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Development and Characterization of Solid Dispersion of Rasagilline Mesylate for Improvement of Dissolution Rate Using Hydrophilic Carriers

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ABSTRACT: The aim of present study was to improve the solubility of Rasagilline mesylate, an Atypical Antipsychotic agent which is BCS Class III drug and thus has very low solubility and hence very poor bioavailability owing to less absorption. Moreover Rasagilline mesylate has a bitter taste. Thus in the present study an attempt was made to taste mask the bitter taste of drug and improve oral bioavailability of drug by formulating the drug into solid dispersion and then formulate the solid dispersions into Fast Dissolving Tablets. Solid Dispersions of Rasagilline mesylate were formulated using various polymers like Plasdone K30, plasdone K90, Eudragit RS100, Eudragit RL 100, Poloxamer 188 and Soluplus in different ratios viz., 1:1 and 1:2 by solvent evaporation method and evaluated for various physicochemical parameters. On the basis of evaluation parameters Solid Dispersion containing Drug : Soluplus :: 1 : 2 was optimized batch having Solubility 1.91 mg/ml, Drug content 102.75 % and % CDR of 98.43 % at 35 mins. For formulating Fast Dissolving Tablets, 3^2 factorial designs was applied where the batch SD12 and Concentration of Chitosan were taken as dependent variable X_1 and X_2, respectively and wetting time (sec.) and in vitro disintegration time (sec.) and % CDR were taken as an independent variables. All the formulation prepared by applying experimental design showed more than 93 % drug release in 15 mins. Batch F9 was selected as an optimized batch from the data of overlay plot, drug release kinetics and checkpoint batch. A stability study for optimized formulation was carried out as per ICH guidelines, showed no significant changes in the evaluation parameters. Thus from the study it can be concluded that Fast Dissolving Tablets of Rasagilline mesylate formulated from solid dispersions can provide rapid drug release within a short period of time.

KEYWORDS: Rasagilline mesylate, Solid Dispersion, solvent evaporation method, Fast Dissolving Tablets, Effervescent method, Wetting time, *In Vitro* disintegration time, % CDR.

INTRODUCTION

The development of many active pharmaceutical ingredients (APIs) has been discontinued because of their low aqueous solubility, which leads to poor bioavailability. Some of these drugs belong to Biopharmaceutical Classification System (BCS) Class II compounds, which are characterized by low aqueous solubility and high permeability. The urgency to 'enhanced solubility' of BCS Class III APIs has generated special interest to the pharmaceutical scientists to achieve better oral bioavailability. Out of numerous formulation strategies. The oral route of administration still continues to be the most preferred route due to its manifold advantages including ease of ingestion, pain avoidance, versatility and most importantly patient compliance. The most popular solid dosage forms are tablet and capsule. One drawback of these dosage forms however is the difficulty to swallow. Dysphasia or difficulty in swallowing is seen nearly 35% in the general population.

Many elderly persons will have difficulties in taking conventional solid dosage form (tablets and capsules) because of their hand tremors and dysphasia. Swallowing problems are also common in young individuals because of their under developed muscular system. In some cases such as motion sickness, sudden episode of allergic attack or coughing and an unavailability of water, swallowing of tablets may become difficult. To fulfill these medical needs, the pharmaceutical technologist have devoted considerable effort to develop a novel type of dosage form for oral administration, the Fast Dissolving Tablet (FDT), tablet that disintegrates and dissolves rapidly in saliva without need of water. The FDT usually dissolve in oral cavity within 15 to 60 s. The faster the drug goes into solution, the quicker the absorption and onset of clinical effects. The development of fast dissolving tablets also provides line extension in the market place. Advantages of rapid disintegrating drug delivery system over conventional dosage forms include fast drug absorption, quick drug therapy intervention, convenience of administration and patient acceptance,

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especially for pediatric, geriatric, dysphagic, psychiatric patients and travelers.

Rasagilline mesylate was selected for the present work because it is BCS class III (high solubility low permeability) drug and has solubility problems. BCS class III (i.e., less water soluble) drugs require innovative approaches to reach a sufficiently high bioavailability when administered by oral route. Poorly water soluble drugs can exhibit a number of negative clinical effects including potentially serious issues of inter patient variability and subsequent erratic absorption.

Rasagiline is a second generation, selective, irreversible inhibitor of mono amine oxidase type B (MAO-B). The Rasagilline mesylate is bitter in taste and which was selected as model drug to formulate rapid disintegrating drug delivery system.

First aim of the study was masking the bitter taste of Rasagilline mesylate. Various methods are available to physically mask the undesirable taste of drugs such as the addition of sweeteners and flavors, coating with water insoluble materials, creating a wax matrix by spray congealing, adsorption to ion-exchange resin, solid dispersions, formation of salts or derivatives, use of amino acids and protein hydrolysates, viscosity modifications, precipitation method and complexing with cyclodextrins.

The main features of the study were to completely mask the bitter taste of Rasagilline mesylate using solid dispersion technique and to develop an optimum formula and process conditions to manufacture a rapid disintegrating drug delivery system. Developed system than serve us as a patient-favorable dosage form.

MATERIALS AND METHODS

MATERIALS: Rasagilline mesylate was a gift from Amneal Pharmaceuticals (Intas Pharmaceuticals (Ahmedabad, India). All polymer used were obtained from Chemdyes Corporation. The superdisintegrants was Chitosan (Chemco Industries). The diluents was Avicel 102 (Grindley Merck: A Pharma Division, Ahmedabad). All other chemicals used in the study were of analytical grade.

PREFORMULATION STUDIES OF RASAGILLINE MESYLATE

Determination of Melting point of Rasagilline mesylate

- Melting point determination is one of the popular techniques used to identify drug using melting point apparatus and melting point of Rasagiline Mesylate was found in the range of 152 - 159 ºC, whereas the reported Melting Point of Rasagiline Mesylate is 155.56 °C.
- This indicates that the observed melting point is in the range of reported melting point and thus it was concluded that the given drug is Rasagiline Mesylate.

Determination of Rasagilline mesylate by FTIR

FTIR spectroscopy of pure drug and physical mixture of drug and excipients was carried out to check the compatibility of drug and excipients.

