



FORMULATION AND EVALUATION OF MATRIX TABLETS OF RASAGILINE MESYLATE USED IN THE TREATMENT OF PARKINSON'S DISEASE

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ABSTRACT

The aim of the present study was to formulate and evaluate Matrixtablet containing Rasagiline Mesylate used in the treatment of Parkinsonism disease. In the present work, an attempt is made to develop controlled-release matrix tablets of Rasagiline Mesylate, with the use of various hydrophilic polymers for their controlling effect. Wet granulation technique is used for tablet formulation along with the addition of suitable additives by using of hydrophilic polymers like Acacia, Ethyl Cellulose. *In vitro* drug release of F6 was 78.125 % with different concentration of Acacia and Ethyl Cellulose shows maximum drug release and good stability than compared to other formulation. In this study, a controlled release matrix tablet of Rasagiline Mesylate was developed with desirable drug release properties. Higher concentration of polymers containing formulation had good stability, better *in vitro* release. Therefore, the higher concentration of polymers containing formulation to have the potential to improve the patient compliance, a controlled release formulation of Rasagiline Mesylate, to minimize the frequent dose, to prolong the pharmacological effect.

KEYWORDS: Matrix tablet, Controlled release, Rasagiline Mesylate, Parkinsonism, *In vitro* release.

INTRODUCTION

Oral drug delivery method is the most widely utilized routes for administration among all alternatives that have been explored for systemic delivery of drug via various pharmaceutical products of different dosage forms. With many drugs, the basic goal is to achieve a steady state blood level that is therapeutically effective and non-toxic for an extended period of time. The design of proper dosage form is an important element to accomplish this goal. prolonged action, controlled release, extended action, timed release and depot dosage form as 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.^[1]

Parkinsonism: Parkinson's disease is a chronic neurodegenerative disorder in which loss of dopamine neurons leads to deterioration of motor and non-motor functions, affecting the quality of life. Motor symptoms associated with Parkinson's disease are tremors, stiffness, bradykinesia, impaired balance, and a shuffling walk. In the later stage, non-motor symptoms such as dementia, anxiety, and depression were also noticed⁽²⁾

Dr. James Parkinson described Parkinson's disease in 1817 as shaking palsy, named after him. Parkinson's disease is a chronic degenerative disorder in which, with

time, degeneration of both motor functions such as immobility of muscles and non-motor functions such as memory gets affected due to which living quality of the patient, its family members, and its caretaker get compromised.^[3]

Parkinson's disease has been recognized as the second most common neurodegenerative disorder and most common movement-related disorder worldwide. Initially, Parkinson's disease was understood as just a movement disorder. However, after so many years of the progression of the disease, it was found that it is not just a movement disorder. However, other symptoms such as postural instability and memory loss were also associated.^[4] Only 10 % of Parkinson's disease cases are found to have a genetic basis; the rest, 90%, are sporadic.^[5] The foremost pathological characteristic of Parkinson's disease is an accumulation of protein α -synuclein in Lewy bodies.^[6] The exact reason for the occurrence of Parkinson's disease is still unclear; however, certain risk factors such as age, brain injury/infection, exposure to toxins/pesticides, and genetic reasons are the cause of Parkinson's disease.^[7]

The main risk factors for Parkinson's disease are elevated cholesterol level, head injury, high calories intake, exposure to environmental toxins such as carbon

disulfide, cyanides, herbicides, pesticides, some organic solvents, oxidative stress, mitochondrial dysfunction, and nitric oxide toxicity.^[8,9,10]

Matrix tablet^[11] A matrix system consists of active and inactive ingredients that are homogeneously dispersed and mixed in the dosage form. It is by far the most commonly used oral extended release technology and the popularity of the matrix systems can be attributed to several factors. The release from matrix type formulations is governed by Fick's first law of diffusion.

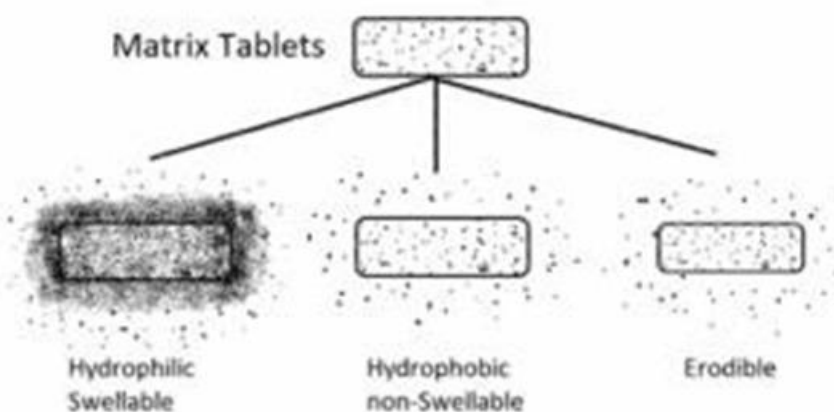
In a matrix system the drug is dispersed as solid particles within a porous matrix formed of a hydrophobic polymer (such as wax, polyethylene, polypropylene, and ethyl cellulose) or hydrophilic polymer (such as Hydroxy propyl cellulose, Hydroxy propyl methyl cellulose, methylcellulose, sodium carboxy methyl cellulose, alginates and Scleroglucan).

In this sense, the term "matrix" indicates the three dimensional network containing the drug and other substances such as solvents and excipients required for the specific preparation. Matrix drug delivery systems release the drug in continuous manner. These release the drug by both dissolution controlled as well as diffusion controlled mechanisms. Initially, drug particles located at the surface of the release unit will be dissolved and the drug released rapidly.

The matrix works as one unit, which dissolves, controlling the release. They're very robust, common, reasonably easy to develop, and inexpensive to make.

Three different types are shown.

- Hydrophilic swellable
- Hydrophobic, non-swellable
- Erodible



Different types of Matrix Tablets^[12]

Advantages of Matrix Tablet

- Easy to manufacture
- Versatile, effective and low cost
- Can be made to release high molecular weight compounds
- The sustained release formulations may maintain therapeutic concentrations over prolonged periods.
- The use of sustain release formulations avoids the high blood concentration.
- Sustain release formulations have the potential to improve the patient compliance.

1.2.3 Disadvantages of Matrix Tablet

- The remaining matrix must be removed after the drug has been released.
- High cost of preparation.
- The release rates are affected by various factors such as, food and the rate transit through the gut.
- Achievement of zero order release is difficult.
- The remaining matrix must be removed after the drug has been released.

