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Formulation Design and in Vitro Evaluation of Oral Disintegrating Tablets of Selegiline

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Keywords: selegiline, sodium starch glycolate, oral disintegrating tablet, formulation; evaluation; design;

Abstract:

In the present work, an attempt has been made to develop fast disintegrating tablets of Selegiline, were as sodium starch glycolate, cross povidone and cross carmellose sodium were employed as super disintegrating agents to enhance the solubility and dissolution rate of drug molecule. Formulations were prepared by direct compression method using 6mm punch on 8 station rotary tablet punching machine. The blend of all the formulations showed good flow properties such as angle of repose, bulk density and tapped density. The prepared tablets have shown good post compression parameters and they passed all the quality control evaluation parameters as per IP limits. Among all the formulations F2 formulation showed maximum percentage drug release i.e., 97.26 % in 45 min, hence it is considered as optimized formulation. The F2 formulation contains SSG as super disintegrate in the concentration of 24mg.

1. Introduction

Drug delivery systems (DDS) are an important tool for expanding markets, extending product life and generating opportunities (Sunil Kumar and Vijay K Sharma 2016). They make a significant contribution to global pharmaceutical sales through market segmentation, and are moving rapidly (Randale SA, 2010; P Govardhan Reddy 2017). New advances have been made in the field of drug delivery systems resulting in development of new dosage forms where in solid dosage forms have greater acceptance because of self-administration, accuracy of dose, patient compliance which make it most preferred route of administration (Gudas GK 2010).

A variety of superdisintegants such as sodium cross carmellose, cross povidone and sodium starch glycolate are used in formulating mouth disintegrating tablets. These disintegrating agents are used alone or in combination in various concentrations. The drug in saliva may be absorbed from mouth, pharynx, esophagus or stomach. Rate of absorption depends on how quickly the drug dissolves and is absorbed (R M Sarfraz et al., 2015).

Selegiline, a white to near white crystalline powder, freely soluble in water, chloroform, and methanol with a melting point of 141-142°C and a Molecular weight of 187.281 g/mol. Selegiline has a bioavailability of 50% with more than 99.5% of protein binding (Achhrish Goel et al., 2013). Excipients used in our study are as follows, Cross Carmellose Sodium, Cross Povidone, Sodium Starch Glycolate, Microcrystalline Cellulose, Magnesium Stearate and aerosil.

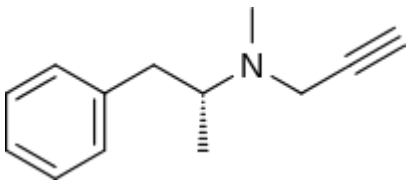

Figure 1: Chemical Structure of Selegiline, $C_{13}H_{17}N$ (Achhrish Goel et al., 2013)

2. Material and methods

Selegiline was obtained from Natco Labs. Microcrystalline cellulose was obtained from Signet Chemical Corporation, Mumbai, India. Sodium starch glycolate and Magnesium stearate were obtained from SD fine chemicalss, Mumbai, India. Cross povidone, cross carmellose sodium and aerosol were obtained from Merck Specialities Pvt Ltd, Mumbai, India.

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2.1 Determination of absorption maximum (λ_{max})

Selegiline (10mg) was weighed accurately and transferred to 100 ml volumetric flask, it was dissolved in phosphate buffer pH 6.8 and the final volume was made up to 100 ml with phosphate buffer and pH was adjusted to 6.8 to get a stock solution (100µg/ml). From the stock solution, 1 ml was pipette out in 10 ml volumetric flask and the final volume was made up to 10ml with phosphate buffer PH 6.8 to get 10µg/ml. This solution was scanned at 200-400nm in UV-Visible double beam spectrophotometer (UV-3200, Labindia, India) to get the absorption maxima (λ_{max}).