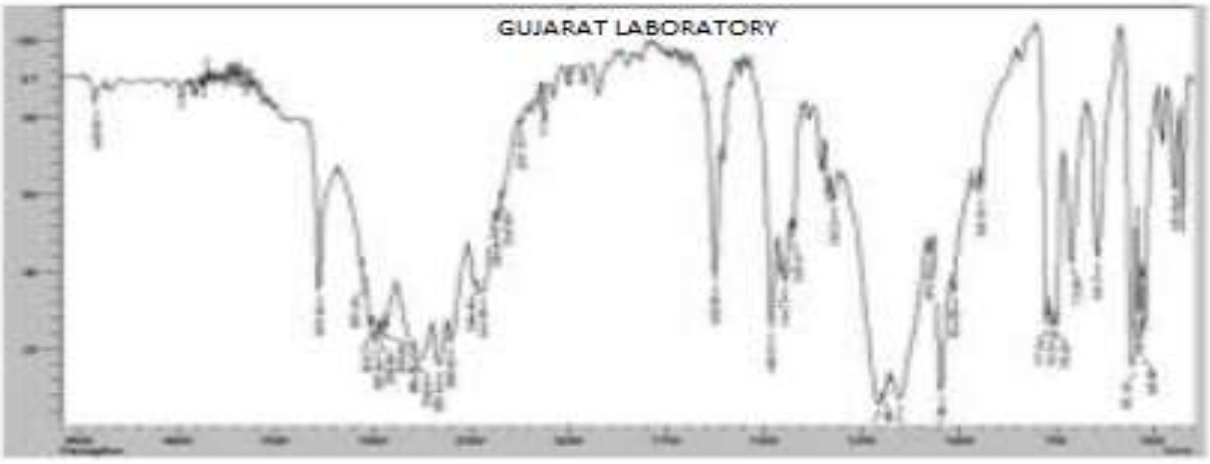

Fig. 1: FTIR of Rasagiline Mesylate

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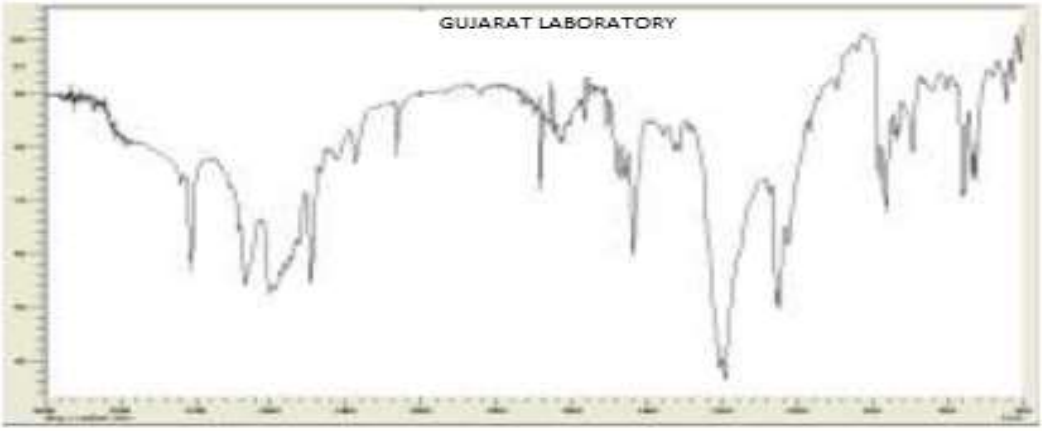

Fig. 2: FTIR spectra of Rasagiline Mesylate and Soluplus

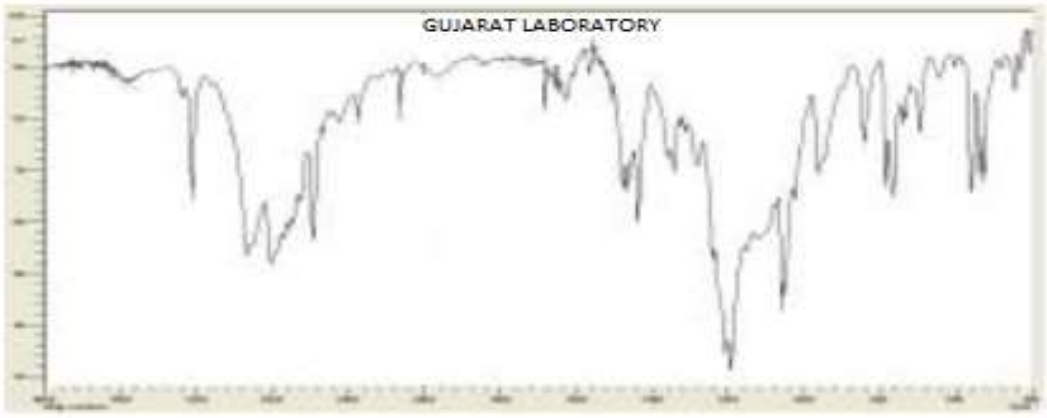

Fig. 3: FTIR spectra of Rasagiline Mesylate and superdisintegrant

Estimation of Rasagilline mesylate by UV-Visible Spectrophotometry

- Standard stock solution of Rasagilline mesylate was prepared by dissolving 10 mg of Rasagilline mesylate in 100 ml phosphate buffer (pH 6.8).
- Working solution of concentration 10, 20, 30, 40 and 50 ppm were prepared by pipette outing 1, 2, 3, 4 and 5 ml respectively from the stock solution of 100 ppm and diluted up to 10 ml volumetric flask.
- Absorbance of working solutions was measured in triplicate at λmax at 271 nm against phosphate buffer (pH 6.8) as a blank.

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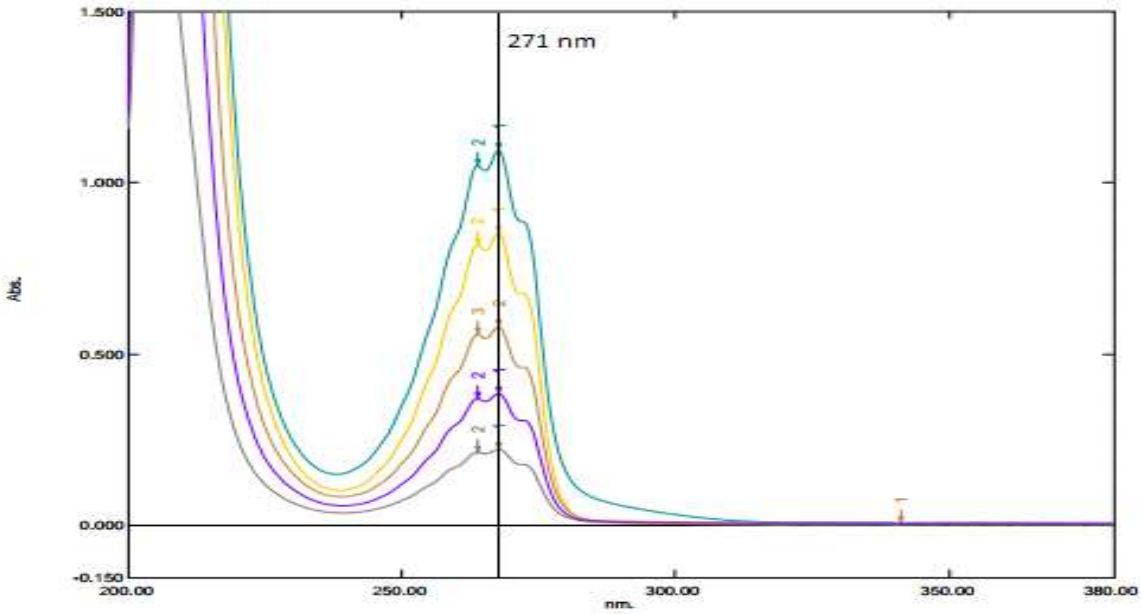

