Innovare Academic Sciences

International Journal of Pharmacy and Pharmaceutical Sciences

ISSN- 0975-1491 Vol 7, Issue 11, 2015

Original Article

KINETIC MODELING OF RASAGILINE MESYLATE FROM NANOSCALE SOLID LIPID PARTICLES

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Received: 23 Aug 2015 Revised and Accepted: 03 Oct 2015

ABSTRACT

Objective: The present study is aimed to investigate the *In-vitro* release behavior of the Rasagiline mesylate loaded nanoscale solid lipid particles to provide the quality based controlled release system.

Methods: The Rasagiline mesylate loaded Nanoscale particles prepared using the microemulsion technique with biodegradable and biocompatible lipid (stearic acid), surfactant (polyethylene-polypropylene glycol) and co-surfactant (polyoxyethylene20 sorbitanmonooleate). The prepared nanoscale solid lipid particles, particle size distribution, polydispersity index, zeta potential, entrapment efficiency, drug loading and drug content were characterized. The fabricated particles surface morphology was examined by transmission electron microscope. *In-vitro* release of Rasagiline mesylate loaded nanoscale solid lipid particles was studied using conical flask method. Release kinetics of Rasagiline mesylate from nanoscale solid lipid particles were studied using mathematical models.

Results: The resulting Rasagiline mesylate loaded nanoscale solid lipid particles were successfully prepared with optimum particle size distribution, polydispersity index, zeta potential, entrapment efficiency, drug loading and drug content. Statistically significant differences were found among the drug release profile from RMSLN-I and RMSLN-II. Applying kinetic mathematical models, the mechanism of Rasagiline mesylate loaded nanoscale solid lipid particles release from the two formulations were found to be followed higuchi model, as the plots showed high linearity, with a correlation coefficient (R^2) value of 0.98 or more. The 'n' value of korsmeyer-Peppas model lies below 0.5 and the mechanism controlling the drug release was Fickian diffusion.

Conclusion: The prepared Rasagiline mesylate loaded nanoscale solid lipid particles controlling the drug delivery through diffusion dominated mechanism.

Keywords: Nanoscale solid lipid particles, Nanoparticle release, Kinetic models, Model dependent method.

INTRODUCTION

In-vitro release kinetics of the active medicament from nanoscale solid lipid particles are providing valuable insight on the time course of drug release. It can be controlled by the structure (e. g., porosity) and fabrication technique of the particles, the molecular mass, polymer degradation and physicochemical properties of the entrapped drug molecule [1, 2]. *In-vitro* release studies are more directly assessing the product performance than does conventional human pharmacokinetics *In-vivo* bio equivalence studies [3]. The drug loaded nanoscale solid lipid particles *In-Vitro* release studies are performed to achieve the following objectives. a) As an indirect measurement of drug absorption, especially in the early stage of product development, b) Repetitive assessment of quality control to support batch release, c) Establishing an *in-vitro in-vivo* correlation/relationship,(d) Validating the product label claims and (e) as a compendial requirement[4, 5]. The fabricated nanoscale solid lipid particles do not have any regulatory standards to predict *In-vitro* drug release studies. The researcher has been implemented numerous techniques to study the *In-Vitro* drug release from drug loaded nanoscale solid lipid particles, includes an incubator shaking method, dialysis bag method, glass basket dialysis method and franz diffusion cell. In the midst of these methods, we have chosen dialysis bag method to study the fabricated Rasagiline mesylate loaded solid lipid particles release profile [6-8]. The kinetics of drug release from controlled release formulation was investigated by using mathematical models, includes zero order, first order, higuchi model and korsmeyer-peppas model [9-11].

In the present study, the selective, irreversible monoamine oxidase (MAO) B inhibitor of Rasagiline (N-Propargyl-1-R-aminoindan) mesylate (RM) was used as a model drug [12, 13]. Rasagiline mesylate was approved for the treatment of Parkinson disease by European drug regulatory authorities in 2005 and by the US FDA in 2006 [14]. The hydrophilic nature of Rasagiline mesylate drug delivery into the brain is highly restricted by the blood brain barrier, the aim being to convey a sufficient dose of Rasagiline mesylate in the brain [15]. To rise above this obstruction, nanoscale solid lipid particles were chosen for the delivery of drugs into the brain in a sustained period of time. Nanoscale solid lipid particles are possessed distinct merits and tremendous tolerability compared with liposomes and polymeric nanoparticles. Several techniques for nanoscale solid lipid particle preparation exist. Among those techniques, we have elected "Micro emulsion" technique, which is thermodynamically stable, most convenient and cost-effective technique to prepare drug loaded nanoscale solid lipid particles [16].

