Formulation and Evaluation of Selegiline Nanoparticles

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Abstract

Due to its reproducibility and ease in formulation, the controlled drug release system is one of the most popular methods of novel drug delivery. Controlling drug release with nanotechnology helps to enhance the medicine's pharmacokinetic and pharmacodynamic parameters.By lowering the dose and frequency of administration and limiting both the local and systemic harmful effects, the approach increases patient compliance. The current study project's objective was to create and assess Selegiline nanoparticles, an anti-Parkinson drug, utilizing the emulsion solvent evaporation process.Selegiline has a very short half-life of 1.5-3.5 hour with bioavailability oral 10%. Sustained release nanoparticles of Selegiline were prepared to increase the drug residence time in gastrointestinal tract and thus improving the bioavailability of drug.According to the findings, formulation F9, which uses a combination of polymers and contains Selegiline nanoparticles, evolved as the best formulation and releases more than 98.9% of the drug in 20 hours.There are no drug-excipient interactions in the improved formulation, according to IR spectroscopic measurements. The improved formulation F9 is a potential Sustained ReleaseSelegiline nanoparticles are a medication delivery method that offers almost zero order drug release over the course of 24 hours.

Keywords: Formulation, Evaluation, Selegiline, Nanoparticles.

1. INTRODUCTION

Nanoparticles are defined as particulate dispersions or solid particles with a size in the range of 10-1000nm. The drug is dissolved, entrapped, encapsulated or attached to a nanoparticle matrix. Depending upon the method of preparation, nanoparticles, nanoparticles or nanocapsules can be obtained. Nanocapsules are systems in which the drug is confined to a cavity surrounded by a unique polymer membrane, while nanoparticles are matrix systems in which the drug is physically and uniformly dispersed. In recent years, biodegradable polymeric nanoparticles, particularly those coated with hydrophilic polymer such as poly(ethylene glycol) (PEG) known as long-circulating particles, have been used as potential drug delivery devices because of their ability to circulate for a prolonged period time target a particular organ, as carriers of DNA in gene therapy, and their ability to deliver proteins, peptides and genes.

ADVANTAGES:

1. Particle size and surface characteristics of nanoparticles can be easily manipulated to achieve both passive and active drug targeting after parenteral administration

2. They control and sustain release of the drug during the transportation and at the site of localization, altering organ distribution of the drug and subsequent clearance of the drug so as to achieve increase in drug therapeutic efficacy and reduction in side effects.
3. Controlled release and particle degradation characteristics can be readily modulated by the choice of matrix constituents.
4. Site-specific targeting can be achieved by attaching targeting ligands to surface of particles or use of magnetic guidance.
5. The system can be used for various routes of administration including oral, nasal, parenteral, intra-ocular etc.

LIMITATIONS:

- Their small size and large surface area can lead to particle-particle aggregation,
- Making physical handling of nanoparticles difficult in liquid and dry forms.
- Small particles size and large surface area

readily result in limited drug loading and burst release.

Preparation of Nanoparticles

Nanoparticles can be prepared from a variety of materials such as proteins, polysaccharides and synthetic polymers. The selection of matrix materials is dependent on many factors including[7]:

(a) size of nanoparticles required;
(b) inherent properties of the drug, e.g., aqueous solubility and stability;
(c) surface characteristics such as charge and permeability;
(d) degree of biodegradability, biocompatibility and toxicity;
(e) Drug release profile desired;
(f) Antigenicity of the final product.

Nanoparticles have been prepared most frequency by three methods: (1) dispersion of preformed polymers; (2) polymerization of monomers; and (3) ionic gelation or coacervation of hydrophilic polymers.

MATERIALS AND METHODS:

Selegiline was purchased from yarrow chemicals, Mumbai, HPMC K_4M HPMC K_{100} Ethyl cellulose, Dichloromethane, Methanol 2% SLS are provided by CMR College of pharmacy

PREPARATION METHOD

Utilizing a variety of polymers, emulsion followed by solvent evaporation was employed to create Selegiline drug nanoparticles.

Making the polymer and medication solution:

1. Placed the necessary amount of polymer in a dry beaker after weighing it.
2. Methanol, the required solvent, was measured out into a cylinder.
3. Methanol was now gradually added to the beaker containing the polymer.
4. To create the polymer solution, it was continually agitated with a glass rod.
5. Add precisely measured amounts of Selegiline 3 mg, and carefully combine.