Fig. 4: Overlay Spectra of Rasagilline mesylate

Table 1: Regression Analysis of Rasagiline Mesylate in phosphate buffer at pH 6.8

Sr. No.	Parameters	Result
1.	Regression equation	y = 0.0456x - 0.0584
2.	Correlation coefficient	R^2 = 0.997
3.	Calibration curve range	10 - 50 ppm

Solubility of Rasagilline mesylate in Different Media

Table 2: Solubility of Rasagilline mesylate in Different Media

Sr. No.	Media	Solubility
1.	Water	Highly soluble
2.	0.1 N HCl	Slightly Soluble
3.	Phosphate Buffer pH 6.8	Slightly Soluble
4.	Methanol	Soluble

RASAGILLINE MESYLATE SOLID DISPERSIONS

Preparation of Solid dispersion of Rasagilline mesylate by Solvent evaporation method:

Solid dispersions of Rasagilline mesylate with different polymers such as Plasdone K30, plasdone K90, Eudragit RS100, Eudragit RL 100, Poloxamer 188 and Soluplus containing drug: polymer (1:1 and 1:2) were prepared by the solvent evaporation method as follows.

To a solution of weighed quantity of Rasagilline mesylate in a minimum amount of Methanol, the appropriate amount of polymer was added. The resulting mixture was stirred for 1 hr and evaporated at temperature of 45-50°C on water bath until nearly dry and then stored in a desiccator over anhydrous $CaCl_2$, to constant weight. The evaporated product was grounded in a mortar and passed through sieve 60# and stored in a desiccator until further evaluation.

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Table 3: Composition of Various Solid Dispersions of Rasagilline mesylate

SR. NO.	FORMULATION CODE	COMPOSITION	RATIO
1.	SD1	Drug : Plasdone K30	1 : 1
2.	SD2	Drug : Plasdone K30	1 : 2
3.	SD3	Drug : Plasdone K90	1 : 1
4.	SD4	Drug : Plasdone K90	1 : 2
5.	SD5	Drug : Eudragit RS 100	1 : 1
6.	SD6	Drug : Eudragit RS 100	1 : 2
7.	SD7	Drug : Eudragit RL 100	1 : 1
8.	SD8	Drug : Eudragit RL 100	1 : 2
9.	SD9	Drug : Poloxamer 188	1 : 1
10.	SD10	Drug : Poloxamer 188	1 : 2
11.	SD11	Drug : Soluplus	1 : 1
12.	SD12	Drug : Soluplus	1 : 2

EVALUATION PARAMETERS OF SOLID DISPERSIONS

Table 4: Flow property data of Rasagilline mesylate Solid Dispersions

S.D. Batch	Bulk Density (gm/ml)	Tapped Density (gm/ml)	Carr's Index (%)	Hausner's Ratio (%)	Angle of Repose (°Θ)	Void Volume	% Porosity
SD1	1.05	1.33	21.05	1.26	38.65	0.4	21.05
SD2	1.17	1.53	23.52	1.30	27.75	0.4	23.52
SD3	1.052	1.42	26.31	1.35	29.05	0.5	26.30
SD4	1.05	1.25	15.78	1.18	32.82	0.3	15.78
SD5	1.052	1.33	21.05	1.26	36.52	0.4	21.05
SD6	1.11	1.42	22.22	1.28	28.39	0.4	22.22
SD7	1.05	1.42	26.31	1.35	43.60	0.5	26.31
SD8	1.11	1.53	27.77	1.38	35.53	0.5	27.77
SD9	1.11	1.33	16.66	1.20	29.05	0.3	16.66
SD10	1.17	1.25	05.88	1.06	27.14	0.1	05.88
SD11	1.17	1.33	11.76	1.13	26.56	0.2	11.76
SD12	1.11	1.25	11.11	1.12	24.94	0.2	11.11

Table 5: Solubility and Drug content data of Rasagilline mesylate Solid Dispersions

Formulation Batch	% Practical Yield	Amount of Drug Soluble (mg/ml)	Drug Content (%)
SD1	81.50	1.10	97.24
SD2	82.66	1.22	97.93
SD3	84.50	1.28	98.96
SD4	89.33	1.64	100.68
SD5	78.50	0.92	96.55
SD6	85.66	1.41	99.31
SD7	73.50	0.61	95.17
SD8	76.33	0.74	95.86
SD9	86.50	1.60	100.34
SD10	91.33	0.81	101.37
SD11	92.50	1.85	102.06
SD12	93.66	1.91	102.75

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Table 6: Drug Release Profile of Rasagilline mesylate Solid Dispersions

Batch	Time (min)									
	0	**5**	**10**	**15**	**20**	**25**	**30**	**35**	**40**	**45**
SD1	0	12.82	34.81	53.68	66.62	74.89	80.84	89.63	97.65	-
SD2	0	16.96	39.72	59.63	71.53	79.29	85.24	93.25	98.43	-
SD3	0	11.27	31.44	55.24	69.98	79.03	86.01	89.63	98.68	-
SD4	0	17.22	39.46	61.44	76.96	84.72	90.67	98.17	-	-
SD5	0	10.75	30.15	48.51	65.06	74.37	80.32	86.53	91.70	99.72
SD6	0	17.22	40.24	55.86	73.08	81.62	87.82	92.22	99.20	
SD7	0	11.53	31.70	48.25	61.44	68.43	73.60	79.03	87.05	97.39
SD8	0	16.18	38.17	56.27	68.68	74.89	79.29	86.27	92.22	98.68
SD9	0	12.82	36.10	62.75	77.48	83.68	87.82	97.13	-	-
SD10	0	17.22	44.63	96.98	83.94	90.41	92.48	98.94	-	-
SD11	0	11.01	35.58	65.06	85.24	93.77	95.43	99.20	-	-
SD12	0	16.18	45.15	70.24	92.48	97.39	98.43	-	-	-