Nanoscale solid lipid particles are developed by using biodegradable and biocompatible lipid (stearicacid), Surfactant (polyethylene-polypropylene glycol) andco-surfactant (polyoxyethylene20 sorbitanmonooleate). Stearic acid is an endogenous saturated fatty acid found in an animal and plant sources, providing better biocompatibility and low toxicity. The melting point of stearic acid is higher than body temperature.

So, it can be compatible with human tissues and neutral with respect to physiological fluids [17, 18]. The novelty of the current investigation was to predict the Rasagiline mesylate release pattern by mathematical models and the mechanism of release from Rasagiline mesylate loaded nanoscale solid lipid particles investigated by korsmeyer-peppas model. Release kinetics of Rasagiline mesylate from nanoscale solid lipid particles were studied using mathematical models [9].

MATERIALS AND METHODS

Materials

Rasagiline mesylate was a kind gift from Orchid Generics (Chennai, India.). Stearic acid and Tween 80 were purchased from SD fine Chem. Ltd. (Mumbai, India.). Kolliphor and HPLC grade acetonitrile were obtained from BASF Chemicals (Mumbai, India.) and Sigma Aldrich (Bangalore, India.). The analytical grade reagents and chemicals were used for all the experiments. Double-distilled water was used after filtration through a 0.45 µm membrane (cellulose acetate).

Fabrication of rasagiline loaded nanoscale solid lipid particles

Rasagiline mesylate loaded nanoscale solid lipid particle were fabricated by microemulsion technique. In this technique, the lipid containing stearic acid was weighed precisely and heated above its melting point. Rasagiline mesylate was added in the molten lipid. The aqueous phase with double distilled water contained polyethylene-polypropylene glycol and polyoxyethylene 20 sorbitan monooleate was heated to 80 °C. The lipid phase was added to the aqueous phase under magnetic stirrer (Remi, India.) at 500rpm for 10-15 min to facilitate o/w emulsion formation. The pre-emulsion was dispersed into clod double distilled water under probe sonicator (Lark, India.) for 20 min to solidify the nanoscale solid lipid particles. The formulations were prepared by different ratio of drug/polymer ratio 1:1 (RMSLN-I) and 1:2 (RMSLN-II). The fabricated Rasagiline mesylate nanoscale solid lipid particles were freeze dried on a lyophilizer (Lark, India.) at-40 °C with 0.4 bar pressures [8, 16, 19, 20].

Physicochemical evaluation of Rasagiline loaded nanoscale solid lipid particles

To evaluate the particle size distribution, poly dispersity index and zeta potential, freeze dried RM nanoscale solid lipid particles were reconstituted with double distilled water. The evaluations were done by dynamic light scattering or photon correlation spectroscopy using malvernzeatsizer Nano ZS (Malvern Instruments, UK). Poly dispersity provide the statistics about the homogeneity of particle size distribution. Zeta potential was used to determine the surface charge of particles and electrostatic stabilization through electrostatic repulsion between particles [8, 17, 19].

Determination of entrapment efficiency (EE %) and drug loading (DL %)

The entrapment efficiency of Rasagiline mesylate loaded nanoscale solid lipid particles were assessed using centrifugation at 16,000rpm for 30 min at 0 °C (Remi C 24, Mumbai, India). After centrifugation process the free unloaded drug content from the supernatant of the formulation was quantified by validated HPLC method(Thermoscientific, spectra system P-4000, USA),which was formerly reported by Kannan *et al.*, 2015 [8], using UV detector (Kromosil 100) and C18 column (particle size 5 µm, 250 mm×4 mm). The entrapped efficiency of the Rasagiline mesylate loaded nanoscale solid lipid particles from lipid matrix was calculated by using following equation [8, 19]

$$\text{Entrapment efficiency (\%)} = \frac{(\text{W1(assay)} - \text{W2})}{\text{W1}} \times 100$$

Where, W1-the initial amount of RM used in nanoscale solid lipid particles,

W2-amount of RM detected in the supernatant.