Making an aqueous solution

One gramme of SLS was added to one thousand millilitres of water as needed, and the mixture was then set aside to remove air bubbles.

SIMPLE MIXING:

As a successful method for creating nanodrugs, emulsion followed by solvent evaporation was used to create Selegilinenanoparticles. Polymers were first dissolved in chloroform, followed by the addition of 10 mg of the drug Selegiline, which was thoroughly mixed into the polymer solution. Next, 1% SLS solution was added to the mixture, which was then stirred continuously for 20 minutes at 400-500 rpm. Finally, the beaker was placed in a probe sonicator for 15 minutes. Nanoparticles formed right away after mixing.

Ingredients	Formulation code								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
Selegiline (mg)	3	3	3	3	3	3	3	3	3
HPMC K4M (mg)	75	150	225	-	-	-	75	150	225
HPMC K 100 (mg)	-	-	-	75	150	225	75	150	225
Ethyl cellulose (mg)	75	150	225	75	150	225	-	-	-
Dichloromethane (ml)	10	10	10	10	10	10	10	10	10
Methanol (ml)	10	10	10	10	10	10	10	10	10
2% SLS (ml)	50	50	50	50	50	50	50	50	50

Table 1: Formulation code for ingredients

Characterization of Nanoparticles

1. Assay

3 mg of Selegiline (manufactured nano crystals) should be precisely weighed. It should then be dissolved in 40 ml of methanol and titrated with 0.1 mol/L sodium hydroxide VS (potentiometric titration, Endpoint Detection Method in Titrimetry).

Each mL of sodium hydroxide at 0.1 mol/L VS equals 35.419 milligrammes of $C_{16}H_{13}Cl_2NO_4$.

When dried, lactidipine has a concentration of 99.0% to 101.0% lactidipine.

2. Modified Dissolution Test:

The open cut boiling tube containing 25mL of the nanoparticle solution and the beaker containing 100mL of the 1% sodium lauryl sulphate (SLS) solution in distilled water were used for the in vitro dissolution investigations. The studies lasted for 24 hours. The temperature of the water bath in which the dissolving medium was kept was thermostatically controlled at 37 0.05 °C. 50 rpm was chosen as the basket rotation speed. 3 ml samples were taken out at regular intervals and examined spectrophotometrically at 275 nm for the drug release. To keep the sink condition, 3 ml of new matching media were added to the dissolution flask each time a sample was withdrawn.

3. FT-IR Spectroscopy:

To identify any potential interactions between medications and the polymers or excipients, IR spectral matching experiments are used. FT-IR was used to assess the medicine Selegiline's compatibility with various polymers in the present (PERKIN ELMER FT-I Insf. USA). . The samples were scanned using an FT-IR spectrophotometer with a range of 4000 to 400 cm-1. Similar to that, all of the individual drugs and created nanocrystals had their IR spectra recorded. To look for any potential physical and chemical interactions, the samples' outward appearance as well as the presence or removal of peaks in the spectra were observed.

4. Scanning Electron Microscopy (SEM):

The particle morphology of the unprocessed drug as well as the manufactured drug nanoparticles was studied using scanning electron microscopy. A small portion of each drug powder sample was glued to a double-sided carbon conductive tape and sputtered with a Pt-Pd alloy coating measuring 5 nm. On a Zeiss DSM 982 Field Emission Gun Scanning Electron Microscope, micrographs were taken (Carl Zeiss AG, Germany).

5.Particle size distribution:

Immediately following precipitation, the size of drug nanoparticles was determined using dynamic laser light scattering (Nanoparticle size analyzer, Malvern). Purified water was used to dilute the drug suspension to 0.2 mg/ml prior to analysis. The outcomes of the particle size study were interpreted using the graphic mean size (Mz) and computed surface area (Cs).

6. Differential scanning calorimetry (DSC) measurement:

Using a DSC-41 instrument, the thermal characteristics of the lyophilized powder samples were studied (Shimadzu, Japan). Each lyophilized powder sample had its scanning temperature adjusted between 25 and 200 °C with a heating rate of 10 °C/min. In an open aluminium pan, 10 mg of each sample were examined, and magnesium served as the standard. Thermal analysis was done on Selegiline and the excipients to assess the internal structure changes following the nanosizing process.