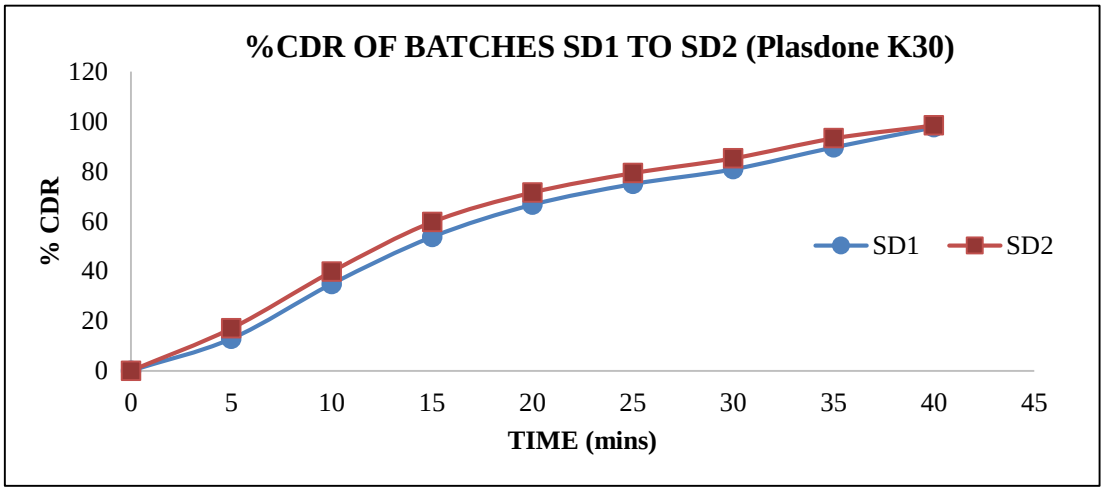

Fig. 5: % Cumulative Drug Release of Batches SD1 & SD2

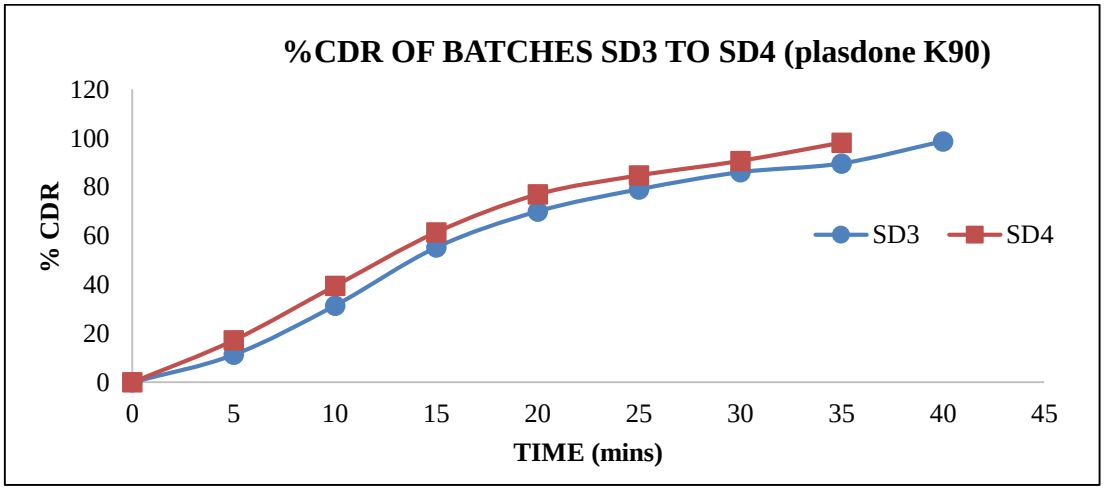

Fig. 6: % Cumulative Drug Release of Batches SD3 & SD4

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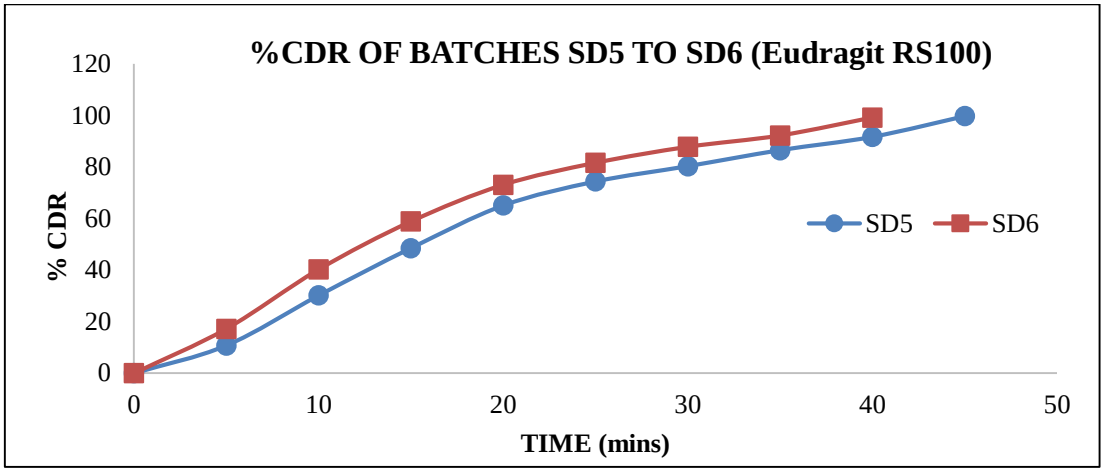