2.1.1 Construction of Selegiline calibration curve with phosphate buffer pH 6.8

100mg of Selegiline was dissolved in 100ml of phosphate buffer pH 6.8 to give a concentration of 1mg/ml (1000µgm/ml). From the above standard solution (1000µgm/ml) 10 ml was taken and diluted to 100ml with phosphate buffer pH 6.8 to give a concentration of 100µgm/ml. From this stock solution aliquots of 0.2, 0.4, 0.6, 0.8 and 1ml were pipette out in 10ml volumetric flask and the volume was made up to the mark with phosphate buffer PH 6.8 to produce concentration of 2, 4, 6, 8 and 10 µgm/ml respectively. The absorbance (abs) of each conc. was measured at respective (λ_{max}) i.e., 258 nm.

2.2 Drug-excipient compatibility studies by FT-IR

The compatibility between the pure drug and excipients was detected by FTIR spectra obtained on Bruker FTIR Germany (Alpha T). The potassium bromide pellets were prepared on KBr press by grounding the solid powder sample with 100 times the quantity of KBr in a mortar. The finely grounded powder was then introduced into a stainless steel die and was compressed between polished steel anvils at a pressure of about 8t/in^2. The spectra were recorded over the wave number of 8000 to 400cm^{-1}.

2.3 Flow properties

Various flow properties have been studied such as angle of repose, loose bulk density, tapped density, carr's consolidation index and hausner's ratio (Addanki Gopikrishna et al., 2016).

2.4 Formulation of Oro dispersible tablets of Selegiline

2.4.1 Preparation of tablets:

Composition of Selegiline oro dispersible tablet by direct compression. All the ingredients were weighed. Required quantity of drug and excipients were mixed thoroughly in a polybag. The blend is compressed using rotary tablet machine-8 station with 8mm flat punch, B tooling. Each tablet contains 50mg Selegiline and other pharmaceutical ingredients. Total weight of tablet was found to be 120 mg.

Table 1: Composition of various tablet formulations

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9
Selegiline (mg)	6	6	6	6	6	6	6	6	6
Sodium Starch Glycollate (mg)	12	24	-	-	-	-	12	-	12
Cross Carmellose Sodium (mg)	-	-	12	24	-	-	12	12	-
Cross Povidone (mg)	-	-	-	-	12	24	-	12	12
Magnesium Stearate(mg)	3.6	3.6	3.6	3.6	3.6	3.6	3.6	3.6	3.6
Aerosil(mg)	3.6	3.6	3.6	3.6	3.6	3.6	3.6	3.6	3.6
MCC(mg)	Qs	Qs	Qs	Qs	Qs	Qs	Qs	Qs	Qs
Total wt(mg)	120	120	120	120	120	120	120	120	120

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2.5 Post compression parameters

Various post compression parameters have been studied such as shape and colour, uniformity of thickness, hardness test, friability test, weight variation test and drug content estimation (Rama Rao et al., 2016).

2.6 In -vitro dissolution studies:

In-vitro studies were carried out using modified USP XXIII dissolution test apparatus (Lab India, DS-800).

The dissolution fluid-500ml of phosphate buffer pH 6.8 at a speed of 50rpm and at a temperature of 37^0c was used in each test. Samples of dissolution medium (5ml) were withdrawn every 2min and assayed for Selegiline by measuring absorbance at 258 nm. For all tests 5ml of the test medium were collected at specified time intervals and replaced with same volume of phosphate buffer pH 6.8 (Sahitha Roopa A et al., 2014).

Details:

Apparatus used	:	modified USP XXIII Lab India DS 800
Dissolution medium	:	Phosphate buffer PH 6.8
Dissolution medium volume	:	500 ml
Temperature	:	37^0C
Speed of paddle	:	50 rpm
Sampling intervals	:	5, 10, 15, 20, 25, 30, 35, 40 and 45 min
Sample withdrawn	:	5ml
Absorbance measured	:	258 nm
Beers Range	:	2-10 µg/ml

3. Results

3.1 Standard Calibration curve of Selegiline

It was found that estimation of Selegiline had good reproducibility by UV spectrophotometric method at λ_{max} 221nm in phosphate buffer pH 6.8, hence this method was used in the study. The correlation coefficient for the standard curve was found to be closer to 1, at the concentration range, 2- 10µg/ml. The regression equation generated was y = 0.049x + 0.009, R^2 = 0.998.