7.Zeta potential

Zeta sizer was used to assess the nanoparticles' size, size distribution, and zeta potential (ZS 90 malvrn). The lyophilized materials were diluted with PBS to a pH of 6.0 on mg/ml and 67 mm before being tested. These samples were stored in another clean cubet during the size analysis process before being placed on the zeta size analysis chamber to obtain distinct peaks and then determine its average zeta size. Surface charge potential or zeta potential samples were kept in the zeta sizer analysis chamber on for analysis and watched for its peak to obtain zeta potential data. When analysing these data, monodisperse rather than polydisperse character is always taken into account.

RESULTS AND DISCUSSION

Characterization of Pharmaceutical Active Ingredients was carried out.

Characterization of API (appearance, identification test by FTIR, assay) was carried out in preformulation investigations, and it was discovered that all fall within the parameters set forth in the pharmacopoeia.

Description	Specifications	Observations
Appearance	White Crystalline powder	White

Identification	FTIR	Complies
Assay	Not less than 99.0% w/w and not more than 101.0% w/w of Carvedilol	99.97%w/w

Table 2: Characterization of active medicinal component

Standard curve for lacedipine in 0.1% SLS solution

Selegiline's standard graph was created using 0.1% SLS. Concentrations ranging from 2 to 10 g/ml were made. At 301 nm, the absorbance of the produced concentrations was measured after being calibrated with a blank sample. Concentration and absorbance were shown on a graph, and the best fit line, regression value, and equation were constructed to describe the data.

Concentration (µg/ml)	absorbance
0	0
4	0.2
8	0.39
12	0.55
16	0.72
20	0.89

Table 3: Concentration and Absorbance values for standard curve for selegiline

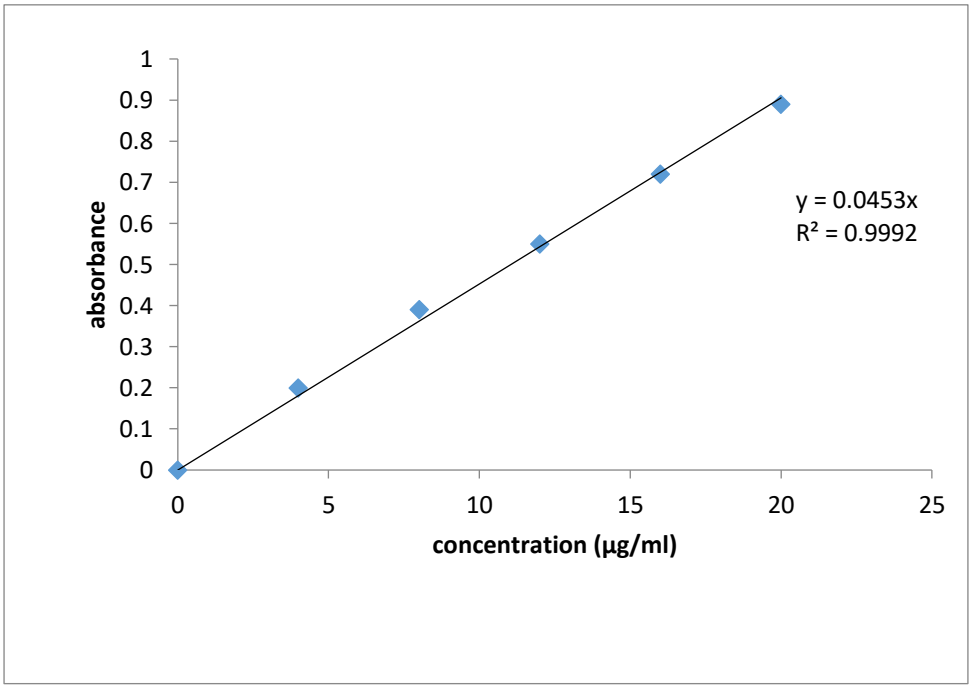


Figure 1: calibration graph for standard curve

Evaluation of nano particles:

Formulation code	Particle size (nm)	% yield	Entrapment efficiency	Drug content
F1	200.5	98.5	77.8	298.5
F2	210.2	80.7	87.5	297.8
F3	246.7	79.5	97.6	298.2
F4	198.2	96.2	75.2	298.0
F5	205.3	87.5	80.2	298.2
F6	226.7	79.8	91.8	297.4
F7	197.2	98.8	77.4	298.4
F8	220.2	84.2	83.4	296.3
F9	245.3	75.8	95.2	295.5

Table 4: Evaluation results of selegiline nanoparticles

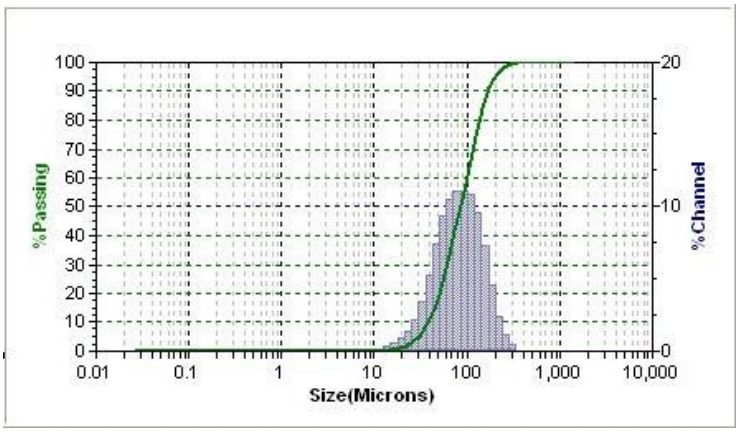


Figure 2: Particle size distribution curve for nanoparticles

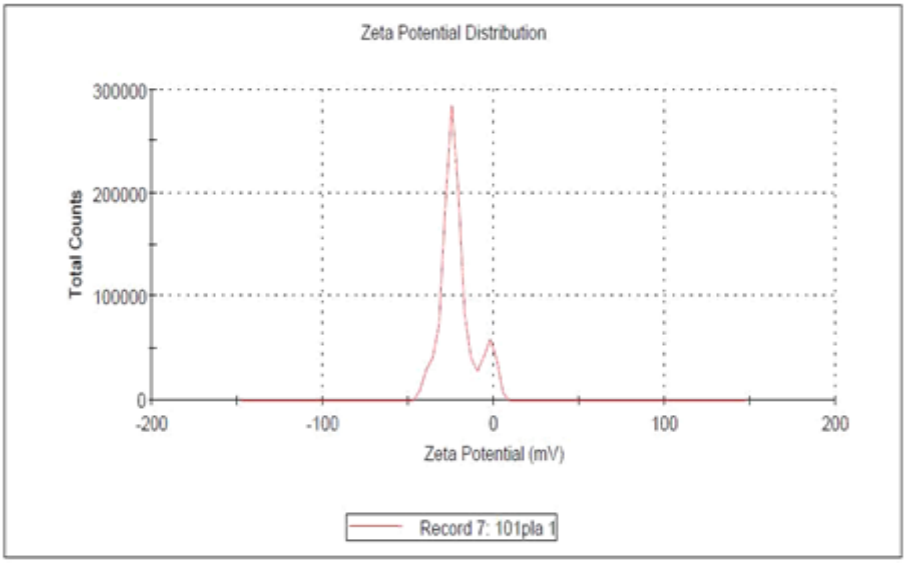


Figure 3: Zeta potential distribution for nano particles

***In-vitro* dissolution study:**

Time (hr)	% drug release								
	Formulation code								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
1	15.2	12.5	10.8	20.8	17.8	15.2	25.4	22.8	9.5
2	38.9	25.9	21.6	28.9	25.9	21.8	38.9	30.2	17.8
4	46.4	34.5	30.8	35.4	31.8	29.6	46.2	42.7	28.3
6	54.8	46.4	42.7	48.9	43.6	40.9	54.8	51.8	39.4
8	68.9	58.5	55.8	56.1	50.7	49.4	61.7	59.7	47.5
10	82.5	67.5	63.7	69.8	59.8	56.8	76.8	71.5	54.5
12	96.7	85.4	81.6	84.7	76.8	71.2	89.5	85.3	67.6
14	-	94.8	90.8	96.8	87.8	83.5	97.6	94.5	79.7
16	-	-	96.2	-	95.5	93.7	-	97.8	87.2
20	-	-	-	-	-	-	-	-	98.9