Fig. 7: % Cumulative Drug Release of Batches SD5 & SD6

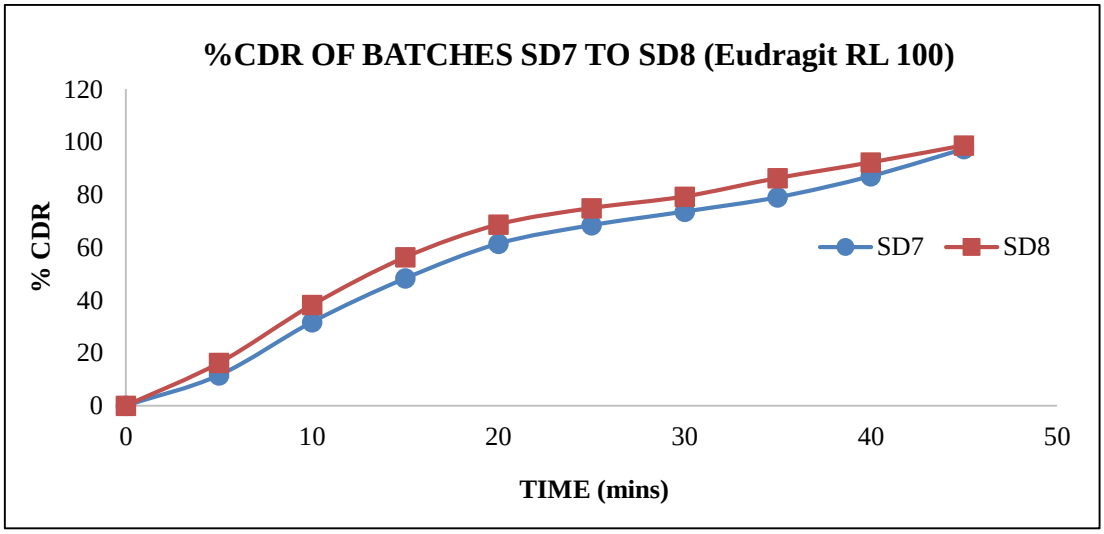

Fig. 8: % Cumulative Drug Release of Batches SD7 & SD8

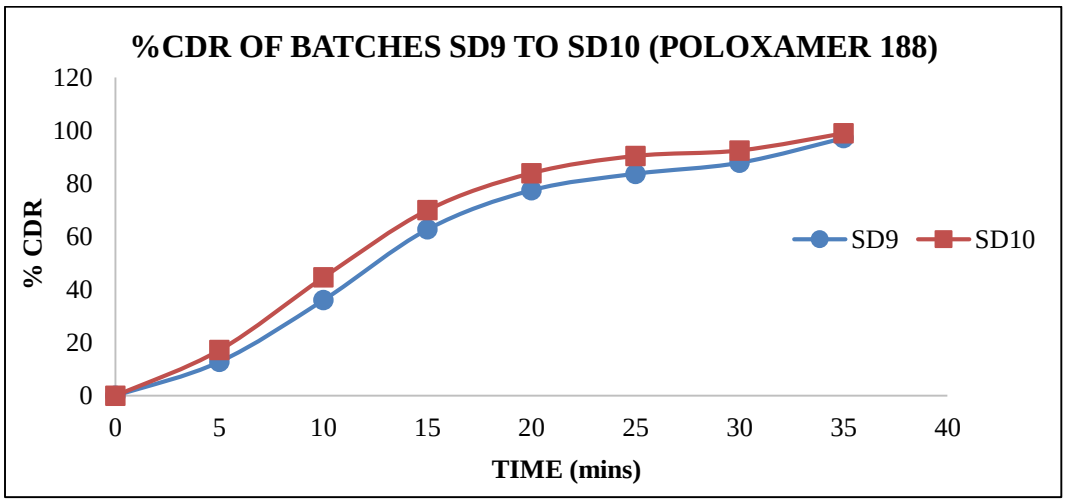

Fig. 9: % Cumulative Drug Release of Batches SD9 & SD10

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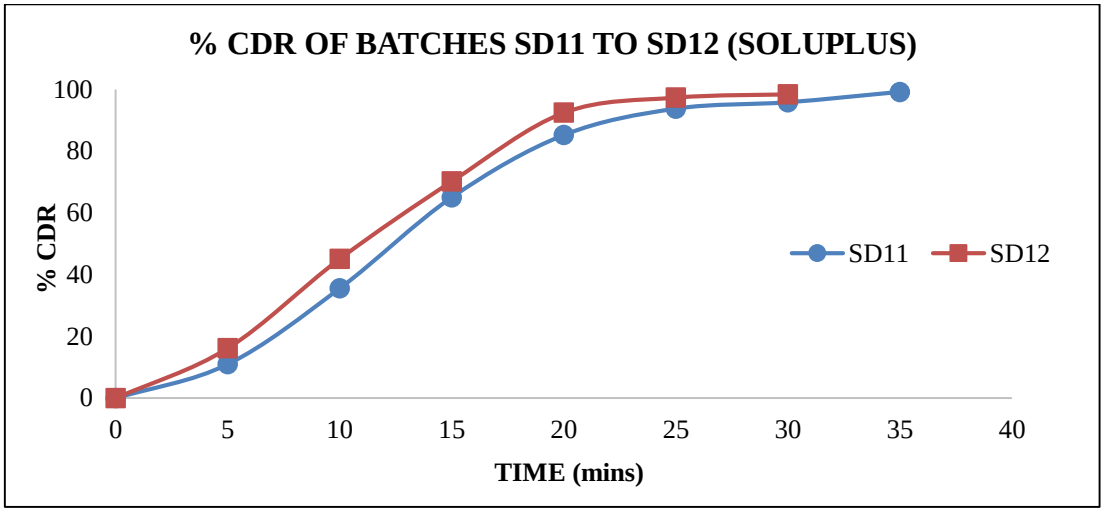

Fig. 10: % Cumulative Drug Release of Batches SD11 to SD12

The dispersion of Rasagilline mesylate in Plasdone K30, plasdone K90, Eudragit RS100, Eudragit RL 100, Poloxamer and Soluplus as an inert carrier or matrix in solid state was used to mask the taste of bitter drugs. On the basis of the results of solid dispersion batch SD1 to SD12 the Formulation Batch SD12 (Drug: Soluplus 1:2) was selected as best taste masked candidate for development of FDTs. The drug release from ratio Formulation Batch SD12 in phosphate buffer pH 6.8 was found 98.43 in 30 mins, thus selected for the development of the FDTs.

RASAGILLINE MESYLATE FAST DISSOLVING TABLETS

Formulation design of Rasagilline mesylate Fast Dissolving Tablets by Effervescent Method

Dispensing: All the ingredients were weighed as per the formulation design.

Sieving: After dispensing of the ingredients, all the ingredients were passed through sieve size of 44 #. This step used for the uniformity of the ingredients and reduction in the size of particles gives uniform particle size distribution.

Mixing: After sieving, Rasagilline mesylate, Avicel PH 102, D-Mannitol, super disintegrants, Citric acid, Sodium bicarbonate were weighed and mixed in a geometric order in a mortar. Weighed quantity of Talc, Magnesium stearate and SLS were mixed with the formulation blend.

Compression: Formulation blend was compressed using 8 mm flat round punch into a tablets using Rimek multi rotary 16 station tablet compression machine.

Evaluation: Prepared tablets were evaluated by various evaluation parameters.

Table 7: Formulation of Fast Dissolving Tablet using 3^2 Factorial design

Ingredients (mg)	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**
S.D. (equivalent to 1 mg drug)	1.85	2.32	2.81	1.85	2.32	2.81	1.85	2.32	2.81
Avicel pH 102	30	30	30	30	30	30	30	30	30
Crospovidone	3	3	3	4.5	4.5	4.5	6	6	6
D-mannitol	61.15	60.68	60.19	59.65	59.18	58.69	58.15	57.68	57.19
Citric acid	15	15	15	15	15	15	15	15	15
Sodium bicarbonate	30	30	30	30	30	30	30	30	30
Aspartame	3	3	3	3	3	3	3	3	3

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SLS	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
Talc	3	3	3	3	3	3	3	3	3
Magnesium stearate	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
Total weight	**150**	**150**	**150**	**150**	**150**	**150**	**150**	**150**	**150**

EVALUATION PARAMETERS OF FAST DISSOLVING TABLET

Table 8: Pre-Compression parameters

Batch code	Bulk density (gm/ml)	Tapped density (gm/ml)	Carr's index (%)	Hausner's Ratio	Angle of repose (°θ)
F1	1.07	1.41	23.70	1.31	46.46
F2	1.06	1.37	22.55	1.29	32.82
F3	1.01	1.21	16.59	1.19	27.14
F4	1.09	1.44	24.45	1.32	43.60
F5	1.01	1.26	19.33	1.23	29.74
F6	1.15	1.32	13.36	1.15	23.96
F7	1.03	1.30	20.66	1.26	35.53
F8	1.02	1.26	18.93	1.23	28.39
F9	1.04	1.16	10.41	1.11	23.49

Post compression parameters

Table 9: Weight variation, Thickness, Diameter, Hardness and Friability

Batch Code	Thickness (mm ± S.D.)	Diameter (mm ± S.D.)	Weight Variation (mg ± S.D.)	Hardness (kg/cm^2± S.D.)	Friability (%)
F1	3.13 ± 0.020	5.76 ± 0.025	150.3 ± 1.25	2.96 ± 0.15	0.86
F2	3.07 ± 0.015	5.80 ± 0.028	150.5 ± 1.64	2.86 ± 0.20	0.78
F3	3.06 ± 0.040	5.75 ± 0.028	151.1 ± 1.60	3.06 ± 0.11	0.41
F4	3.11 ± 0.100	5.75 ± 0.011	150.2 ± 1.24	2.86 ± 0.05	0.49
F5	3.12 ± 0.023	5.80 ± 0.015	149.5 ± 1.49	2.56 ± 0.28	0.54
F6	3.07 ± 0.040	5.82 ± 0.015	149.8 ± 1.39	3.08 ±0.005	0.79
F7	3.06 ± 0.005	5.85 ± 0.025	150.7 ± 1.51	2.63 ± 0.11	0.86
F8	3.09 ± 0.015	5.87 ± 0.017	150.8 ± 1.87	3.03 ± 0.15	0.74
F9	3.04 ± 0.005	5.84 ± 0.015	149.9 ± 1.58	2.96 ± 0.057	0.58