MATERIALS AND METHODS

Materials: Rasagiline Mesylate (Indoco Remedies Ltd, Navi Mumbai 400701), Acacia, Ethyl Cellulose, Starch, Lactose, Purified Talc, Magnesium stearate (SD fine chemical ltd, Mumbai, India) all other chemicals used where of laboratory reagent grade (LR grade).

Methods

Qualitative estimation of Rasagiline Mesylate by UV Spectrometric method Determination of absorption maxima: The Absorption Spectra of Rasagiline Mesylate in Phosphate buffer pH 6.8 was observed by UV Spectrophotometer.

Standard calibration curve of Rasagiline Mesylate

The standard curve with a regression value of 0.9987 and a slope of 0.0036 in Phosphate buffer pH 6.8 was observed. The curve is linear in the concentration range from 50 to 250 µg/ml, and it obeys Beer's law. UV spectra of different concentrations are shown in Fig 3. The calibration data was given in Table 3 and the calibration curve was constructed and confirmed the linearity.

Preparation of granules

Granules of Rasagiline Mesylate matrix tablets were prepared by wet granulation technique using various ratios of Acacia and Ethyl cellulose separately and mixture of both as release retardant polymers. All the powders passed through sieve No.120. The required quantity of drug, various polymers and other ingredients were mixed thoroughly and a sufficient volume of

granulating agent was added slowly.

After enough cohesiveness was obtained, the wet mass was sieved through sieve No.12. The granules were dried at 60°C for 30 minutes and then the dried granules were passed through Sieve No. 40. Talc and magnesium Stearate were finally added as a Glidant and Lubricant respectively.

Table 1: Composition of Rasagiline Mesylate Matrix Tablets

Ingredients (mg/tablet)	F1	F2	F3	F4	F5	F6
Rasagiline	2	2	2	2	2	2
Mesylate						
Acacia	20	40	-	-	10	20
Ethyl cellulose	-	-	20	40	10	20
Lactose	176	156	176	156	176	156
Magnesium Stearate	1	1	1	1	1	1
Talc	1	1	1	1	1	1
Total weight	200	200	200	200	200	200

Preparation of tablet⁽¹³⁾

The evaluation of granules showed excellent flow properties. The granules were compressed into tablets on 16 station rotary tablet compression machine using 8 mm round, flat punches with break line. The compressed

tablets were evaluated for various parameters viz. appearance, thickness, diameter, hardness, friability, weight variation, drug content and *in vitro* drug release studies.

RESULTS

a) Melting Point Determination.

Table 2: Melting Point report of Rasagiline Mesylate.

Reported	Method	Observed
152 ⁰ C-159 ⁰ C	Thiel’s tube method	154.35 ⁰ C

b) Solubility Study

Solubility analysis of Rasagiline Mesylate was carried out in various solvents and Phosphate buffer. The

obtained results are in agreement with other researchers as showed in the Figure 1.

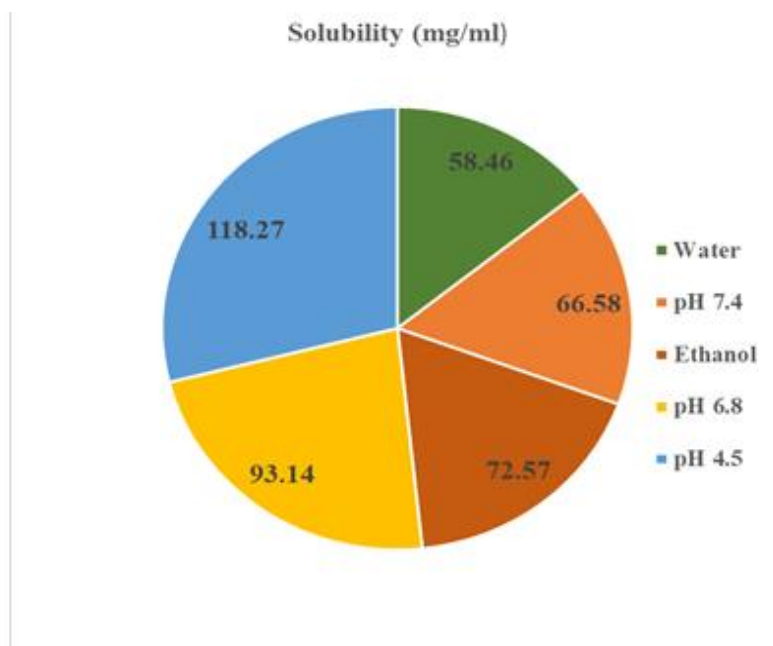


Fig. 1: Graphical representation of solubility analysis of Rasagiline Mesylate.

c) Determination of λ max

The absorption spectrum of pure drug was scanned between 200-400 nm with 10 μ g/ml concentration in pH

6.8 phosphate buffer solution using UV Spectrophotometer. The maximum peak was obtained at 271 nm that was taken as λ max.

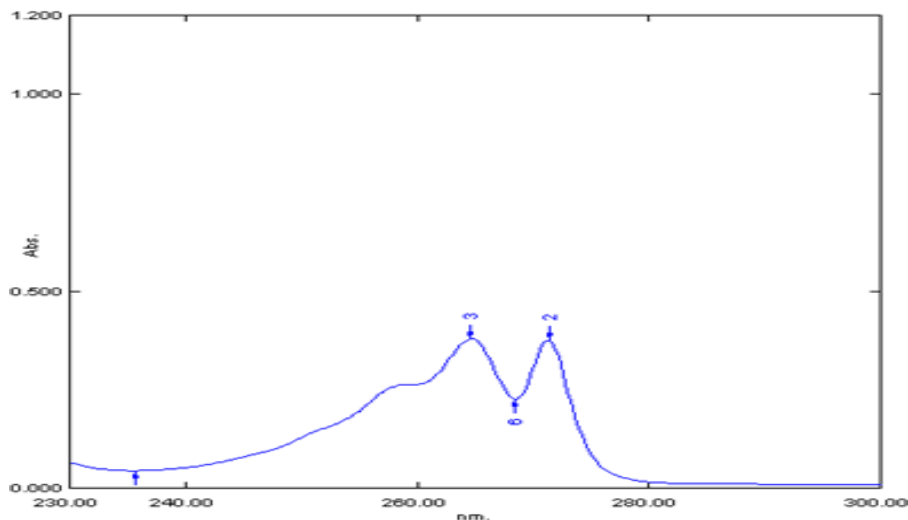


Fig. 2: UV Spectrum of Rasagiline Mesylate 10 μ g/ml concentration.

d) Standard Calibration curve of Rasagiline Mesylate

The standard curve with a regression value of 0.9987 and a slope of 0.0036 in Phosphate buffer pH 6.8 was observed. The curve is linear in the concentration range from 50 to 250 μ g/ml, and it obeys Beer's law. UV

spectra of different concentrations are shown in Fig 3. The calibration data was given in Table 3 and the calibration curve was constructed and confirmed the linearity.

