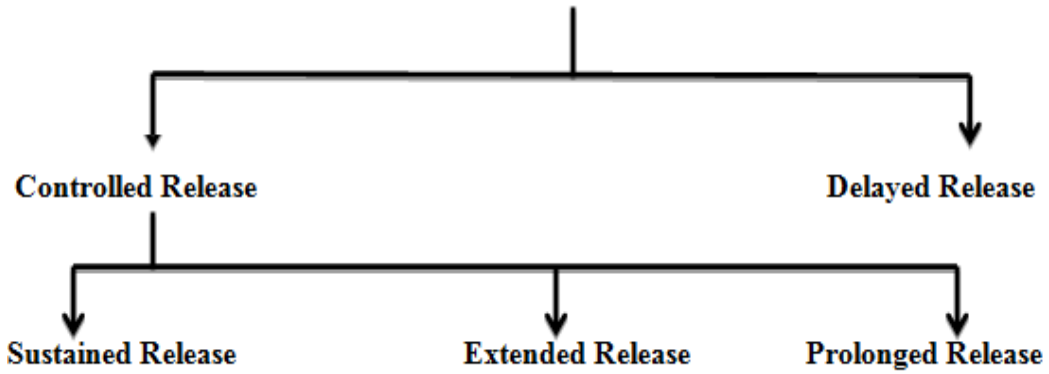

Fig. 1: Classification of modified release drug delivery system.

MODIFIED RELEASE DRUG DELIVERY SYSTEM [3, 4,12,15]

- **Extended release system**: The drug delivery system that allows at least two folds reduction in dosage frequency as compared to that drug presented as an immediate release system.
- **Sustained release system:** It includes any drug delivery system that achieves slow release of drugs over an extended period of time not particularly at pre-determined rate.
- **Controlled release system:** It includes any drug delivery system from which the drug is delivered at a predetermined rate over a long period of time.
- **Prolonged release system:** It is designed to release the drug slowly and to provide a continuous supply of drug over an extended period.
- **Delayed release system:** This are the system which designed to release a discrete portion of drug at a time or other than promptly after administration, although one portion may be release promptly after administration of dosage form.

Sustained Release Dosage Forms: [5,10,11]

The term 'Sustained Release' is known to have existed in the medical and pharmaceutical literature for many decades. Sustained release has been constantly used to retard the release of therapeutic agent such that its appearance in the circulation is delayed and/or prolonged and its plasma profile is sustained in duration. The onset of its pharmacological action is often delayed and duration of therapeutic action is sustained.

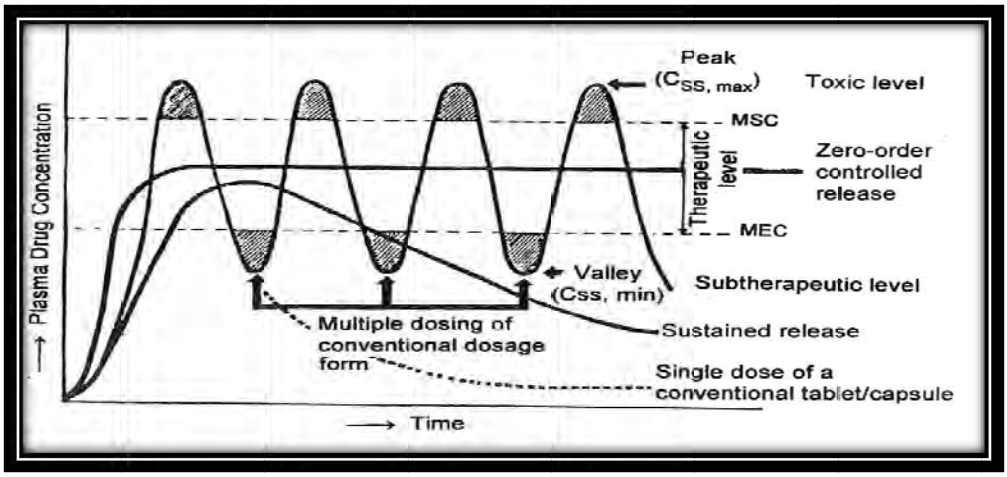

Fig. 2: Hypothetical plasma concentration-time profile from conventional multiple dosing and single doses of sustained and controlled delivery formulations