The entrapped RM concentration was calculated as the initial amount of Rasagiline mesylate minus the free RM subtracting from the initial amount of drug used in the formulation. The loading capacity was calculated as amount of RM in nanoparticles subtracting from total weight of nanoscale solid lipid particles by following equation [21, 22],

$$\text{Drug loading (\%)} = \frac{\text{W1}}{\text{W2}} \times 100$$

Where, W1-amount of RM in nanoscale solid lipid particles,

W2-total amount of nanoscale solid lipid particles.

Determination of drug content

The HPLC method with ultraviolet (UV) detector was used to quantify the Rasagiline mesylate. Accurately, weighed amount of RM loaded nanoscale solid lipid particles were diluted with the mixture of acetonitrile: water (5:95, v/v) and analyzed using HPLC system (Thermoscientific, spectra system P-4000, USA) using UV detector (Kromosil 100). The analytical conditions were as follows: column C18 (particle size 5 µm, 250 mm×4 mm), detection of wavelength was 265 nm, flow rate 1 ml/mins and the injection volume was 25 µl. Under these conditions the retention time of Rasagiline mesylate was at 4.627 min and the concentration was calculated by relative to a calibration curve [8, 16].

Transmission electron microscope (TEM)

TEM used to characterize the surface morphology of Rasagiline mesylate loaded nanoscale solid lipid particles. The samples were negatively stained with 0.5% (w/v) phosphotungstic acid solution and fixing on coated copper grids with carbon film and dried under vacuum pressure. The samples were diluted to 5 ml in the buffer to obtain a clear solution and scanned by using a JEOL JEM-2000 EXII TEM (Tokyo, Japan) [16, 19].

***In-Vitro* release study**

Rasagiline mesylate loaded nanoscale solid lipid particle drug release study was carried out by using the incubator shaking method. Accurately weighed quantities of RM-SLNs were suspended in a conical flask containing 50 ml phosphate buffers at pH 7.4 at 37±0.5 °C. The conical flask was sealed tightly and kept in an incubator shaker (Lark, India), which was agitated at 50 strokes per minute and maintained at 37 °±0.5 °C. At schedule time intervals, the withdrawn samples were centrifuged and then the supernatant was completely extracted with a syringe. The release medium was and replaced with the same volume of fresh PBS. The samples were immediately filtered through a 0.45 µm membrane filter (Elix, Mill-Q) and the content of Rasagiline mesylate was estimated after suitable dilution with a Thermoscientific HPLC (spectra system P-4000, USA) with UV detector (Kromosil 100) and C18 column (particle size 5 µm, 250 mm × 4 mm) at 265 nm [16, 20].

Kinetics of drug releases

There are a number of model-dependent methodologies used to describe the drug release pattern and mechanism from fabricated nanoscale solid lipid particles. The release of drug loaded nanoscale solid lipid particle statistics was studied using, zero-order (cumulative amount of drug release versus time), first-order (log cumulative percentage of drug remaining versus time), higuchi (cumulative percentage of release versus square root of time), Hixson Crowell and korsmeyer-Peppas (log cumulative percentage of drug released versus log time) equation models [22].

The qualitative and quantitative changes in the fabricated of nanoscale solid lipid particles can change the drug release pattern and *In-vivo* performance, evolving tools that facilitate the formulation development by reducing the necessary of bio-studies were always desirable. In this respect, use of *In-vitro* drug release data to calculate *In-vivo* bio-performance can be considered as the rational development of controlled drug delivery. The controlled release formulation kinetics modeling was investigated three methods includes, statistical methods, model dependent methods and model independent methods [24-27]. Among, these models the model dependent methods used to describe the pattern of drug release pattern and mechanism of RMSLNs.

Model dependent methods

The model-dependent approaches are constructed by different mathematical functions and that can describe the drug dissolution release profile.

Zero-order

The drug release from nanoscale solid lipid particles that are not disaggregates and the release of the particles slowly can be expressed by this equation [28]:

$$Q_o - Q_t = K_o\, t \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (1)$$

Where, the Q_o is the initial amount of drug in the formulation,-Q_t is the amount of drug in the formulation at time t and K_o is the zero order release constant (Units: concentration/time). This model can be used to describe the release of drug from the oral osmotic system, transdermal systems and low soluble matrix coated tables.