Table 3: Data for Standard calibration curve of Rasagiline Mesylate

Sl. No.	Conc. (μ g/ml)	Absorbance			Standard deviation (SD)
		Trial 1	Trial 2	Trial 3	
1	0	0	0	0	0
2	50	0.218	0.224	0.208	0.216 \pm 0.008
3	100	0.384	0.395	0.376	0.385 \pm 0.0095
4	150	0.563	0.574	0.556	0.564 \pm 0.009
5	200	0.737	0.751	0.722	0.736 \pm 0.014
6	250	0.916	0.926	0.906	0.916 \pm 0.01

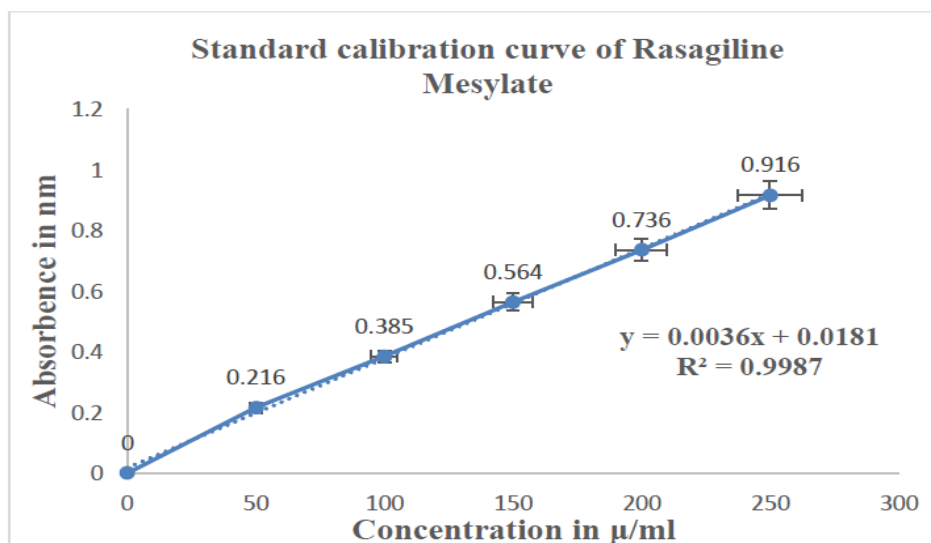


Fig. 3: Plot of standard calibration curve of Rasagiline Mesylate.

e) Compatibility Studies

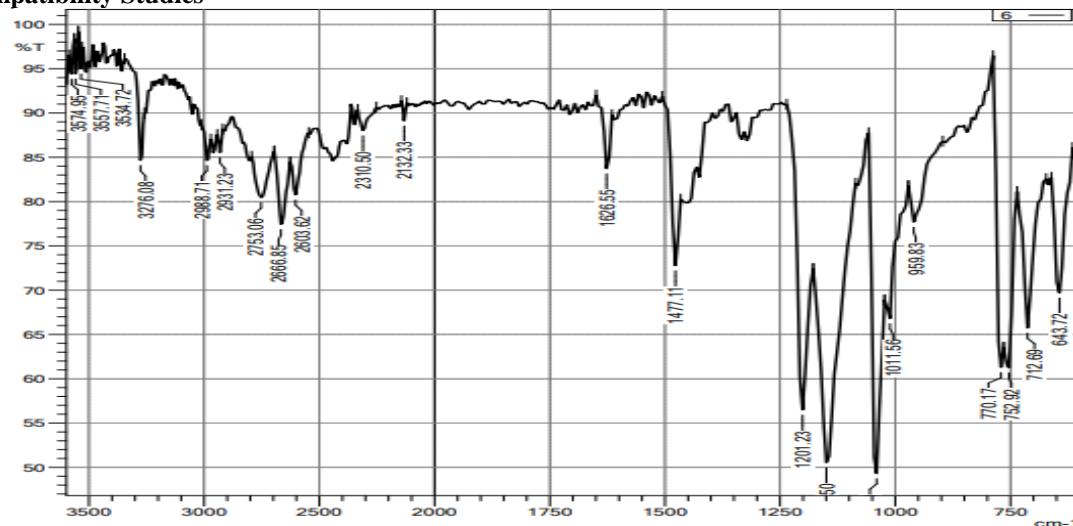


Fig. 4: FTIR Spectra of Rasagiline Mesylate.

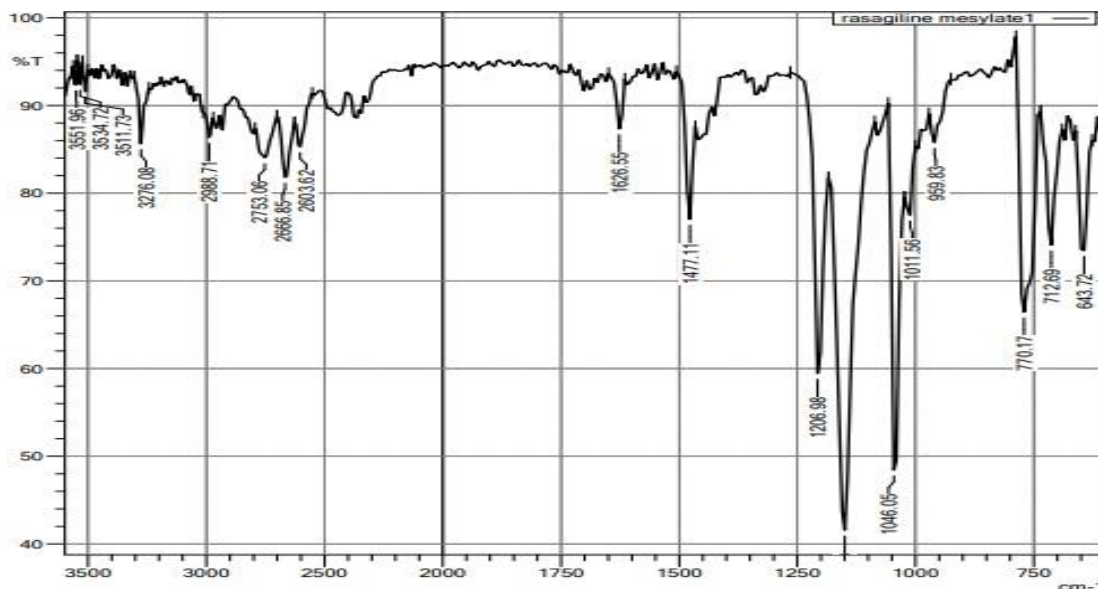


Fig. 5: FTIR Spectra of Rasagiline Mesylate + Acacia.