Table 5: Formulation code for *in vitro* dissolution studies

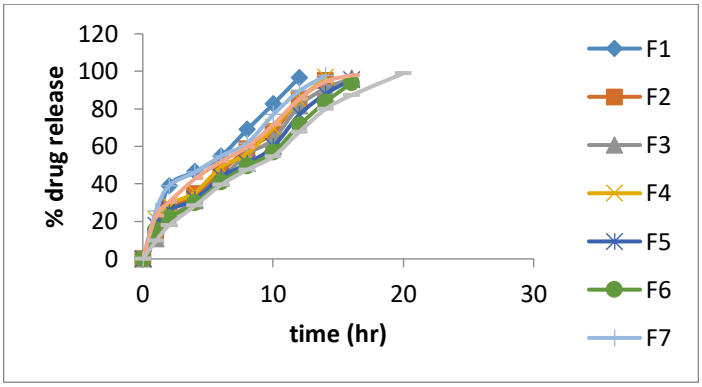


Figure 4: Dissolution studies spectra of selegiline

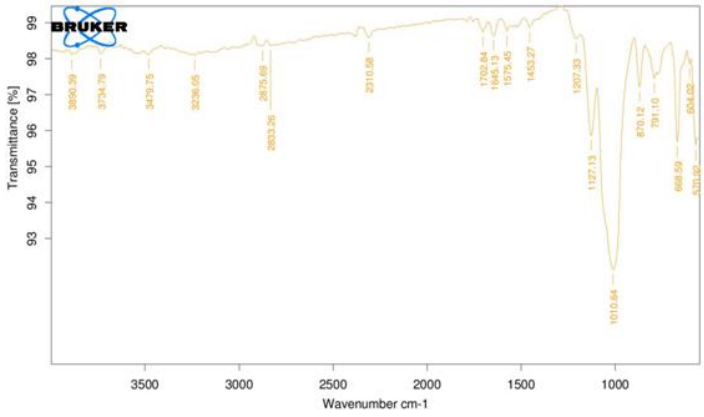


Figure 5: FTIR Spectra For Selegiline

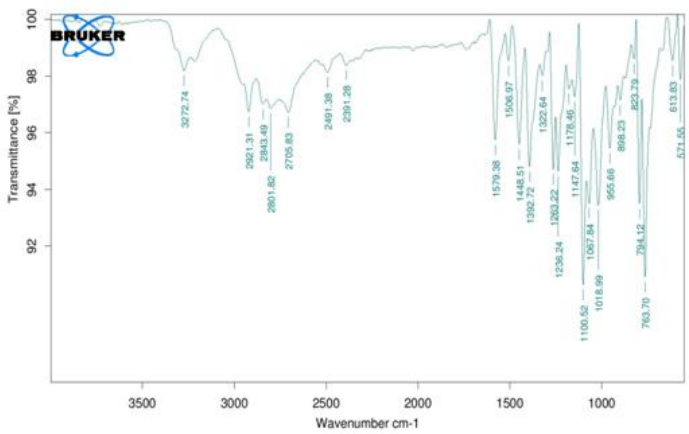
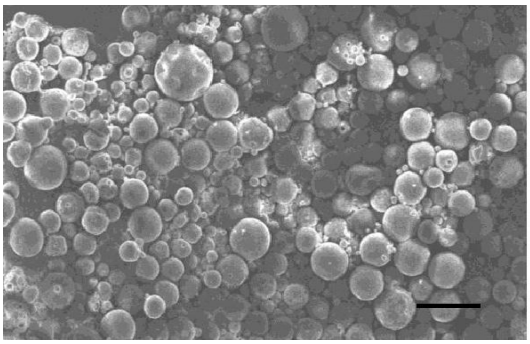