First-order

Gibaldi and Feldman (1967) and later Wagner (1969) were proposed this model to study the drug release kinetics. Kitazawa

(1975 & 1977) also proposed different model, which is achieved practically the same decisions. The first order model is used to describe the drug loaded nanoscale solid lipid particles absorption and/or elimination, whereas it is problematic to conceptualize this mechanism on a theoretical basis.

$$\frac{dC}{dt} = -K_c \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (2)$$

Where, K is the first order rate constant (Units: time) and the equation (2) in logarithms

$$\log C = \text{Log } C_o - Kt/2.303 \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (3)$$

Where, C_o is the initial concentration of drug, K is the first order rate constant and t is the time. This model can be used to describe the formulations contain hydrophilic drugs in porous system [29-32].

Higuchi model

The mathematical model for a matrix system of drug release was first proposed by higuchi (1961 &1963), who studied the release of hydrophilic and low hydrophilic drugs incorporated in semi-solid and/or solid matrix. The model can be expressed by following equation:

$$f_1 = Q = A\sqrt{D(2C - C_s)\, C_s\, t} \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (4)$$

Where, Q is the amount of drug release in time t per unit area A, C is the drug initial concentration, Cs is the drug solubility of the drug in the matrix media andD is the diffusivity of the drug molecules in the matrix system.

This relation is effective for all time, except when the total depletion of the drug in therapeutic system is achieved. Higuchi also developed another model to study the dissolution of the drug from a planar heterogeneous matrix system, where the drug concentration is lower than its solubility in matrix system; the drug release occurs through pores in the matrix. It can be expressed by the following equation

$$f_1 = Q = A\sqrt{\frac{D\delta}{\tau}(2C - \delta C_s)\, C_s\, t} \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (5)$$

Where, D is the diffusion coefficient of the drug molecule in the solvent, δ is the porosity of the matrix, τ is the tortuosity of the matrix, Q is the amount of drug release in time t per unit area A, C is the drug initial concentration and Cs is the drug solubility of the drug in the matrix media.

Tortuosity is defined as a property of the curve being tortuous and it's commonly used to describe the diffusion of pores in the matrix. The drug release from an insoluble matrix is a function of the square root of time as shown in the Higuchi equation,

$$f_t = Q = K_H \times t^{\frac{1}{2}} \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (6)$$

Where, KH is the Higuchi rate constant, which represents the design variables of the system [33, 34].

Hixson-crowell model

Hixson-Crowell (1931) recognized that the cylindrical surface of a dissolving substance changes within the particle. This model derived an equation [35],

$$W_0^{\frac{1}{3}} - W_t^{\frac{1}{3}} = K_s t \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (8)$$

Where, W_o is the initial amount of drug in the pharmaceutical dosage form, W_t is the remaining amount of drug in the pharmaceutical dosage form at time t and Ks is a constant incorporating the surface-volume relation.

Korsmeyer-peppas model

To determine the mode of drug release from polymeric system korsmeyer (1983) proposed the model. The mechanism of drug loaded nanoscale solid lipid particles release can be finding by incorporating the initial 60% of the release data in korsmeyer-Peppas model.

$$M_t/M_\infty = Kt^n \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (7)$$

Where, M_t/M_∞ is the fraction of drug released at time t, K is the drug release rate constant and n is the release exponent

The n value is employed for the characterization of different release modes for cylindrical-shaped matrix. The drug release exponent (n) and mechanism of drug release are related as: n = 0.45, Fickian diffusion; 0.45<n<0.89, Anomalous (non-Fickian) diffusion; n = 0.89, Case-II transport; and n>0.89, Super case-II transport [36-39].

RESULTS

The Rasagiline mesylate loaded nanoscale solid lipid particles successfully fabricated by microemulsion technique. The particle size distribution of RM solid lipid nano particles, entrapment efficiency, drug loading and drug content are given in Table1. The Rasagiline mesylate loaded nanoscale solid lipid particles successfully fabricated by microemulsion technique. The formulations were found narrow particle size distribution. The formulae RMSLN-I exhibited the least particle size of 145.21±0.3 nm followed by formulae RMSLN-II, which had the particle size of 195.01±1.04 nm (Fig.1 & 2). The formulations particle size increased with increasing drug-polymer ratio. The polydispersity index is a ratio provides the evidence of the particles homogeneity in a given colloidal system. Ideally, it should be 0.3. The formulation of RMSLN-I and RMSLN-II particle size distribution has a narrow size of 0.248 and 0.315, respectively. Zeta potential of Rasagiline mesylate loaded nanoscale solid lipid particles provide the surface charge of the particle and electrostatic stabilization through the electrostatic repulsion between particles. The results of RMSLN-I and RMSLN-II zeta potential values were-34.60±1.20 and-35.14±1.04 mV, respectively. The high positive or negative results minimize the aggregation/flocculation of particles.