2. MATERIAL AND METHODS

2.1 MATERIALS:

Ropinirole HCl was received as a gift sample from Ind-Swift Labs, Mohali (Punjab).Polyox WSR303 was received as agift sample from Accela Pharmaceuticals, Pune HPMC K100M was received as a gift sample from Colorcon, Mumbai, while other chemicals and solvents were procured from LobaChemie, Mumbai.

2.2 METHODOLOGY

2.2.1 Preformulation study

Preformulation testing is the primary and first step of development of any dosage form. Preformulation study involves investigation of physical and chemical properties of drug alone or in combination with excipients. Preformulation data of physical and chemical properties of drug and excipients helps in development of desirable dosage forms. Preformulation study was done at the primary level of development of dosage form.

2.2.2 Characterization of Ropinirole HCl

Characterization of drug and excipients are necessary to identify particular drug and excipients, to check purity of drug and excipients, to determine physicochemical properties which help for development of desired formulation. Ropinirole HCl Drug sample was characterized by identification test, solubility study, melting point, UV analysis, IR analysis.

a. Identification of Ropinirole HCl: [9]Identification of Ropinirole HCl was done to ensure that available sample is of same drug or not. For identification Infrared spectrum was taken.

Infrared spectrum of Ropinirole HCl:

Infrared spectrum of pure drug was determined by ATR technique using FT-IR(Bruker alpha-T) instrument.

b. Solubility study

The main purpose of solubility study is to check in which solvent drug dissolves and suitability of solvent for development of dosage form. Solubility study of Ropinirole HCl was carried out by dissolving 10 mg of drug sample in different solvents like water, ethanol, methanol, acetic acid, acetone, dichloromethane. The results are as shown in **Table 4.**

c. Melting point

Melting point is used for determination of purity and identification of drug. The melting point of Ropinirole HCl was determined by melting point apparatus using capillary method. Fine powder of Ropinirole HCl was filled in glass capillary tube which was previously sealed on one end. The capillary tube was tied with thermometer and then immersed into melting point apparatus. The temperature was observed at which drug started to melt by thermometer which was already immersed into the Thiele's tube. The results are as shown in **Table 4 .**

d. Loss on drying

1 gm of Ropinirole HCl was taken in petriplate and weight of petriplate and drug was measured. Petriplate containing API was placed at 105 ^{0}C for 15 min. in oven and again weight of petriplate and API was measured and LOD was calculated by using following formula. The results are as shown in **Table 4.**

LOD = Initial weight – final weight / Initial weight x 100

e. Determination of absorption maxima (λ_{max})

UV spectrophotometric study of Ropinirole HCl was carried out to identify λ_{max} of drug in 0.1 N HCl and 6.8 pH buffer solution. The prepared solution was scanned in the range of 200 to 400 nm using UV spectrophotometer (UV-3000 Labindia) and the spectrum was recorded.**Table 4.**

f. Calibration curve of Ropinirole HCl

Calibration curve is the standard plot of linear concentration of drug in solution versus absorbance. From that graph, slope and intercepton y axis is determined and it is used to determine concentration of drug in solution.

g. Calibration curve of RopiniroleHClin1.2 pH

Preparation of pH 1.2 Acid Buffer[6]

Place 50ml of 0.2M Potassium Chloride in 200ml of volumetric flask and add 85 ml of 0.2M Hydrochloric Acid and then add water to the volume.