3.2 Pre-compression parameters

The data is shown in Table 3. The values for angle of repose were found in the range of 25-30. Bulk densities and tapped densities of various formulations were found to be in the range of 0.41 to 0.49 (gm/cc) and 0.50 to 0.57 (gm/cc) respectively. Carr's index of the prepared blends fall in the range of 13% to 18%. The Hausner ratio fall in range of 1.12 to 1.20. From the result it was concluded that the powder blends had good flow properties and these can be used for tablet manufacturing.

3.3 Post compression Parameters

3.3.1 Weight variation test

Tablets of each batch were subjected to weight variation test, difference in weight and percent deviation was calculated for each tablet and was shown in the Table 4. The average weight of the tablet is in range of 127 to 118.5mg, so the permissible limit is ±10%. The results of the test showed that the tablet weights are within the pharmacopoeia limit.

3.3.2 Hardness test

Hardness of the three tablets of each batch was checked by using Monsanto hardness tester and the data were shown in Table 4. The results showed that the hardness of the tablets is in range of 2.5 to 3.00 kg/cm^2, which was within IP limits.

3.3.3 Thickness

Thickness of three tablets of each batch was checked by using Vernier Caliper and data shown in Table 4.The result showed that thickness of the tablet is raging from 3.54 to 3.67.

3.3.4 Friability

Tablets of each batch were evaluated for percentage friability and the data was represented in the Table 4. The average friability of all the formulations lies in the range of 0.34 to 0.49% which was less than 1% as per official requirement of IP indicating a good mechanical resistance of tablets.

3.3.5 In vitro disintegration time

Tablets of each batch were evaluated for in vitro disintegration time and the data was shown in the Table 4. The results showed that the disintegration time of prepared tablets were in the range of 16.76 to 28.63 seconds.

Assay:

Assay studies were performed for the prepared formulations. From the assay studies it was concluded that all the formulations were showing the % drug content values within 97.23 -99.2%.

3.4 Invitro Dissolution studies

Invitro dissolution studies were carried out by using 500ml of pH 6.8 phosphate buffer in USP dissolution apparatus by using paddle method. The dissolution studies were carried out for about 30 min.

From the Table 5 it was evident that the formulations prepared with super disintegrate SSG showed maximum % drug release in 45 min i.e.97.26% (F2 formulations and the concentration of super disintegrate was 24 mg). So the principle of super disintegrates was found to be useful to produce oro dispersible tablets. F2 formulation was considered as optimized formulation. The formulation followed zero order release mechanism. As the time increases the percentage drug release was increased.

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Table 2: Concentration and absorbance obtained for calibration curve of Selegiline in pH 6.8 Phosphate buffer