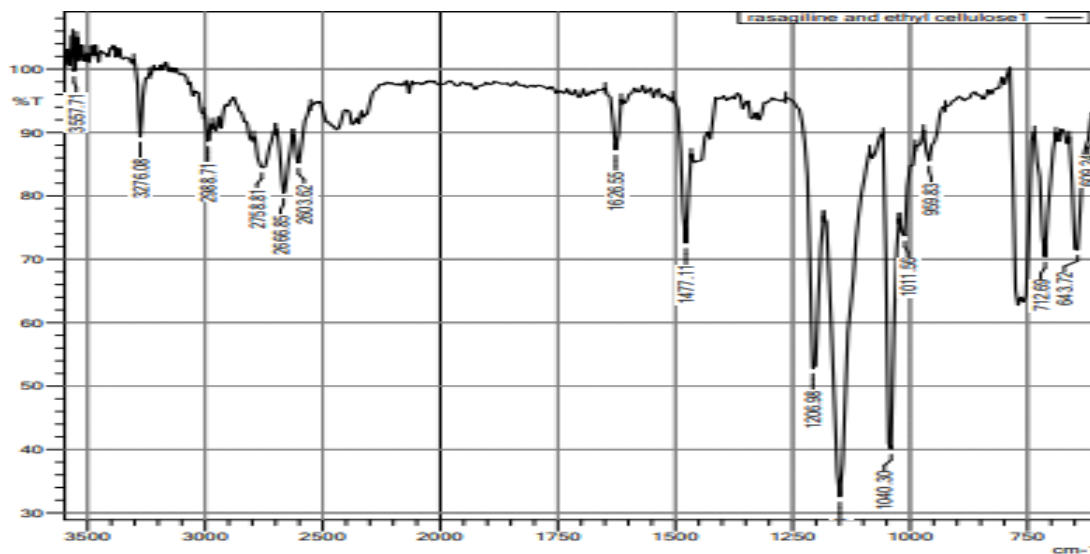


Fig. 6: FTIR Spectra of Rasagiline Mesylate + Ethyl cellulose.

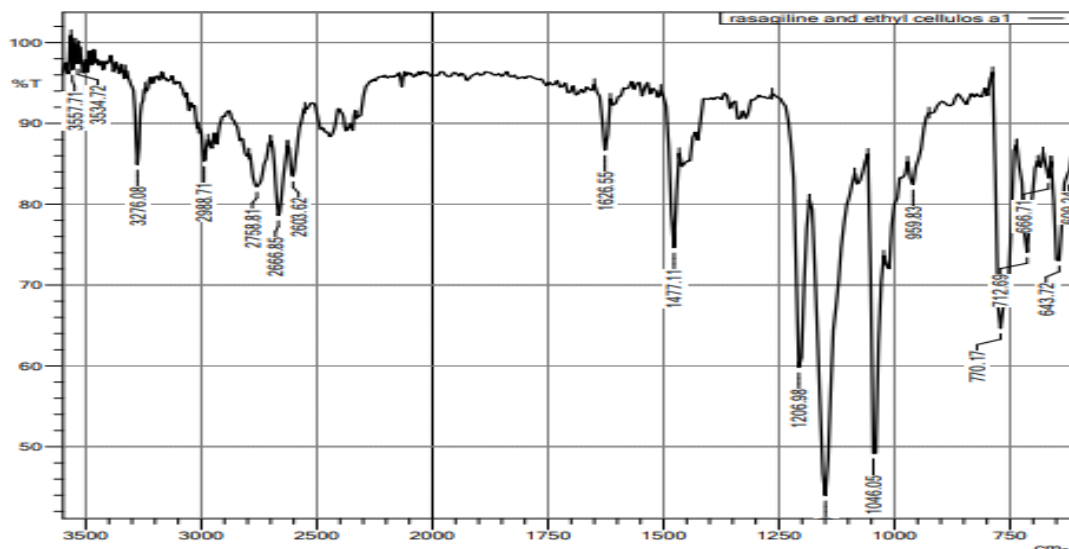


Fig. 7: FTIR Spectra of Rasagiline Mesylate + Acacia + Ethyl cellulose.

Table 4: Compatibility studies by FTIR

Functionalgroup	Wave number (cm ⁻¹) of	Wave number (cm ⁻¹) RM+Acacia	Wavenumber (cm ⁻¹) RM+Ethyl cellulose	Wavenumber (cm ⁻¹) RM+Acacia+ Ethylcellulose
O-H (Stretching)	3557.75	3551.96	3557.71	3557.71
N-H (Bending)	1626.06	1626.55	1626.55	1626.55
C-H Ar(Stretching)	3276.08	3276.08	3276.08	3276.08
C-H (Bending)	1327.07	1477.11	1477.11	1477.11
C=C (Stretching)	2123.33	2603.63	2603.62	2603.62
S=O (Bending)	1011.56	1011.56	1011.56	959.83
C-H Alkane(Stretching)	2988.71	2988.71	2988.71	2988.71

Evaluation of granules

Table 5: Evaluation of granules.

Formulation Code	Angle of Repose (°)	Loose Bulk Density (g/ml)	Tapped Bulk Density (g/ml)	Carr's Index (%)	Hausner's Ratio
F1	23.30±0.04	0.58±0.19	0.62±0.19	6.817±0.22	1.068
F2	34.32±1.76	0.40±0.50	0.44±0.36	10.01±0.64	1.1
F3	16.29±1.32	0.42±0.20	0.50±0.27	19.16±0.56	1.19
F4	14.06±0.02	0.41±0.54	0.47±0.23	14.07±0.99	1.14
F5	27.30±1.03	0.42±0.20	0.45±0.29	7.14±0.20	1.07
F6	24.02±0.04	0.58±0.20	0.59±0.15	7.27±0.24	1.072

Evaluation of Controlled Release Matrix Tablet of Rasagiline Mesylate.

Table 6: Characterization of Controlled Release Matrix Tablet of Rasagiline Mesylate.

Formulation Code	Thickness (mm)	Hardness (kg/cm ²)	Friability(%)	Weight Variation(mg)	Drug Content (%w/w)
F1	3.95	4.83	0.62±0.03	206	98.86±0.02
F2	4.02	5.33	0.62±0.02	186	98.65±0.01
F3	3.99	4.83	0.42±0.05	198	98.98±0.06
F4	4.00	4.83	0.49±0.04	190	98.86±0.01
F5	3.98	4.83	0.65±0.03	190	97.65±0.07
F6	3.94	6.33	0.59±0.04	212	98.45±0.02

In vitro Dissolution Studies

Table 7: In vitro Dissolution Study of Formulation F1 – F6.