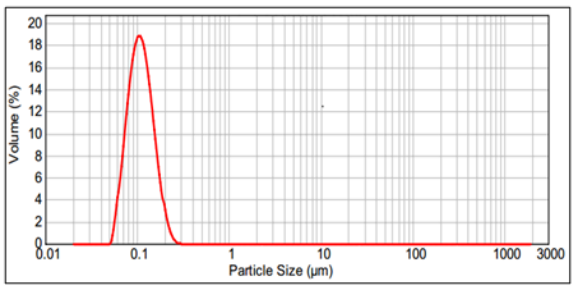

Fig. 1: Particle size distribution of RMSLN-I

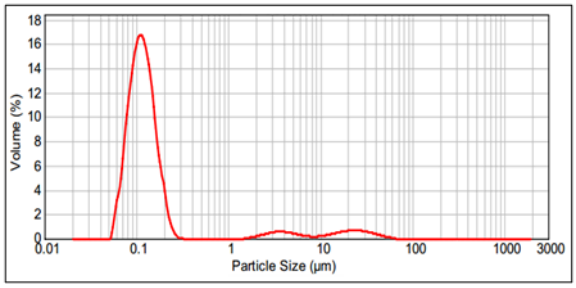

Fig. 2: Particle size distribution of RMSLN-II

Entrapment efficiency of RMSLN-I was shown 81.27±2.14%, which was fabricated with drug: lipid ratio of 1:1. The formulation RMSLN-II entrapment efficiency found 79.73±2.05% as the drug: lipid ratio was 1:2, surfactant concentration of the formulation was same as RMSLNs-I. EE (%) was validated as previously reported method. The drug loading of Rasagiline mesylate loaded nanoscale solid lipid particle formulation RMSLN-I and RMSLN-II were found 35.21±0.14 % and 26.04±1.32%, respectively. The results of drug loading were increased with increasing drug: lipid ratio. The RM content of RMSLN-I and RMSLN-II was 96.29±2.4 % and 98.37±1.7 %, respectively.

Table 1: Characterization of RM-loaded nanoscale solid lipid particles

Evaluation parameters	Formulations code	
	RMSLN-I	RMSLN-II
Mean particle size (nm)	145.21±0.3	145.21±0.3
Polydispersity Index (Pdi)	0.248	0.315
Zeta potential (mV)	-34.60±1.20	-35.14±1.04
Drug loading (%)	32.21±0.14	26.04±1.32
Entrapment efficiency (%)	81.27±2.14 %	79.73±2.05 %
Drug content (%)	96.29±2.4 %	98.37±1.7 %

*(n=3±SD)

The fabricated Rasagiline mesylate loaded nanoscale solid lipid particle formulation transmission electron microscope studies were carried out to attain more insight about the surface morphology of the colloidal system. The TEM photomicrographs of formulation RMSLN-I and RMSLN-II reveals almost uniform spherical shapes and rarely particles aggregate into secondary particles because of their very small dimension and high surface energy (Fig.3&4). The *In-Vitro* release from Rasagiline mesylate loaded nanoscale solid lipid particles formulation RMSLN-I and RMSLN-II is shown in (Fig.5). The formulation RMSLN-I and RMSLN-II released 94.70±2.16 % and 98.2±1.03 %, respectively, of their Rasagiline mesylate content at the end 24 h. Each data point of the in the release profile represents the mean of three determinations. Formulation RMSLN-I fabricated by the ratio of drug: lipid (1:1), failed to controlled release beyond 94.70 % at the end of 24 h.