S. No.	Concentration (µg/ml)	Absorbance* (at 221 nm)
1	2	0.107
2	4	0.215
3	6	0.299
4	8	0.402
5	10	0.507

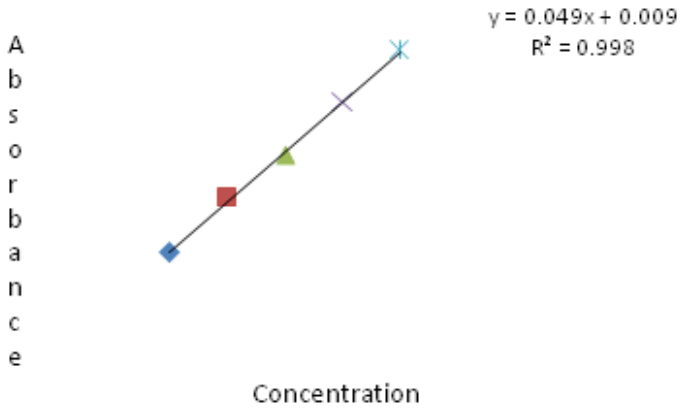

Figure 2: Standard graph of Selegiline in pH 6.8 phosphate buffer

Table 3: Pre-compression parameters

Formulations	Bulk Density (gm/cm^2)	Tap Density (gm/cm^2)	Carr's Index (%)	Hausner ratio	Angle Of Repose(Θ)
F_1	0.41	0.51	17.68	1.18	26.89
F_2	0.43	0.53	16.54	1.20	25.09
F_3	0.48	0.57	13.76	1.12	28.43
F_4	0.46	0.51	16.36	1.16	27.81
F_5	0.47	0.57	13.78	1.18	29.54
F_6	0.42	0.54	14.54	1.19	26.23
F_7	0.49	0.52	13.98	1.12	29.54
F_8	0.42	0.51	17	1.20	27.78
F_9	0.43	0.53	17.50	1.18	26.58

Table 4: Post compression parameters

Formulation code	Weight variation (mg)	Hardness (kg/cm^2)	Thickness (mm)	Disintegration Time (sec)	Friability (%)	Assay (%)
F1	120	2.6	3.55	17.84	0.48	97.23
F2	124	2.5	3.66	16.76	0.36	98.54
F3	119	2.5	3.54	28.63	0.49	98.12
F4	121	2.7	3.58	16.00	0.47	99.35
F5	122	2.7	3.59	30.33	0.49	98.23
F6	123	2.9	3.67	22.66	0.34	98.58
F7	122	2.5	3.58	19.87	0.49	98.17
F8	120	2.6	3.59	17.00	0.37	99.22
F9	122	2.5	3.59	23.94	0.34	99.21

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Table 5: Invitro dissolution studies of all formulations

TIME (min)	% drug release of F1	% drug release of F2	% drug release of F3	% drug release of F4	% drug release of F5	% drug release of F6	% drug release of F7	% drug release of F8	% drug release of F9
0	0	0	0	0	0	0	0	0	0
5	18.8	28.94	16.1	14.47	29.42	26.56	16.14	11.12	16.4
10	24.87	37.88	29.74	24.89	32.05	34.92	27.35	33.45	26.7
15	36.12	48.2	30.56	32.11	44.1	44.52	30.73	45.62	34.6
20	45.25	55.45	48.29	41.82	51.25	54.85	45.24	58.73	42.4
25	51.24	69.52	57.1	56.01	63.33	67.21	51.27	62.64	55.4
30	57.35	71.53	65.25	67.35	69.24	70.05	57.83	70.43	67.4
35	62.17	87.37	70.32	76.25	70.01	74.16	62.19	76.21	76.13
40	68.65	90.12	76.25	80.24	76.45	79.61	67.02	81.26	79.17
45	71.26	97.26	79.23	85.16	84.29	82.83	72.01	89.75	85.26

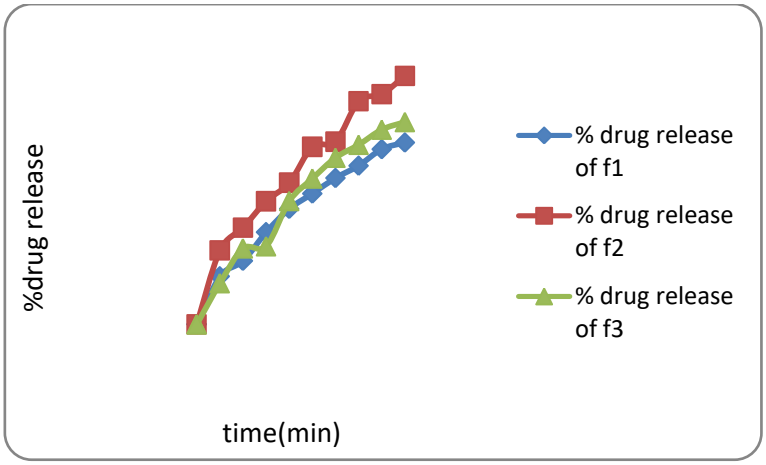

Figure 3: Dissolution profile of formulations prepared with Sodium starch Glycolate as super disintegrate