The standard stock solution was prepared by dissolving API (10 mg) in 100 ml of1.2 pH solution to make final concentration of 100 µg/ml. Different aliquots were taken from stock solution and diluted with 1.2 pH to prepare series of concentrations from 4-20 µg/ml. The λ_{max} was found to be 249.5 nm from UV spectrum of RopiniroleHCldurin scanning in the range of 200-400 nm. Absorbance was measured at 249.5 nm against1.2 pH on UV-Visible Spectrophotometer (UV-3000 Labindia).Calibrationcurve was prepared by plotting absorbance versus concentration of Ropinirole HCl.

i. Calibration curve of Ropinirole HCl in phosphate buffer pH 6.8

Preparation of Phosphate buffer pH 6.8[6]

Place 50ml of 0.2M Potassium Dihydrogen Phosphate in 200ml of volumetric flask and add 22.4 ml of 0.2M Sodium Hydroxide and then add water to the volume.

2.88 gm of disodium hydrogen phosphate, 1.145gm of potassium dihydrogen phosphate were dissolved in sufficient quantity of distilled water to produce 100 ml.

The standard stock solution was prepared by dissolving Ropinirole HCl(10 mg) in 100 ml of phosphate buffer to make final concentration of 100 µg/ml. Different aliquots were taken from stock solution and diluted with phosphate buffer to prepare series of concentrations from 4-20 µg/ml. The λ_{max} was found to be 249 nm from UV spectrum of Ropinirole HCl during scanning from 200-400 nm. Absorbance was measured at 249 nm against phosphate buffer on UV-visible Spectrophotometer. Calibration curve was prepared by plotting absorbance versus concentration of Ropinirole HCl.

2.2.3 TRIAL BATCHES FOR SELECTION OF CONCENTRATION OF POLYOX WSR303

Table 1: Trial batches for selection of polymer concentration

Code / Ingredients**(mg)**	**Trial A**	**Trial B**	**Trial C**	**Trial D**
Ropinirole	4	4	4	4
PolyoxWSR303	30 (20%)	45 (30%)	60 (40%)	75 (50%)
Maltodextrin	7.5	7.5	7.5	7.5
Magnesium stearate	1.5	1.5	1.5	1.5
Microcrystaline Cellulose	107	92	77	62
Total weight	**150**	**150**	**150**	**150**

2.2.4 FORMULATION OF SUSTAINED RELEASE MATRIX TABLET BY DIRECT COMPRESSION

Sustained release matrix tablet of Ropinirole HCl were prepared by direct compression technique using rotary tablet compression machine. The drug was blended with the excipients. All the ingredients of the formulations (except lubricant) were passed through sieve no.40. The final blend was compressed into tablets using8 station rotary tablet compression machine (Jaguar JMD 4-8) using 8 mm flat die & punches. Tablet weight was 150 mg and kept constant for all the formulations.

2.2.5 OPTIMIZATION

Statistical Experiment Design

A three-level, three-factor Box Behnken design of response surface methodology was employed for the formulation optimization using statistical software, Design expert version 9.0.1 (Stat-Ease Inc., Minneapolis, MN). Three components, Polyox WSR303,HPMC K100M &Maltodextrin were screened from preliminary experimental work and used for optimization study as independent variables. These components tested at three different concentrations. Total 15 formulations including 3 replicates of central points were prepared to investigate the influence of screened polymers concentration on drug release.

Table 2: Formulation of SR Tablets Trial Batches F1 –F8

Code / **Ingredients (mg)**	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**
Ropinirole	4	4	4	4	4	4	4	4
Polyox WSR303	52.5	52.5	52.5	52.5	52.5	60	60	52.5
HPMC K100M	60	15	60	15	37.5	60	37.5	37.5
Maltodextrin	7.5	7.5	15	156	11.25	11.25	7.5	11.25
Magnesium stearate	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
Microcrystalline Cellulose	23.94	68.98	16.44	61.44	42.69	12.59	38.94	42.69
Total weight	**150**	**150**	**150**	**150**	**150**	**150**	**150**	**150**