Table 10: Wetting time, *In vitro* disintegration time and Drug Content

Batch code	Wetting time (sec. ± S.D.)	*In vitro* disintegration time (sec. ± S.D.)	Drug content (%)
F1	54.33 ± 1.53	58.33 ± 0.58	92.41
F2	42.33 ± 0.58	45.33 ± 1.53	95.05
F3	25.33 ± 1.53	28.33 ± 1.15	98.96
F4	52.33 ± 0.58	55.33 ± 0.58	93.56
F5	39.67 ± 1.15	40.67 ± 1.15	97.24
F6	23.67 ± 0.58	26.67 ± 1.15	100.34
F7	48.33 ± 0.58	51.33 ± 0.58	93.90
F8	35.33 ± 1.53	39.67 ± 1.15	98.50
F9	20.33 ± 1.15	23.33 ± 1.15	101.72

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Table 11: Percentage Cumulative Drug Release of Batches F1 to F9

TIME (MIN)	BATCH								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
2	10.24	15.41	19.81	11.27	15.41	18.77	16.7	18.25	30.41
4	32.48	39.2	43.08	34.03	39.46	45.93	34.81	38.68	45.41
6	49.03	58.6	62.48	50.48	59.37	63.25	44.37	52.65	59.89
8	69.72	73.6	79.55	66.1	73.6	76.96	55.75	63.25	70.24
10	81.36	84.46	91.7	78.25	80.32	83.94	69.2	74.37	78.00
12	84.46	88.34	93.25	84.46	87.82	94.29	82.13	85.24	86.53
14	89.89	91.7	95.84	90.41	93.77	96.87	89.12	92.48	94.29
16	93.25	95.58	97.65	94.29	96.87	98.43	94.81	97.39	99.46
18	96.1	97.39	98.17	95.58	97.65	99.98	98.17	98.94	-
20	98.43	99.72	-	97.39	-	-	98.68	-	-