Figure 6: FTIR Spectra For Selegiline and Polymers

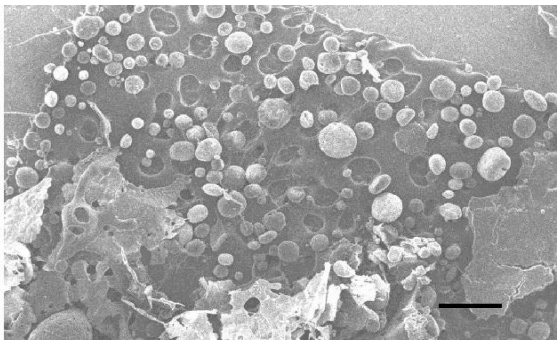
Morphology

Utilizing a scanning electron microscope, the shape of these Selegilinenano particles was determined to be spherical structures (SEM). The particles have rough and rounded surfaces. According to reports, the ratio of the polymer grew along with the tendency for the pores' relative diameters to grow (Nayak et al., 2009).



1 µm

Figure 7: Surface structure of Selegiline with GMS(80mg)



1 µm

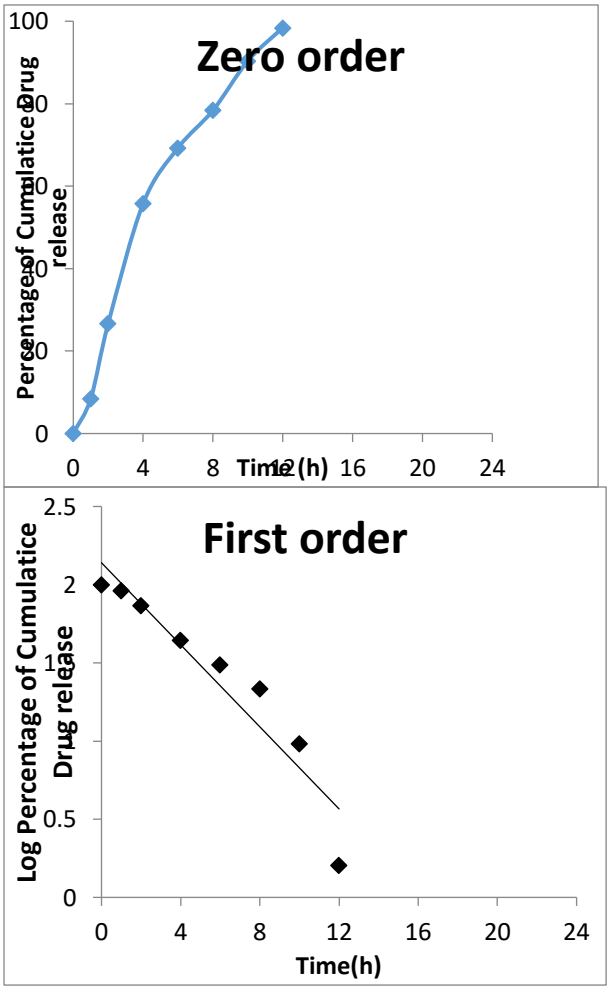
Figure 8: Surface structure of Selegiline with GMS(100mg)

KINETIC ANALYSIS OF DISSOLUTION DATA:

The in-vitro release data was fitted into different release equations and kinetic models, including zero order, first order, Higuchi and KorsmeyerPeppasmodel, to analyse the drug release mechanism. The release kinetics of the optimised formulation is displayed in TABLE.

Formulation code	Zero order	First order	Higuchi	Peppas	
	R2	R2	R2	R2	n
F9	0.99	0.8	0.96	0.99	0.8