Table 3: Formulation of SR Tablets Trial Batches F9 –F15

Code / **Ingredients (mg)**	**F9**	**F10**	**F11**	**F12**	**F13**	**F14**	**F15**
Ropinirole	4	4	4	4	4	4	4
Polyox WSR303	60	45	52.5	45	60	45	45
HPMC K100M	15	37.5	37.5	37.5	37.5	15	60
Maltodextrin	11.25	7.5	11.25	15	15	11.25	11.25
Magnesium stearate	1.5	1.5	1.5	1.5	1.5	1.5	1.5
Microcrystalline Cellulose	57.69	53.94	42.69	46.44	31.44	72.69	27.69
Total weight	150	150	150	150	150	150	150

2.2.6 POST COMPRESSION EVALUATION OF PREPARED ROPINIROLEHCl SR TABLETS [6,7,10]

General parameters: Tablets were evaluated for hardness (Pfizer tablet hardness tester), friability (Roche friabilator), and weight variation.

a) **Hardness**:
The crushing strength of the tablets was measured using a Pfizer tablet hardness tester. Three tablets from each formulation batch were tested randomly.

b) **Friability:**
Twenty tablets were weighed and placed in a Roche friabilator and the equipment was rotated at 25 rpm for 4 min. The tablets were taken out, dedusted, and reweighed. The percentage friability of the tablets was calculated using Equation.

$$\% \, \boldsymbol{Friability} = \frac{\boldsymbol{Initial\,weight - Final\ weight}}{\boldsymbol{Initial\,weight}} \times \mathbf{100}$$

e) Uniformity of content.

Five tablets were selected randomly and dissolved in 100 mL of 0.1 N HCl, stirred for 60 min, and filtered. One milliliter of the filtrate was diluted to 100 mL with 0.1 N HCl. Absorbance of this solution was measured at 249.5 nm using 0.1 N HCl as blank and content of RopiniroleHCl was estimated.

g) Weight Variation:

Randomly, 20 tablets were selected after compression and the mean weight was determined. None of the tablets deviated from the average weight by more than ±7.5%.

2.2.7 IN-VITRO RELEASE STUDIES

In-vitro release of Ropinirole HCl SR Tablets was carried out using the USP dissolution test apparatus Type-II (paddle).SR Tablets were placed in dissolution jar. Dissolution medium used was 500 ml of 0.1 N HCI (pH 1.2) maintained at 37 ± 0.5°Cand stirred at 50 rpm for 2 hrs. At predetermined time intervals of 1 hr, 5 ml of sample was withdrawn and replaced with equal amount of 0.1 N HCI (pH 1.2). After that dissolution medium was made upto6.8 pH for further dissolution testing. The 5 ml withdrawn samples were filtered and suitably diluted if needed with 0.1 N HCI and 6.8 pH buffer solution and analyzed spectrophotometrically. It is shown in **Table 8-10** and **Fig.3-5.**

2.2.8 ASSAY OF SR TABLETS OF ROPINIROLE HCl[9]

Five tablets of Ropinirole hydrochloride were weighed and powdered in glass mortar. Powder equivalent to 10 mg of the drug was transferred to 100 ml volumetric flask, dissolved in about 50ml distilled water and made up the volume to the mark with distilled water to obtain the concentration of 100 µg/ml. Aliquots of 0.4 to 4.0 ml portions of the standard solution were transferred to a series of calibrated 10 ml corning test tubes and the volume in each test tube was adjusted to 10 ml with distilled water. The absorbance of solutions was measured at 250 nm against reagent blank and calibration curve was constructed. Similarly absorbance of sample solution was measured and amount of Ropinirole hydrochloride in the tablet was determined by referring to the calibration curve. The assay results are shown in **Table 11.**

3. RESULTS AND DISCUSSION

3.1 Preformualtion study of Ropinirole HCl

Table 4: Preformualtion study of Ropinirole HCl

Parameter	Standard	Observation
Solubility study of Ropinirole HCl	Freely soluble in water, Methanol, acetonitrile.	Freely soluble in water, Methanol, acetonitrile.
Loss on drying	NMT 0.5%	NMT 0.3%
λmax of Ropinirole HCl	250 nm	249.5 nm&249.0
Melting point of Ropinirole HCl	243-250^{0}C	247-248^{0}C