Time (Hrs.)	Percentage Cumulative Drug Release					
	F1	F2	F3	F4	F5	F6
0	0	0	0	0	0	0
1	16.25	10.62	15.00	11.25	8.75	8.70
2	26.25	18.12	25.62	22.50	19.37	18.12
3	35.62	26.25	36.87	30.62	28.75	25.62
4	46.87	41.87	48.75	42.50	43.12	40.62
5	61.87	57.50	60.62	60.62	54.37	56.87
6	78.75	67.49	73.75	71.25	63.75	65.00
7	86.25	75.62	81.87	80.62	74.37	70.62
8	96.23	86.25	92.50	89.37	81.87	78.12

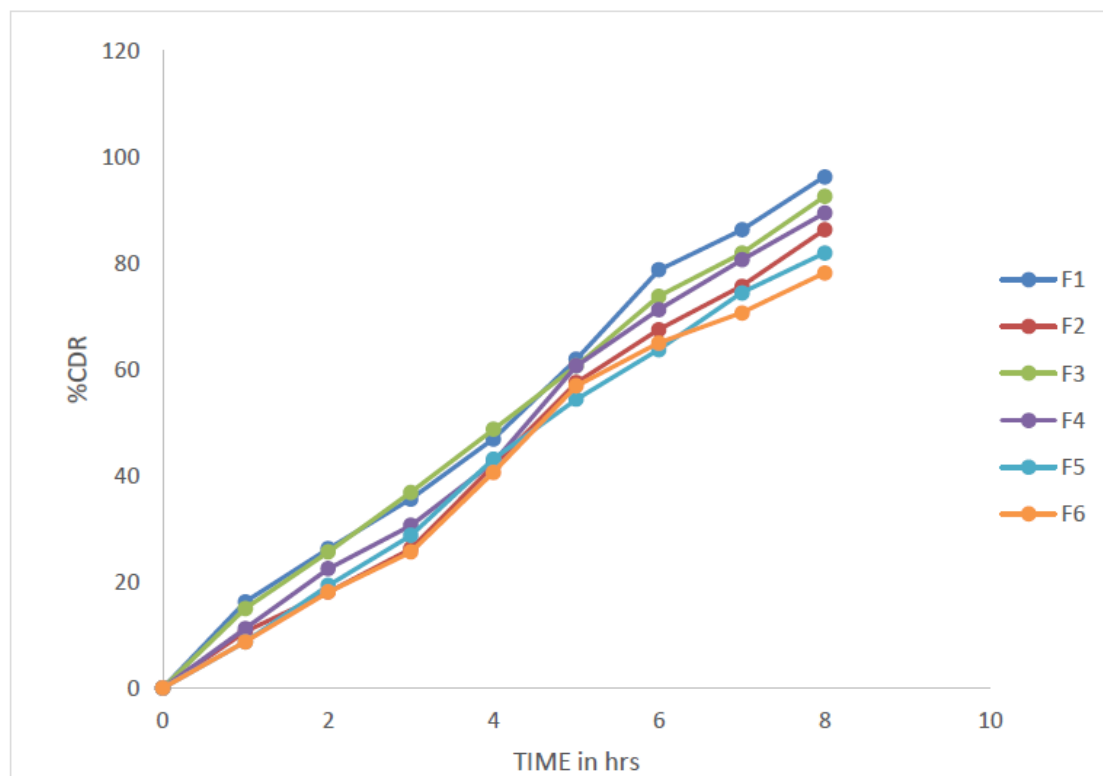


Fig.8: Percentage Cumulative Drug Release from Formulation F1 – F6Release Kinetics Profiles.

Table 8: Zero Order Release Kinetics Profile of Formulation F1 – F6.

Time (Hrs.)	Percentage Cumulative Drug Release					
	F1	F2	F3	F4	F5	F6
0	0	0	0	0	0	0
1	16.25	10.625	15	11.25	8.75	8.75
2	26.25	18.125	25.625	22.5	19.375	18.25
3	35.625	26.25	36.875	30.625	28.75	25.625
4	46.875	41.875	48.75	42.5	43.125	40.625
5	61.875	57.5	60.625	60.625	54.375	56.875
6	78.75	67.5	73.75	71.25	63.75	65
7	86.25	75.625	81.875	80.625	74.375	70.625
8	96.25	86.25	92.5	89.375	81.815	78.125

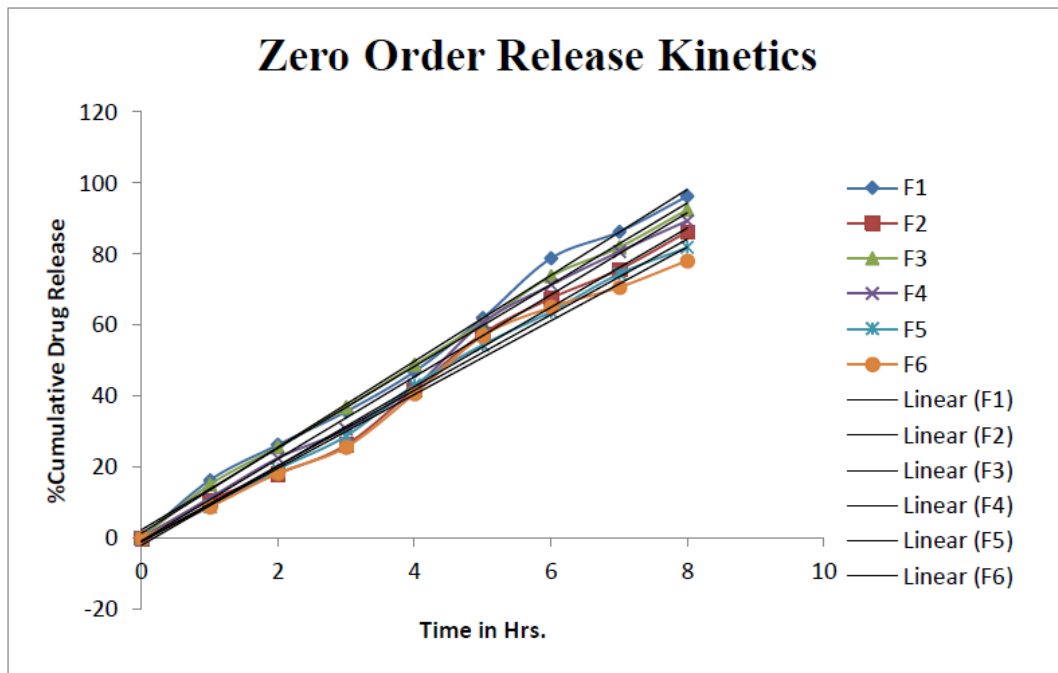


Fig. 9: Zero Order Release Kinetics Profile of Formulation F1 – F6.