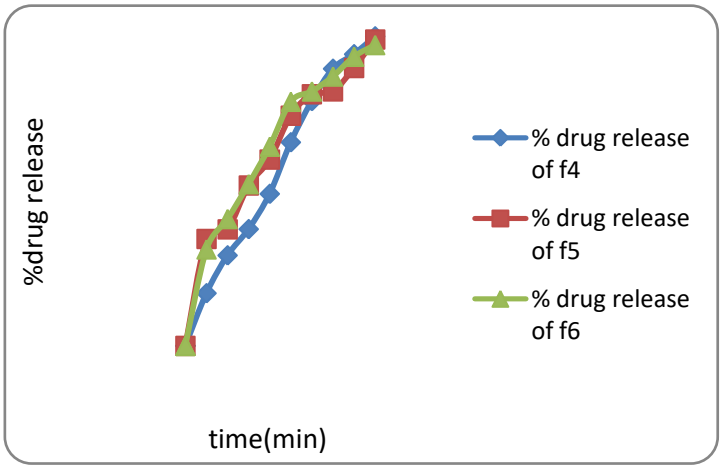

Figure 4: Dissolution profile of formulations prepared with Cross caramellose sodium as super disintegrate

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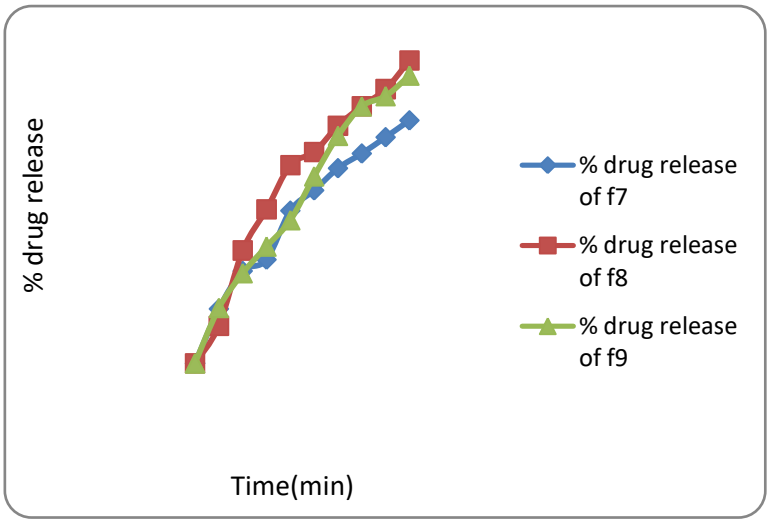

Figure 5: Dissolution profile of formulations prepared with Cross povidone

4. Conclusion

In the present work, an attempt has been made to develop fast disintegrating tablets of Selegiline. Here sodium starch glycolate, cross povidone and cross carmellose sodium were employed as super disintegrating agents to enhance the solubility and dissolution rate of selected drug molecule. All the formulations were prepared by direct compression method using 6mm punch on 8 station rotary tablet punching machine. The blend of all the formulations showed good flow properties such as angle of repose, bulk density, tapped density. The prepared tablets were shown good post compression parameters and they passed all the quality control evaluation parameters as per I.P limits. Among all the formulations F2 formulation showed maximum % drug release i.e., 97.26 % in 45 min, hence it is considered as optimized formulation. The F2 formulation contains SSG as super disintegrate in the concentration of 24 mg.

Conflict of interest

None declared

5. References

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