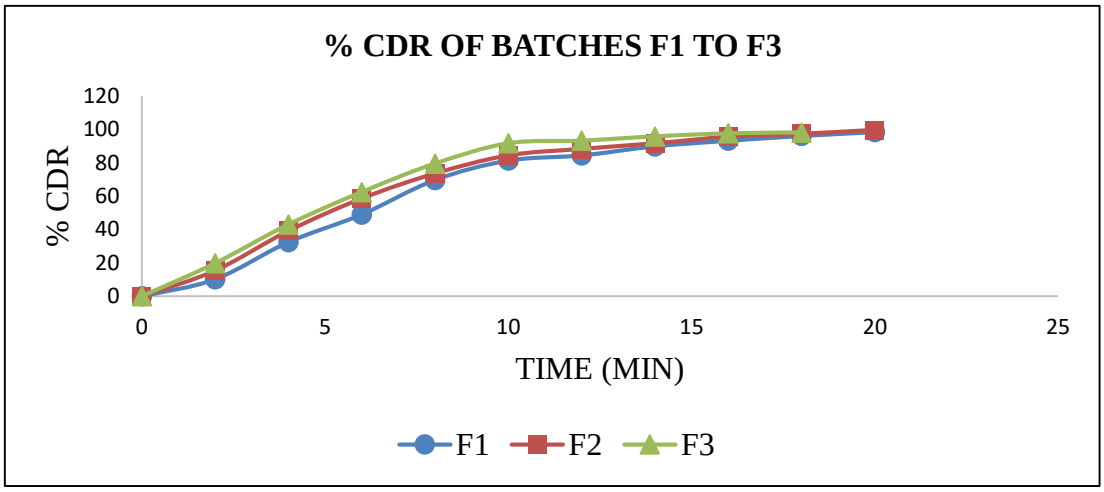

Fig. 11: % Cumulative Drug Release of Batches F1 to F3

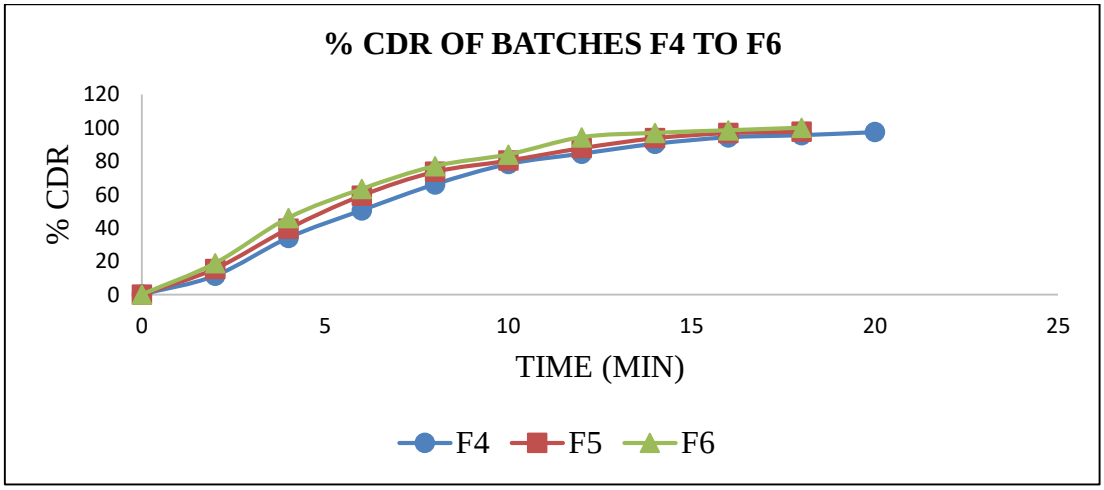

Fig. 12: % Cumulative Drug Release of Batches F4 to F6

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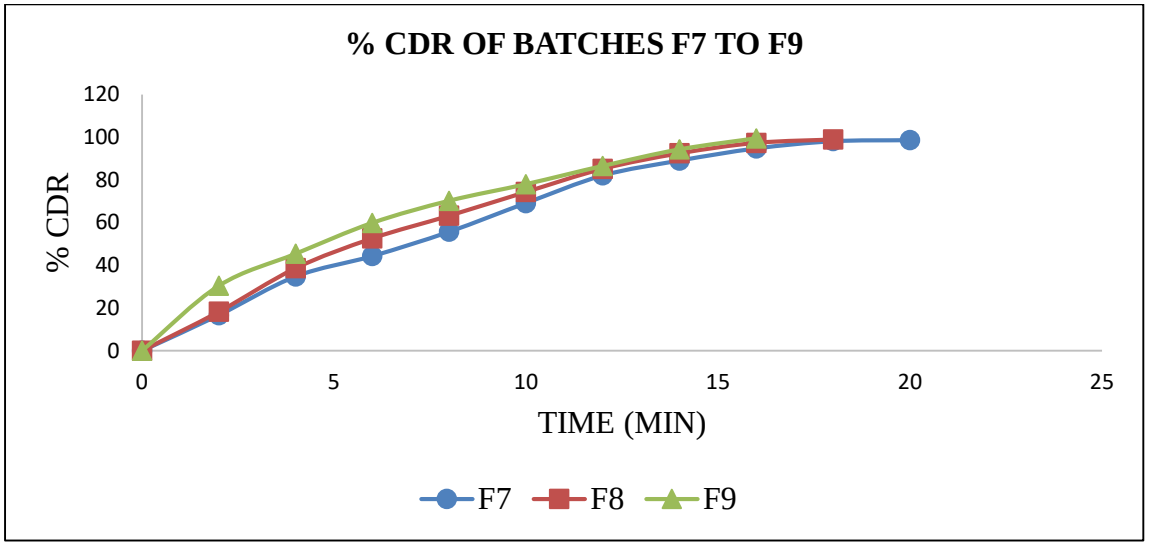

Fig. 13: % Cumulative Drug Release of Batches F7 to F9

DRUG RELEASE KINETICS OF OPTIMIZED BATCH

Dissolution profile of optimized batch was fitted to various model and release data were analysed on the basis of Korsmeyer Peppas equation, Zero order, first order and Higuchi kinetics.

Table 12: Drug Release Kinetics of Optimized Batch

Model	First order	Zero order	Higuchi release model	Korsmeyer Peppas release model
R^2	0.5416	0.9981	0.9967	0.1733
Slope	0.0845	76.82	0.2573	0.1781
Intercept	0.9424	-29.686	-0.029	-0.2961

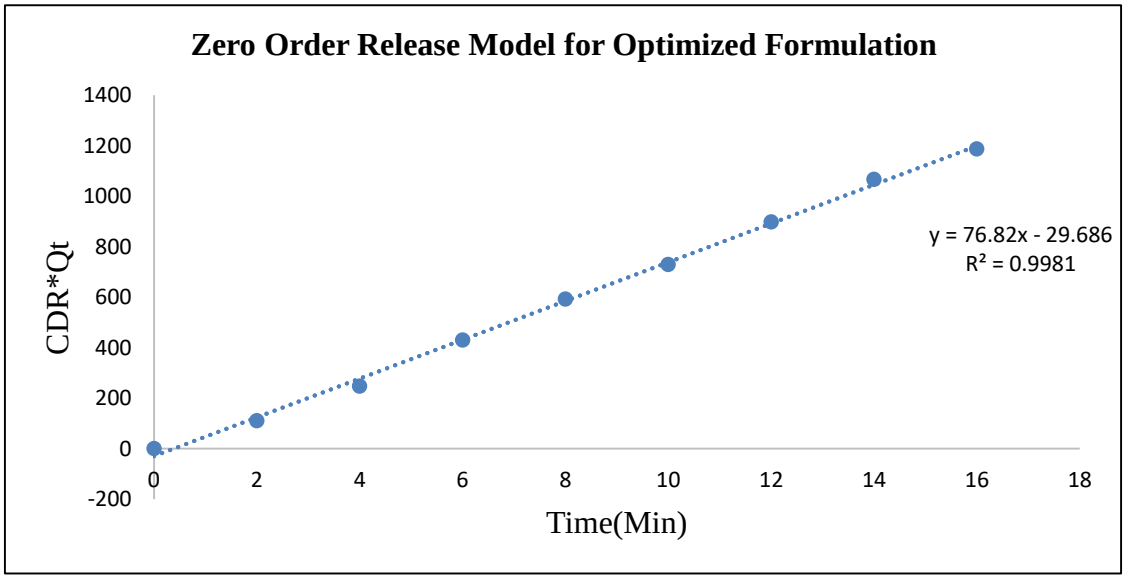

Fig. 14: Zero Order Release Model for Optimized Formulation

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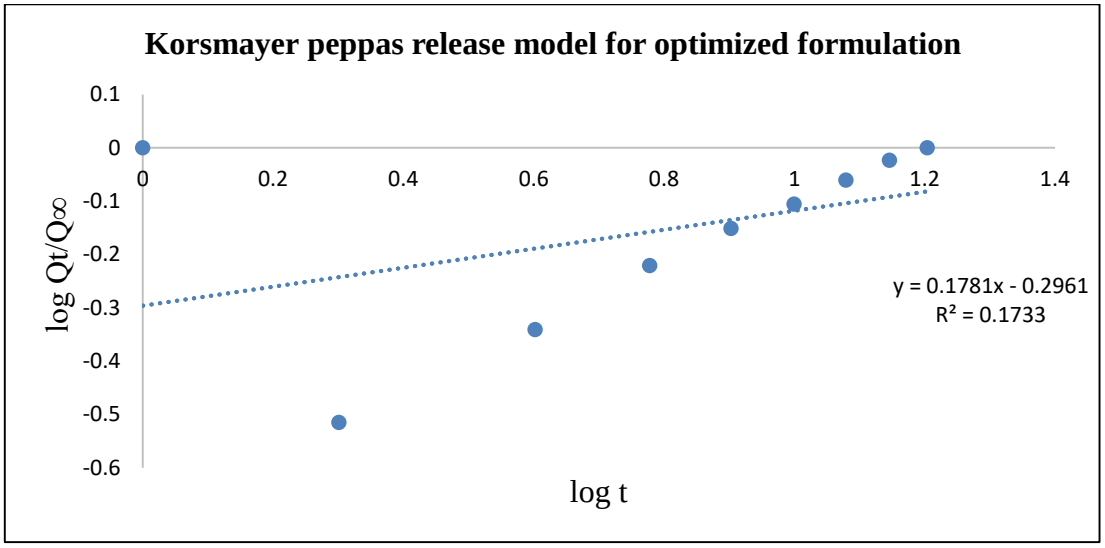

Fig. 15: Korsmayer Peppas Release Model for Optimized Formulation

From the above data it can be concluded that optimized formulation followed Zero order release kinetics as the R^2 value of the Zero order graph was found to be nearer to 1 which indicates that the drug release was constant over a period of time. Moreover from Korsemeyer Peppas model it was concluded that the value of n = 0.178**,** which indicates that the diffusion followed was quasi-fickian diffusion.

Stability study of optimized batch: In the present study, stability study of optimized batch was carried out at 40 ± 2°C/ 75 ± 5% RH for time period of 1 month by wrapping the formulation in aluminum foil to prevent the formulation from exposure to light under the 40 ± 2°C/ 75 ± 5% RH for 1 month as prescribed by ICH guidelines for accelerated stability study.