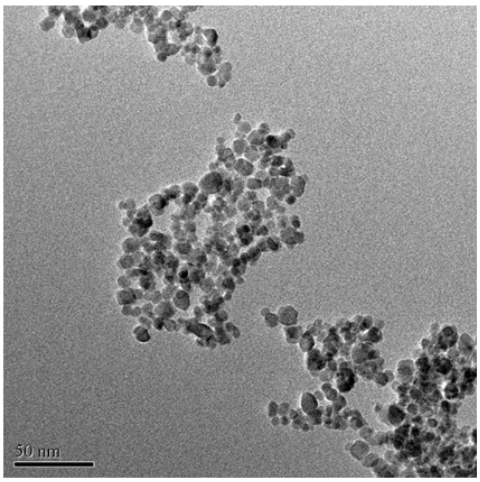

Fig. 3: TEM micrograph of RMSLN-I

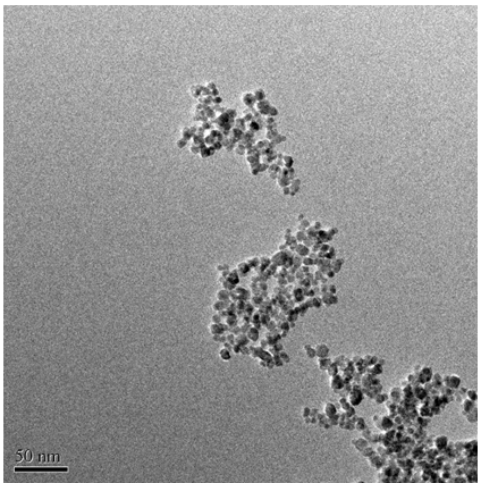

Fig. 4: TEM micrograph of RMSLN-II

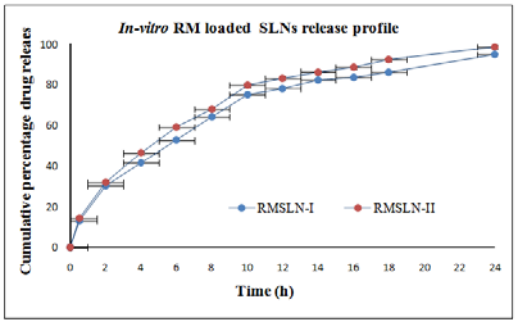

Fig. 5: *In-Vitro* rasagiline mesylate loaded solid lipid particles release profile

Table 2: Kinetic modelling of RM-loaded nanoscale solid lipid particles

Formulations	Zero order	First order	Higuchi	Korosmeyer-Peppas		Hixson-Crowel
	R^2	R^2	R^2	R^2	N	R^2
RMSLN 1	0.6456	0.9859	0.9789	0.9834	0.449	0.9629
RMSLN 2	0.6048	0.9911	0.9743	0.9829	0.432	0.9718

Zero order equation: F=k0*t, First order equation: F=100*[1-Exp(-k1*t)], Higuchi equation: F=kH*t^0.5, Korosmeyer-peppas equation: F=kKP*t^n, Hixson-crowel equation: F=100*[1-(1-kHC*t)^3]

The release data from Rasagiline mesylate loaded nanoscale solid lipid particles of RMSLN-I and RMSLN-II formulations were fitted to zero order, first order, higuchi model, hixson crowell and korsmeyer-peppas model(fig. 6-9) (table 2). The kinetic modeling results shown the Rasagiline mesylate loaded nanoscale solid lipid particles formulation RMSLN-I and RMSLN-II were diffusion controlled as indicated by the higher correlation coefficient (R^2) values in the higuchi model. The formulations 'n' values from the korsmeyer-Peppas model were shown less the 0.45, the mechanism of Rasagiline mesylate release from nanoscale solid lipid particles followed fickiandiffusion [36, 37].

DISCUSSION

Rasagiline mesylate loaded nanoscale solid lipid particles were fabricated using the microemulsion technique with biodegradable and biocompatible lipid, non-ionic surfactant and non-ionic co-surfactant. The endogenous saturated fatty acid of stearic acid was selected as lipid, which has the melting point higher than body

temperature and low toxicity. The molecular weight of the stearic acid was 248.477 Da. Ideally, the lipophilic compound with a molecular weight below 500 Da can only cross the blood brain barrier by transcellularlipophilic diffusion [38]. Polyethylene-polypropylene glycol has long been used as a stearic stabilizer for obtaining nanoscale solid lipid particles. In the presence of polyethylene-polypropylene glycol, following a period of equilibration, stable colloidal particles form, but in the absence of polyethylene-polypropylene glycol the particles are colloidally unstable and rapidly coalesce [39]. Polyoxyethylene 20 sorbitanmono oleate was used as the Co-surfactant and it was coated the surface of nanoparticles then the particles are binded with apolipoprotein E from the blood after administration intravenous route. The particles are taken up by the brain endothelial cell via receptor-mediated endocytosis [40, 41].