3.2 In Vitro Drug Release Study For Selection Of Concentration Of Polymer.

The trial batches were subjected to the in vitro drug release study. Results are shown in **Table 5.**

Table 5: In vitro drug release of preliminary trial batches using PolyoxWSR303**.**

Time(Hr)	Drug Release (%)			
	T_A	T_B	T_C	T_D
1	21.5	18.5	14	11.5
2	25.5	21.5	19.5	15.5
3	33.25	30	24.5	21.75
4	43	41.12	38.37	32.87
5	53.62	48.5	44.37	40.27
6	63.87	56.37	50.37	45.83
7	65.25	61.5	54.12	51.38
8	77.75	69.87	59.62	56.94
9	90.6	81.37	67.12	62.96
10	101.85	85.12	80	68.05
11		89.25	84.25	73.61
12		95.75	88.87	79.16

From the above experimental trial batches it was inferred that the release of the drug was sustained uptoa considerable time period of '12 hours' by Trial batches B,C & D. As trial batches T_B & T_C showed release near about 100% in 12hours. So 30% to 40% concentration of polyox WSR303 can be considered as a optimized concentration for next trial batches.

3.3 Determination Of Precompression Parameters For Sustained Release Matrix Tablets Of Ropinirole HCl

Table 6: Evaluation of precompression material.

Batch	Bulk Density (gm/cm^3)	Tapped Density (gm/cm^3)	Hausner ratio	Carr's Index	Angle of Repose(θ)
F1	0.357	0.425	1.19	16	30.07
F2	0.322	0.377	1.17	14.58	30.01
F3	0.370	0.454	1.22	18.50	30.00
F4	0.312	0.392	1.25	20.40	30.97
F5	0.333	0.392	1.17	15.05	30.01
F6	0.370	0.454	1.22	18.50	32.40
F7	0.357	0.434	1.21	17.74	30.09
F8	0.333	0.40	1.20	16.75	30.04
F9	0.327	0.384	1.17	14.84	30.07
F10	0.312	0.392	1.25	20.40	31.48
F11	0.322	0.384	1.19	16.14	30.05
F12	0.344	0.416	1.20	17.30	30.04
F13	0.357	0.408	1.14	12.5	30.09
F14	0.303	0.370	1.22	18.10	30.01
F15	0.370	0.444	1.20	16.66	31.07

The precompression material for the preparation of SR Tablets of Ropinirole HCl was evaluated for the parameters like bulk density, tapped density, Carr's compressibility index and Hausner ratio. The outcomes of these parameters are tabulated in the above table.

Bulk density of all the 12 batches was in the range of **0.30-0.37** gm/cm^3.

Tapped density was in the range of**0.37-0.354** gm/cm^3.

Carr's index was in the range of **12.5-20.40.**

Hausner ratio was in the range of **1.14-1.25.**

Angle of repose was also found in the prescribed range showing good flow characteristics. It was in the range **30.01-32.40.**

Carr's index value was in the range of 11 to 15 & 16 to 20 which shows good& fair flow properties respectively. Carr's index of all batches was in the range of 11-20. Hence these batches show Good & Fair flow properties. Hausner ratio of all the batches was in the range showing good& fair flow properties. Hence selected for the compression.