Table 9: First Order Release Kinetics Profile of Formulation F1 – F6.

Time (Hrs.)	Log Percentage Drug Remaining					
	F1	F2	F3	F4	F5	F6
0	2	2	2	2	2	2
1	1.922	1.951	1.929	1.948	1.960	1.960
2	1.867	1.913	1.871	1.889	1.906	1.912
3	1.808	1.867	1.800	1.841	1.852	1.871
4	1.725	1.764	1.709	1.759	1.754	1.773
5	1.581	1.628	1.595	1.595	1.659	1.634
6	1.327	1.511	1.419	1.458	1.559	1.544
7	1.138	1.386	1.258	1.287	1.408	1.467
8	0.574	1.138	0.875	1.026	1.259	1.339

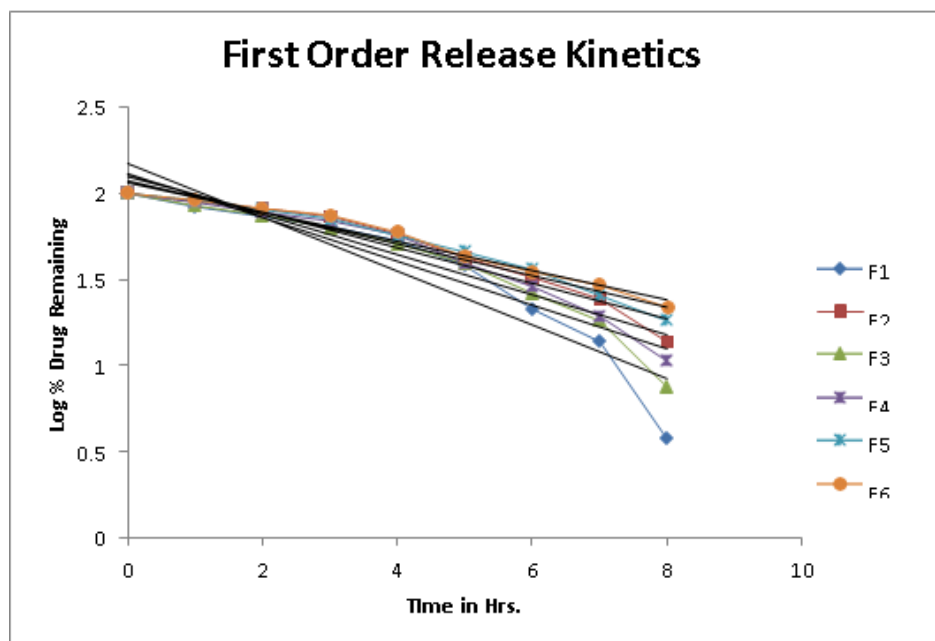


Fig. 10: First Order Release Kinetics Profile of Formulation F1 – F6.

Table 10: Higuchi Release Kinetics Profile of Formulation F1 – F6.

SQRT	Percentage Cumulative Drug Release					
	F1	F2	F3	F4	F5	F6
0	0	0	0	0	0	0
1	16.250	10.625	15	11.250	8.750	8.750
1.414	26.250	18.125	25.625	22.500	19.375	18.250
1.732	35.625	26.250	36.875	30.625	28.750	25.625
2	46.875	41.875	48.750	42.500	43.125	40.625
2.236	61.875	57.500	60.625	60.625	54.375	56.875
2.449	78.750	67.500	73.750	71.250	63.750	65
2.645	86.250	75.625	81.875	80.625	74.375	70.625
2.828	96.250	86.250	92.500	89.375	81.815	78.125

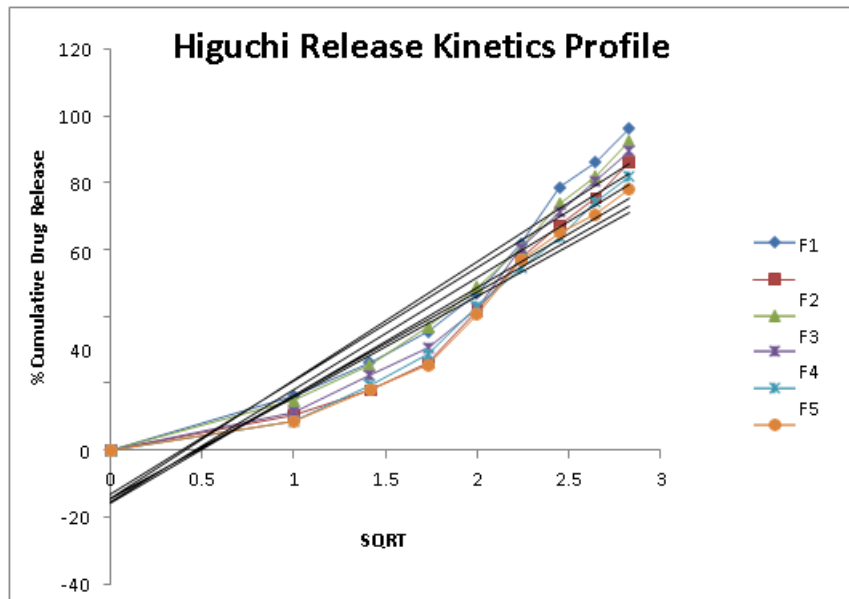


Fig 11: Higuchi Release Kinetics Profile of Formulation F1 – F6.

Table 11: Peppas Release Kinetics Profile of ormulation F1 – F6.