Table 6: kinetic analysis of dissolution data



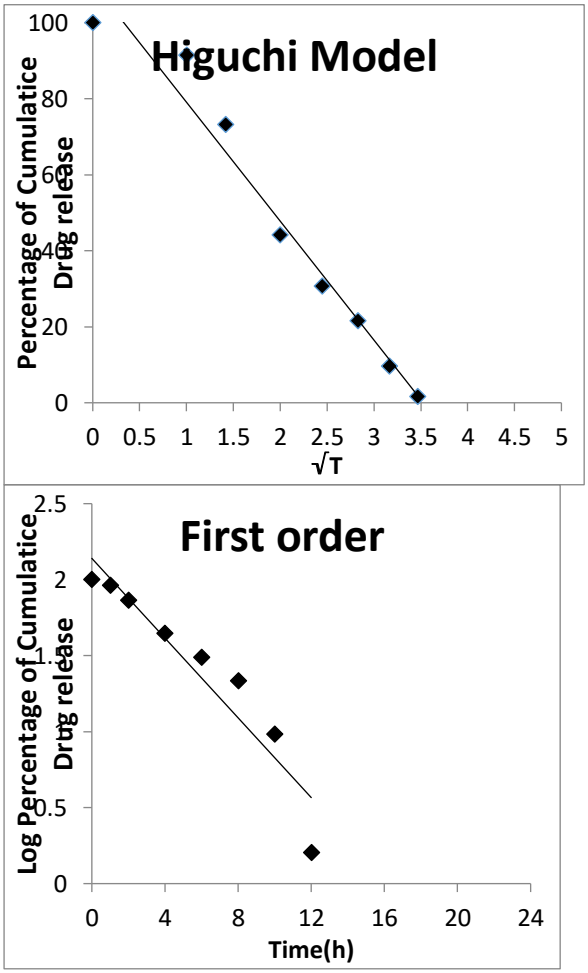


Figure 9: Graphs on kinetic analysis of dissolution data

Stability Studies

After three months, there was no discernible change in the physical or chemical characteristics of the tablets of formulation F-9. The parameters that were quantified at different times were displayed.

S.NO	Parameters	Initial	1 month	2 month	3 month	Limits as per specification
1	40^0C/75% RH % Release	98.9	98.52	97.79	96.56	Not less than 85 %
2	40^0C/75% RH Assay Value	98.9	97.96	96.22	96.00	Not less than 90 % Not more than 110 %

Table 7.Results of stability studies of optimized formulation F-9

Discussion

The goal of the current work was to create Selegiline-solid lipid nanoparticles.

Solid lipid nanoparticles:

GMS, Chitosan, PEG6000 SLN, and other additives were made using a variety of polymers. The

preparation of the nanoparticles was done using the solvent evaporation method. Nine formulations in total were created and assessed.

Particle Size Analysis:

The presence of stabiliser has an effect on particle size, according to the particle size study for the Selegilinefabricated nanoparticles utilising different polymers. The results of the particle size study were interpreted using the graphic mean (Mz) and computed surface area (Cs). While it includes the median value, Graphic Mean provides a different and potentially better control value since both small particles and large particles are included in the calculation. This results in a mean particle size that is less coarse-particle weighted than the mean diameter of the volume distribution. When GMS (F3) was utilised at 10%, smaller graphic mean (Mz) values suggesting smaller particles were discovered.The greatest Mz value for formulation F7 (275 nm) was discovered, indicating larger particles. The polymer concentration was shown to affect particle size. The particle size was reduced when the concentration of the majority of the investigated polymers was raised from 6 to 10%.

***In vitro* dissolution:**

Using a modified dissolving method apparatus and a solvent solution containing 0.1% SLS, in vitro dissolution investigations are carried out on prepared nanoparticles. It was discovered that the dissolving rate increased linearly with polymer concentration. The best formulations are (F9), and in 24 hours, the formulation recorded 98.9 percent of the medication.

Drug Release Kinetics:

To determine the mechanism of drug release, in vitro drug release data from all Sustained formulations was subjected to a goodness of fit test by linear regression analysis in accordance with zero order and first order kinetic equations, Higuchi's, and Korsmeyer-models. Peppa'sAs can be observed from the data above, all of the formulations showed first order release kinetics ('r' values between 0.900 and 0.965). According to Higuchi and Peppas' study, the medication is delivered through a non-fickian diffusion process (n = 0.5).It is clear from the factorial formulations kinetic data that the F9 formulation exhibits zero order kinetic drug release. The r values for Higuchi's formulation equation. This information demonstrates that the Higuchi model of non-Fickiandiffusion governs drug release.

Conclusion

Success of the in vitro drug release experiments suggests the product be used in future in vivo research, which might increase patient compliance. According to the findings, formulation F9, which uses a combination of polymers and contains Selegiline nanoparticles, evolved as the best formulation and releases more than 98.9% of the drug in 20 hours.

There are no drug-excipient interactions in the improved formulation, according to IR spectroscopic measurements. The improved formulation F9 is a potential Sustained Release

Selegiline nanoparticles are a medication delivery method that offers almost zero order drug release over the course of 24 hours.

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