3.4 Evaluation Of Sustained Release Matrix Tablets For Post Compression Parameters:

Table 7: Post compression characterization of tablets

Batch Code	Hardness (Kg/cm^3)	Friability (%)	Thickness (mm)	Weight variation (%)
F1	7.8	0.45	2.7	1.06
F2	7.9	0.47	2.8	1.04
F3	7.7	0.49	2.5	1.01
F4	7.8	0.41	2.6	0.99
F5	7.8	0.43	2.5	1.06
F6	7.8	0.40	2.6	1.05
F7	7.9	0.48	2.6	0.98
F8	7.6	0.46	2.8	1.02
F9	7.8	0.41	2.6	0.99
F10	7.8	0.40	2.7	1.02
F11	7.7	0.44	2.6	1.04
F12	7.6	0.45	2.6	1.05
F13	7.9	0.43	2.5	1.02
F14	7.8	0.81	2.6	0.98
F15	7.8	0.47	2.7	1.06

The tablets were evaluated for post compression parameters like Hardness,Friability,thickness & Weight variation.Hardness was between 7.6-7.9Kp. All the formulations also passed the friability &Weight variation limits which were within 0.40-0.49 % and 0.98-1.06 % respectively.

3.5 *In-Vitro* Drug Release Study

Table 8: *In Vitro* % Cumulative Drug Release of SR Tablets.Batch F1-F5

Time(Hr)	Drug Release (%)				
	F1	F2	F3	F4	F5
1	7.5	16.5	9.5	24.53	14.5
2	19.5	36.5	17.5	28.70	23.5
3	21.75	42.59	21.29	37.5	30.09
4	25.46	50.46	26.38	43.05	34.25
5	33.79	54.16	35.18	47.22	45.83
6	43.51	58.79	43.98	50.92	51.85
8	52.77	70.37	51.85	57.87	57.87
10	56.94	74.07	56.01	61.11	64.35
12	62.5	78.24	63.42	70.83	70.37
14	67.59	85.18	66.66	79.16	77.31
16	70.37	89.81	69.90	87.5	82.87
20	80.55	99.53	77.31	98.14	89.37
24	90.27		88.88		96.75

Table 9: *In Vitro* % Cumulative Drug Release of SR Tablets.Batch F6-F10

Time(Hr)	Drug Release (%)				
	F6	F7	F8	F9	F10
1	7.5	24.07	13.5	11.5	28.5
2	16	33.5	21	19.5	32.5
3	18.98	34.72	31.94	36.5	36.57
4	27.31	36.57	35.64	40.27	38.42
5	32.87	42.59	45.37	42.59	43.51
6	41.20	49.07	52.37	45.83	48.61
8	49.53	56.94	58.79	56.01	56.94
10	55.09	61.57	66.66	62.5	61.11
12	61.11	65.27	70.83	68.28	68.98
14	65.27	69.44	74.53	70.37	72.68
16	68.98	72.68	80.55	86.57	80.09
20	75	84.72	88.88	96.75	96.75
24	86.11	93.98	95.83		102.31

Table 10: *In Vitro* % Cumulative Drug Release of SR Tablets.Batch F11-F15

Time(Hr)	Drug Release (%)				
	F11	F12	F13	F14	F15
1	11	21	12.5	26	8.7
2	21.5	29	21.5	33.33	18.5
3	29.62	33.33	23.61	41.20	24.53
4	37.96	41.20	27.77	49.07	36.57
5	46.76	48.61	38.42	57.87	44.90
6	53.24	55.09	45.37	67.12	53.24
8	59.26	62.5	54.16	73.61	59.25
10	65.74	69.90	59.72	75	65.27
12	69.90	75	65.27	81.94	68.51
14	73.61	80.55	70.83	87.96	70.83
16	79.63	84.72	77.31	92.12	74.01
20	86.57	91.20	78.87	100.46	81.48
24	94.90	100.46	92.12		91.20