Log T	Log Percentage Cumulative Drug Release					
	F1	F2	F3	F4	F5	F6
0	0	0	0	0	0	0
0	1.210	1.026	1.176	1.051	0.942	0.942
0.301	1.419	1.258	1.408	1.352	1.287	1.261
0.477	1.551	1.419	1.566	1.486	1.458	1.409
0.602	1.670	1.621	1.687	1.628	1.634	1.608
0.698	1.791	1.759	1.782	1.782	1.735	1.755
0.778	1.896	1.829	1.867	1.852	1.804	1.812
0.845	1.935	1.878	1.913	1.906	1.871	1.848
0.903	1.983	1.935	1.966	1.951	1.912	1.893

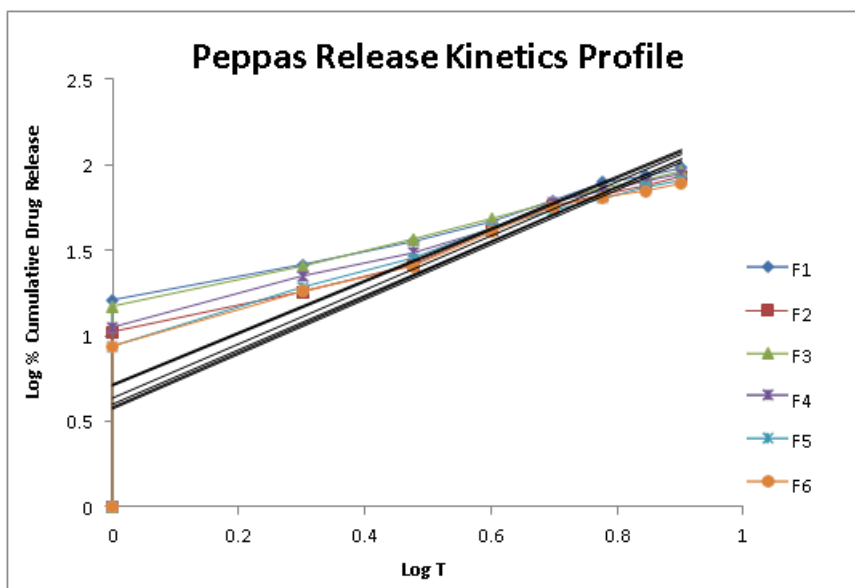


Fig. 12: Peppas Release Kinetics Profile of Formulation F1 – F6.

Table 12: Data for different Kinetic Models.

Formulation Code	Zero Order	First Order	HiguchiPlot	Peppas Plot	
				r ²	n
F1	0.994	0.853	0.915	0.721	1.520
F2	0.992	0.932	0.889	0.800	1.590
F3	0.997	0.906	0.931	0.726	1.517
F4	0.994	0.926	0.903	0.781	1.582
F5	0.996	0.958	0.908	0.814	1.605
F6	0.986	0.970	0.899	0.817	1.601

DISCUSSION

Pre-formulation Studies Identification of Drug

a. Melting point

Melting point of sample was found to be 154.35°C by the Thiel’s tube method which complied with I P standard, thus indicating the purity of drug.

b. Solubility analysis

Solubility analysis of Rasagiline Mesylate was done in different solvent and it was observed that it is soluble in water, slightly soluble in Ethanol, soluble in Phosphate buffer pH 4.5, 6.8 and 7.4.

c. Absorption Maxima Determination

In Phosphate buffer pH 6.8 the absorption maximum for Rasagiline Mesylate was found to be 271 nm, shown in Fig.2.

d. Preparation of Standard Calibration curve of Rasagiline Mesylate

The standard curve with a regression value of 0.9987 and a slope of 0.0036 in Phosphate buffer pH 6.8 was observed. The curve is linear in the concentration range from 50 to 250µg/ml, and it obeys Beer’s law. The calibration data is given in Table 3 and the Calibration curve was constructed and confirms the linearity.

e. Compatibility Studies by FTIR

FTIR spectra of Pure Rasagiline Mesylate showed sharp characteristic peaks at 3557.75 cm⁻¹, 1626.06 cm⁻¹, 3276.08 cm⁻¹, 1327.07 cm⁻¹, 2123.33 cm⁻¹, 1011.56 cm⁻¹, and 2988.71 cm⁻¹. The physical mixture of drug and excipient showed the entire characteristic peaks of pure drug, which confirms there is no interaction between the drug and excipient. Comparative studies of FTIR graphs are shown in (Fig.4-7) and spectral values are mentioned in Table 4.

Evaluation of granules

The blended granules of different formulation were evaluated for Angle of Repose, Loose Bulk density, Tapped Bulk density, Compressibility Index and Hausner ratio.

Angle of Repose

Angle of repose ranged from 14.06±0.02 to 34.32±1.76. The results were found to be below 35° and hence the blend was found to have better flowability.

Loose Bulk density and Tapped Bulk density

Loose Bulk and Tapped Bulk densities are used for the measurement of Compressibility index. (Table 5). The Loose bulk density and Tapped bulk density for all the formulations varied from 0.40±0.50 to 0.58±0.20 and 0.44±0.36 to 0.62±0.19 respectively.

Hausner Ratio

The Hausner's ratio ranged from 1.06 to 1.19 (Table 5). The result indicates the free – flowing properties of the granules.

Carr's Compressibility Index

The compressibility index (%) ranged from 6.817 ± 0.22 to 19.16 ± 0.56 (Table 5). The blend was found to have better flowing property as the result were found to be below 20%.

Evaluation of Controlled Release Matrix Tablet of Rasagiline Mesylate Physical Characteristic:

The physical characteristic of Rasagiline Mesylate controlled release matrix tablets (F1 to F6) such as thickness, diameter, hardness, friability, weight variation and drug content were determined and results of the formulations (F1 to F6) found to be within the limits specified in official books. (Table 6)

Appearance

The tablets were observed visually and did not show any defect such as capping, chipping and lamination.

Dimension (Thickness and Diameter)

Thickness and diameter specifications may be set on an individual product basis. Excessive variation in the tablet thickness and diameter can result in problems with packaging as well as consumer acceptance. The size (diameter) of the tablets of all formulations was found to be 3.95 to 4.02 mm.

Weight Variation Test

A tablet is designed to contain a specific amount of drug. When the average mass of the tablet is 200 mg the Pharmacopoeial limit for percentage deviation is $\pm 5\%$. The percentage deviation from average tablet weight for all the tablet was found to be within the specified limits and hence all formulations complied with the test for weight variation according to the monograph specifications

Hardness Test

A difference in tablet hardness reflects difference in tablet density and porosity, which in turn result in different release pattern of the drug by affecting the rate of penetration of dissolution fluid at the surface of the tablet and formation of gel barrier. The hardness of tablets was found to be in the range of 4.83 kg/cm^2 to 6.33 kg/cm^2 . This indicates good tablet strength.

Friability Test

Percentage friability of all the formulations was found between 0.34 to 0.64 This indicated good mechanical strength and handling property of the prepared matrix tablet.

Content Uniformity Test

The content of active ingredients in the formulation was found to be between 97.65% w/w to 98.98% w/w, which

is within the specified limit as per Indian Pharmacopoeia 1996 (i.e. 90-110% w/w).

In vitro Dissolution Studies

In vitro release behavior of all formulations is summarized Table 7 *in vitro* release was performed by using Phosphate buffer pH 6.8 as medium. The concentration of polymer in the controlled release layer was a key factor in controlling the drug release.