The size of the nanoscale solid lipid particles can play a significant role in the cellular uptake, biodistribution and interaction with the biological cells[23]. Nanoscale solid lipid particles below 1 µm size is accessible for intravenous administration. The formulated Rasagiline mesylate loaded solid lipid particle formulations particle size distribution was acceptable for transport the blood brain barrier. The particle size was depended directly on lipid concentration. The resultant curves from particle size distribution graphs shown, both formulations were unimodal. Nanoscale solid lipid particles poly dipersity in the formulations decreased with an increase in lipid concentration and particle size distribution. The RMSLN-I and RMSLN-II polydispersity index shows narrow size distribution and the formulated particles were monodispersity. Zeta potential directly influences the particle stability and it can determine the particle interaction in biological cells. The repulsive interactions between the particles will be larger as the zeta potential increases in the case of charged particles leading to the formation of more stable particles with a more uniform size distribution. The formulated RMSLN-I and RMSLN-II results had shown electrochemically stable. Which zeta potential values were more than 30mV [8, 19].

An increase in Rasagiline mesylate concentration with respect to lipid indicates high drug loading and also shown the higher entrapment efficiency. Maximum drug loading and entrapment was found in the formulation having drug: ratio of 1:1. It can be an important factor for estimating the best particulate drug-carrier system. An absorbed Rasagiline mesylate on the surface of nanoscale solid lipid particles was considered as entrapment of RM loaded nanoscale solid lipid particles. EE (%) was inversely related to free unloaded RM. However, it was directly related to the amount of lipid used. The results of EE (%) were found greater than 84.73 %. The drug content of the formulation results was satisfactory. TEM photomicrographs of formulation RMSLN-I and RMSLN-II reveals almost uniform spherical shapes.

The release kinetics was aiming to find the formulation release behavior at a slow zero or first order rate and those that provide an initial fast release, followed by zero or first order release by controlling manner. That can be maintained the drug concentration in the blood or target tissue at a desired value as long as possible [24, 42]. The formulated RMSLN-I and RMSLN-II percentage release was 94.70±2.16 % and 98.2±1.03 %, respectively. The results of Rasagiline mesylate release indicate, the formulation exhibited a biphasic release pattern. The burst release was happens within 30 min and the left over the drug was found to be released in a controlled manner, over the period of 24 h. The burst release of Rasagiline mesylate was associated with the drug entrapped in the surface layer of the nanoscale solid lipid particles directly dissolves when it comes in contact with the release medium [23]. The formulated particles showed a biphasic release pattern with the initial burst release followed by controlled release. Statistically significant differences were found among the drug release profile from RMSLN-I and RMSLN-II formulations. Applying kinetic mathematical models, the mechanism of Rasagiline mesylate loaded nanoscale solid lipid particles release from the two formulations were found to be followed higuchimodel, as the plots showed high linearity, with a correlation coefficient (R^2) value of 0.98 or more. The 'n' value of korsmeyer-peppasmodel lies below 0.5 and the mechanism controlling the drug release by diffusion dominated mechanism [22]. The mechanism of Rasagiline mesylate loaded nanoscale solid lipid particles release was found by incorporating the initial 60% of the release data in korsmeyer-peppasmodel.

CONCLUSION

The methodology of the present study was to make an evaluation of nanoscale solid lipid particles as controlled release for hydrophilic drug Rasagiline mesylate and to assess the kinetics of drug release mechanism. Biodegradable and biocompatible lipid (Stearic acid), Surfactant (polyethylene-polypropylene glycol) and co-surfactant (polyoxyethylene20 sorbitanmonooleate) used for controlled release drug delivery through the blood brain barrier to optimum particle size. The study exposes that, the release of hydrophilic drug, Rasagiline mesylate loaded nanoscale solid lipid particles exhibited diffusion conquered mechanism. The prepared Rasagiline mesylate loaded nanoscale solid lipid particles are an auspicious methodology to attain the appropriate controlled release dosage.

ACKNOWLEDGMENT

The authors are thankful to Department of Pharmacy, Faculty of Engineering and Technology, Annamalai University, Annamalai Nagar, Tamil Nadu, India.

CONFLICT OF INTERESTS

There are no conflicts of interest

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