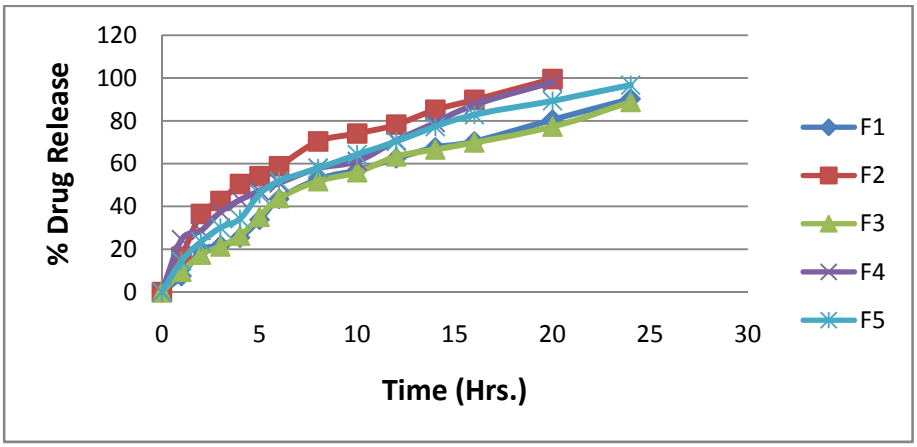

Fig 3: *In- Vitro* % DR of RopiniroleHCl SR Tablet of F1 to F5 Batches

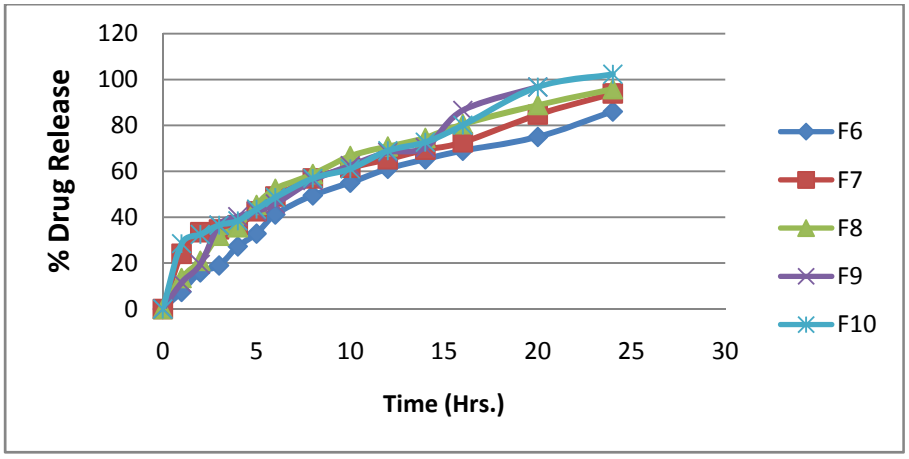

Fig 4: *In- Vitro* % DR of RopiniroleHCl SR Tablet of F6 to F10 Batches

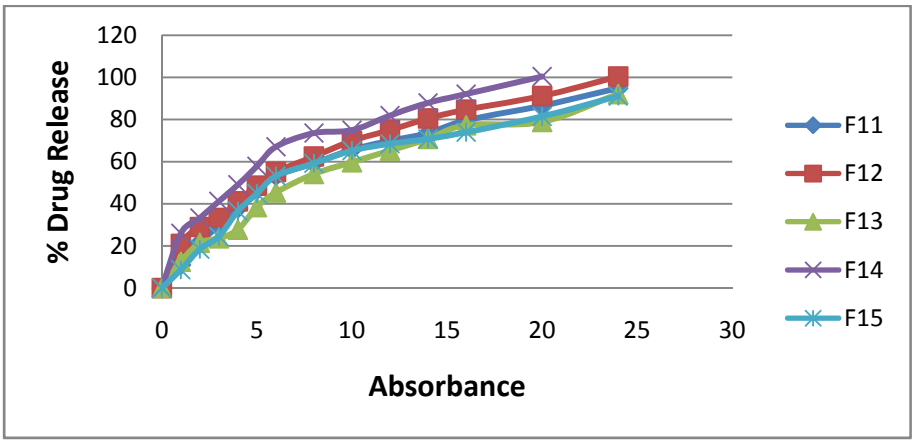

Fig 5: *In- Vitro* % DR of RopiniroleHCl SR Tablet of F11 to F15 Batches

The above In-vitro drug release data it shows that Batch F12 showed expectable drug release profile at different time interval as compared to other batches.So,Batch F12 considered as optimized batch.