Various controlled release formulations were formulated with Acacia and Ethyl cellulose, Starch as binder and Magnesium Stearate and Talc as a Lubricant. The drug released from formulation F1 to F6 were found to be 96.23%, 86.25%, 92.50%, 89.37%, 81.87% and 78.12% for Rasagiline Mesylate respectively.

The release rate of F1 was found to be higher when compared to other formulations this is due to increase in the concentration of polymer. The overall release rate of Rasagiline Mesylate from Ethyl cellulose, Acacia matrices are significantly higher than that from individual polymer matrices that is shown in Fig. 8. These results indicate that the formulation having both Acacia and Ethyl cellulose are having good controlled release.

Release Kinetic Profile

The release profile of Rasagiline Mesylate from all formulations was processed into graphs (Figure 9, 10, 11 and 12) for comparison of different order of drug release and, to understand the linear relationship, i.e., kinetic principles. The data were processed for regression analysis using MS-Excel statistical functions.

For calculation, *in vitro* release data time points between (0 to 8 hrs.) were considered. The data were evaluated for Zero order, First order, Higuchi plot and Peppas plot, and slope and R^2 value obtained are as shown in the Table 12. The plots of Zero order, First order, Higuchi and Peppas are shown in Fig. 9, 10, 11 and 12 respectively.

A pre usual Fig. 9 indicates that release kinetics of Rasagiline Mesylate from all formulation seem to follow Zero order, because the values of regression coefficient obtained for zero order release profiles are higher as compared to first order, Higuchi plot and Peppas Plot.

SUMMARY AND CONCLUSION

Controlled release matrix tablets were successfully prepared by wet granulation method. Pre – formulation studies of Rasagiline Mesylate was carried out by determination of Melting point, Solubility, λ max, and FTIR. The obtained results complied with IP standards, thus indicating the purity of drug.

In vitro drug release study confirmed that the Rasagiline Mesylate controlled release matrix tablet F6 formulation has better potential of controlled drug release.

In present investigation an attempt has been made to design and develop Rasagiline Mesylate controlled release matrix tablets using Acacia and Ethyl cellulose as release retarding polymers. Rasagiline Mesylate was evaluated for its physical characteristics, analytical profiles and drug polymer compatibility studies. The granules were prepared by wet granulation method.

The active pharmaceutical ingredient of Rasagiline Mesylate was evaluated for its physical characteristics, analytical profiles and drug polymer compatibility study. The granules were prepared by wet granulation method. The prepared granules were evaluated for Angle of repose, Bulk density, Hausner's ratio, Tapped density and Carr's index. The results obtained were found to be satisfactory and within the specified limits.

After compression parameters like Thickness, Hardness, Weight variation, Friability, content uniformity and *in vitro* release studies were evaluated. In the present study the effect of types and concentration of polymer were studied on *in vitro* drug release. It shows that increase in concentration of polymer results in the controlled drug release for 8 hours. The study has revealed that by increasing concentration of polymer, release rate of drug was retarded and results confirmed that the release rate from hydrophilic matrix tablets depends on type and concentration of polymer. In present studies, matrix formulation containing Acacia and Ethyl cellulose is probably showing release up to 78.125% within 8 hrs.

In present investigation an attempt has been made to design and develop Rasagiline Mesylate controlled release matrix tablets using Acacia, and ethyl cellulose as release retarding polymers. Rasagiline Mesylate is widely used as Anti – Parkinson's drug; therefore have been selected to prepare controlled release dosage forms. This can be expected to reduce the frequency of administration and decrease the dose dependent side effects.

REFERENCE

1. Thomas LM. Formulation and evaluation of floating oral *in situ* gel of Metronidazole. *Int. J. Pharm. Pharm Sci*, 2014; 6(10): 265-269.
2. Heyn S, Davis C, Stoppler MC. Parkinson's Disease Symptoms, Causes, Stages, Treatment, and Life Expectancy. (2018 https://www.medicinenet.com/parkinsons_disease/article.htm#parkinsons_definition_and_disease_facts)
3. DeMaagd G, Philip A. Parkinson's Disease and Its Management: Part 1: Disease Entity, Risk Factors, Pathophysiology, Clinical Presentation, and Diagnosis. *Pharm. Ther*, 2015 Aug; 40(8): 504-32. PMID: 26236139; PMCID: PMC4517533.
4. Tysnes OB, Storstein A. Epidemiology of Parkinson's disease. *J. Neural Transm. Suppl*, 2017 Aug; 124(8): 901-905.
5. Belin AC, Westerlund M. Parkinson's disease: a genetic perspective. *FEBS J*, 2008 Apr; 275(7):

- 1377-1383. doi: 10.1111/j.1742-4658.2008.06301.x. Epub 2008 Feb 12. PMID: 18279377.
6. Hsieh CJ, Ferrie JJ, Xu K, Lee I, Graham TJ, Tu Z, Yu J, Dhavale D, Kotzbauer P, Petersson EJ, Mach RH. Alpha synuclein fibrils contain multiple binding sites for small molecules. *ACS chemical neuroscience*, 2018 May 11; 9(11): 2521-2527.
7. Bhat S, Acharya UR, Hagiwara Y, Dadmehr N, Adeli H. Parkinson's disease: Cause factors, measurable indicators, and early diagnosis. *Comput. Biol. Med*, 2018 Nov1; 102: 234-241.
8. DeMaagd G, Philip A. Parkinson's Disease and Its Management: Part 1: Disease Entity, Risk Factors, Pathophysiology, Clinical Presentation, and Diagnosis. *Pharm, Ther*. 2015 Aug; 40(8): 504-32. PMID: 26236139; PMCID: PMC4517533.
9. Santiago JA, Scherzer CR, Potashkin JA. Network analysis identifies SOD2 mRNA as a potential biomarker for Parkinson's disease. *PLoS One*, 2014 Oct 3; 9(10): e109042. doi: 10.1371/journal.pone.0109042. PMID: 25279756; PMCID: PMC4184821.
10. Van der Merwe C, Haylett W, Harvey J, Lombard D, Bardien S, Carr J. Factors influencing the development of early-or late-onset Parkinson's disease in a cohort of South African patients. *S. Afr. Med. J*, 2012; 102(11): 848-854.
11. Mandal UK, Chatterjee B, Senjoti FG. Gastro-retentive drug delivery systems and there *in vivo* success: A recent update. *Asian J. Pharm Sci*, 2016; 11(5): 575-584.
12. <https://www.societalcdmo.com/blog/pros-and-cons-of-matrix-vs-multiparticulate-formulations/>
13. Lieberman H.A., Lachman L. and Schwartz J.B. *Pharmaceutical Dosage Forms: Tablets Vol-I and III, Revised and Expanded, 2nded.*, Marcell Dekker, New York, 1999; 131-245, 199-213.