Table 13: Result of the Stability Study

Evaluation parameter	Results of optimized batch	Result after 1 month at 40 ± 2 °C and 75 ± 5 % RH
Hardness (kg/cm^2 ± S.D.)	2.96 ± 0.057	2.8667 ± 0.11
Wetting Time (sec. ± S.D.)	20.33 ± 1.15	21.33 ± 0.58
In vitro Disintegration Time (sec. ± S.D.)	23.33 ± 1.15	24.67 ± 0.58
Drug Content (%)	101.72	100.68

Table 14: Cumulative Drug Release Study of Stability Batch

Time (Min.)	% CDR of Optimized Batch (%)	% CDR of batch After Time Period of1 Month (%)
0	0	0
2	30.41	17.50
4	45.41	37.39
6	59.89	54.98
8	70.24	69.98
10	78	79.03
12	86.53	83.43
14	94.29	92.22
16	99.46	98.17

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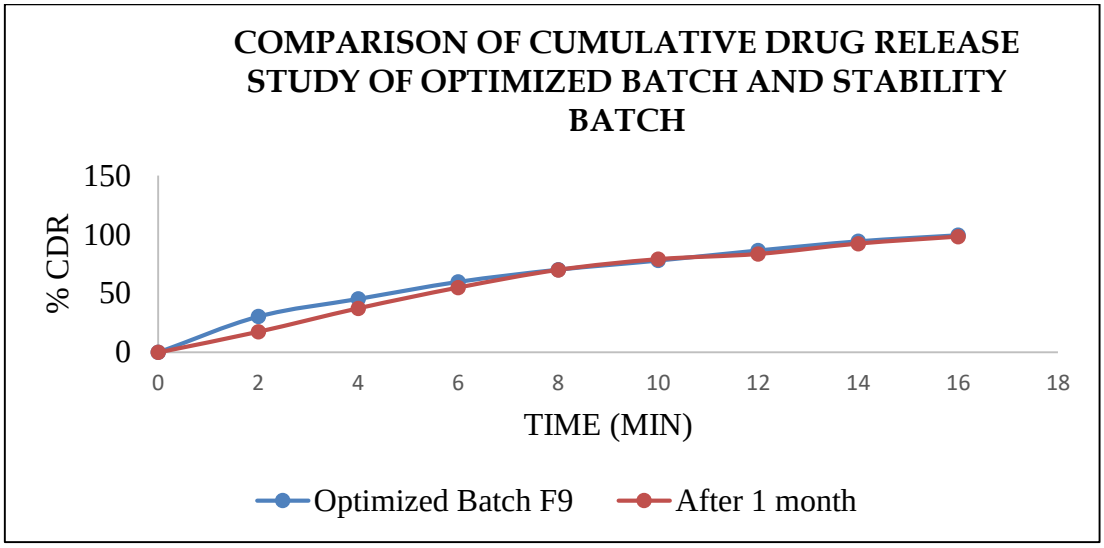

Fig. 16: Comparison of Cumulative Drug Release study of Optimized batch and Stability batch

CONCLUSION

- Rasagiline is a second generation, selective, irreversible inhibitor of mono amine oxidase type B (MAO-B). It is BCS Class III drug hence having high solubility and 36 % bioavailability. Rasagiline Mesylate has the unpleasant taste. Based on the taste of the Rasagiline Mesylate was selected as a drug candidate for masking its unpleasant taste.
- Hence the main objectives of this study was to taste mask the unpleasant taste by formulating solid dispersions using different carriers by solvent evaporation method. Further formulating fast dissolving Tablets of the Solid Dispersions giving desired drug release profile and other physicochemical parameters.
- Compatibility studies were performed through FT-IR on Rasagiline Mesylate and carriers used in the formulations and they were found to be compatible.
- Solid dispersions were prepared using different carriers at 1:1 and 1:2 ratio and they showed enhanced solubility as compared to pure drug. Carriers such as Plasdone K30, Plasdone K90, Eudragit RS100, Eudragit RL100, Poloxamer and Soluplus showed enhanced dissolution rate. The flow properties such as Angle of Repose and Carr's Index were evaluated and gave excellent flow characteristics and Carr's Index.
- From the results of evaluation parameters batch SD12 containing Drug:Soluplus (1:2) was found to be excellent which showed Drug Content 102.75 %, Solubility 2.12 µg/ml and Cumulative drug release of 98.43 % in 30 mins as compared to all other batches and hence this batch was used for formulating Fast Dissolving Tablets.
- The concept of Fast Dissolving Tablet containing Rasagiline Mesylate solid dispersion offers a suitable and practical approach in serving the desired objective of management of psychosis or schizophrenia. The excipients used in the formulation were water-soluble and hence have a better patient acceptability.
- Fast Dissolving Tablets of Rasagiline Mesylate were prepared by effervescent method using natural Superdisintegrants. A 3^2 factorial design was applied to optimize the formulation where solid dispersion Drug : Soluplus ratio was selected as an independent variable (X_1) and Crospovidone was selected an independent variable (X_2) at 3 different levels, whereas Wetting time, *In Vitro* Disintegration time and % Cumulative Drug Release at 16 mins were selected as dependent variables Y_1, Y_2 and Y_3 respectively.
- For the preparation of Fast Dissolving Tablet Crospovidone was used as Superdisintegrant which was screened to achieve rapid disintegration and acceptable hardness, Avicel PH 102 as binder, Mannitol as diluent, Aspartame as sweetening agent, Magnesium stearate as lubricant and Talc was used as glidant, Sodium bicarbonate and Citric acid were used as effervescence forming agent.
- All Precompression parameters like Carr's Index, Hausner's Ratio and Angle of Repose met the standard values indicating good flow properties. The average weight, friability and hardness were within compendia limits which showed that all

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formulations possessed good mechanical strength. Drug content uniformity was within acceptable limits, which indicated a homogeneous distribution of drug in tablets.

- Two check point batches were selected from the yellow region of overlay contour plot, which shows that the % error of actual and predicted value were less than 5 for all the response. Thus the model was significant.
- Formulation F9 was optimized from the overlay contour plotn which showed minimum disintegration time of 23.33 ± 1.15 secs, wetting time of 20.33 ± 1.15 secs and % cumulative drug release of 99.46 % in just 16 mins.
- Thus, batch F9 of Fast Dissolving Tablet was selected as an optimum batch by using desirability function. The results of comparison of predicted response and obtained response were found in good agreement and evaluated for further parameters like stability study.
- Moreover the graphs and data obtained from Design Expert software showed that the batch F9 gave all the desired results as well as ANOVA analysis stated that the values of independent variables were in the acceptable limits. From the contour plot and overlay plot also, the batch F9 was the optimized batch.
- The result of stability study of the batch F9 showed that there was no significant change in Hardness, Wetting time, *In-vitro* Disintegration time, Drug content and *In Vitro* dissolution profile for a period of one month when stored in stability chamber at 40 ± 2 °C/ 75 ± 5 % RH for period of one month.
- From the study it was concluded that taste masked solid dispersions of Rasagiline Mesylate can be successfully formulated in to Fast Dissolving Tablets using Natural Superdisintegrants by effervescent method, which can provide rapid drug release within a short period time.
- Thus, it will be an important factor in improving patient compliance which is prerequisite for Parkinson's disease for all age groups.

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