3.4 In vitro drug release study of RopiniroleHCl SRT formulation F12 in triplicate:

Table 11: In vitro drug release study of selected formulation

Time (Hrs)	% DRUG RELEASE			
	F12a	F12b	F12c	Avg.
1	18.05	19	20.5	19.18
2	29	28	27.5	28.15
3	33.79	32.87	34.25	33.63
4	40.88	41.21	40.69	40.92
5	47.68	48.14	49.53	48.45
6	54.16	54.16	55.09	54.47
8	64.35	65.27	66.20	65.27
10	70.83	69.90	69.44	70.05
12	76.38	77.31	78.24	77.31
14	82.40	81.01	81.94	81.78
16	86.11	87.03	87.5	86.88
20	90.74	90.27	91.20	90.73
24	99.53	100.46	99.07	99.68

The in vitro drug release of the selected formulation was repeated thrice to study the reproducibility of the results. The sustained drug release was found to be reproducible in case of the selected SRT formulation F12.

3.5 Comparison of In vitro drug release study of Tablet with Polymers

Table 12: Comparison of In vitro drug release study of Tablet with Polyox WSR303 and HPMC K100M alone & in combination (F12 Batch)

Time(Hr)	Drug Release (%)		
	Polyox WSR303 (55%)	HPMC K100M (55%)	Combination of Both (F12 Batch)
1	26	28	21
2	34.5	33.5	29
3	37.5	38.88	33.33
4	44.44	44.90	41.20
5	51.38	50.46	48.61
6	55.09	53.70	55.09
8	60.04	59.25	62.5
10	66.20	64.35	69.90
12	70.83	69.90	75
14	78.24	79.62	80.55
16	85.18	86.57	84.72
20	101.85	96.75	91.20
24			99.53

The above study clears that when Polyox WSR303 & HPMC K100M used separately sustained drug release upto 20 Hrs. But, when used in combination it retards drug release upto24 Hrs. So, it can be concluded that when both Polyox WSR303 & HPMC K100M are used in combination increases sustained action than using separately.

3.6 Assay of Ropinirole HCl Sustained release tablet (F12)

Table 13: Assay of Ropinirole HCl SR Tablet

Assay	Limit
98.86	NLT 98.7%and NMT 101.0%

SUMMARY AND CONCLUSION

In the present work sustain release matrix tablets of RopiniroleHClwere prepared by Direct compression technique by using Polyox WSR303 & HPMC K100M. These polymers are used in combination and individually. Optimization done by using Box Behnkenmodel with the help of Design Expert Software. Among the formulated batches F12 batch showed best results.All tablets were subjected to hardness, friability, weight variation,In vitrodrug release study and short term stability study.

Based on the above study following conclusions were drawn:

i. IR spectra revealed that, the drug matches with standard functional group frequencies of drug.
ii. There was no interaction between excipients and drug. All the excipients used were compatible with the drug.IR studies indicated that there was no drug-excipients interaction.
iii. Evaluation parameters like hardness and friability indicated that tablets so prepared were mechanically stable and complied with necessary pharmacopoeial specifications.
iv. Drug content was found to be98.86% which is within the limit NLT 98.7%and NMT 101.0%.
v. From the In vitro drug release study; it is clear that batch F12 gives maximum drug release that is 99.53 in 24 Hrs. Thus F12 batch formulation achieved the aim of sustaining the drug release upto 24 hrs. Thus from above all study it was clear that Batch F12 formulation achieved all aim and objective of the research work.
vi. The study clears that when Polyox WSR303 & HPMC K100M used separately sustained drug release upto 20 Hrs. but, when used in combination it retards drug release upto24 Hrs. So, it can be concluded that when both Polyox WSR303 & HPMC K100M are used in combination increases sustained action than using separately

From the results; direct compression of drug with Polyox WSR303 and HPMC K100M in combination is promising approach to Sustained drug release up to 24 hrs.

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