RESEARCH ARTICLE

Preparation and Characterization of Sustained Release Risperidone Loaded Eudragit Microparticles by Spray-Drying Technique

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ABSTRACT

The goal of this work was to create novel risperidone-containing spray-dried microparticles using Eudragit® L100, a methacrylic polymer. Microparticles were designed with controlled release and enhanced *in-vitro* effects in mind and were meant to be taken orally. Spray-drying was used to create Eudragit® L100 microparticles loaded with risperidone. Risperidone-loaded Eudragit® L100 was successfully prepared to treat mental/mood disorders, according to an investigation into its physicochemical properties *in-vitro*. Spray-drying was an effective method for producing Eudragit® L100 microparticles loaded with risperidone. Formulations displayed a suitable drug entrapment percentage or nearly 89.94%. The mean diameter of the nearly spherical and spherical microparticles ranged from 30 to 50 µm, and they had a smooth surface. The distinctive peak of risperidone loaded with Eudragit L100 was visible in the fourier-transformed infrared (FTIR) spectra, indicating that the medication was fully encapsulated in the polymer. The dissolution rate of risperidone-loaded microparticles was slower than that of the pure medication. The use of spray-dried risperidone microparticles as a practical oral drug delivery method for more effective and regulated risperidone release is supported experimentally by our results.

Keywords: Schizophrenia, Autistic, Microparticle, Encapsulated, Controlled release.

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INTRODUCTION

Schizophrenia is a severe and incapacitating psychiatric disorder that impacts around 1% of the global population. There is no known treatment for this severe, persistent illness. Schizophrenia patients have suicide rates between 9 to 13%, and 50% of those who are diagnosed with the disorder will attempt suicide at some point in their lifetime. Affective alterations and social disengagement are examples of premorbid behavioral aberrations that often occur before the onset of schizophrenia.[1] Individuals diagnosed with schizophrenia may exhibit a range of symptom severity. Typically, the symptoms can be classified into three distinct categories: good symptoms, negative symptoms, and cognitive impairments.[2-4]

Since long, antipsychotic medication noncompliance has been a serious issue.[5] Noncompliant mental health patients experienced nearly twice as many re-hospitalizations due to relapse, which decreased their quality of life and raised their financial burden.[6] The main reasons for noncompliance with antipsychotic medication were side effects,[7] which included extrapyramidal side effects and dose-dependent cardiac arrest deaths.[8] Good compliance and a higher rate of therapy success are known to be linked to good tolerance in the case of schizophrenia. We all know mental illness is a very common problem nowadays. We prepared Microparticles of risperidone, (Figure 1) which would target on brain *via* transiently occupying and inhibiting D2 dopaminergic receptors and the patient will get relief from schizophrenia, bipolar disorder or irritability associated with autistic disorder.

MATERIALS AND METHODS

Materials

Risperidone (pure 99.80%; Padmavati Pharmachem, Kandivali West, Mumbai, India) and poly(methyl methacrylate-co-

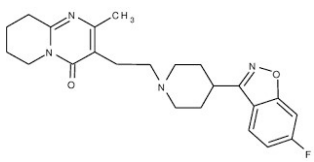

Figure 1: Structure of risperidone

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acrylic acid; Eudragit® L100; mass = 125.000 g.mol^{-1}, Evonik Rohm, Germany) were utilized exactly as supplied. Fisher Scientific India Pvt. Ltd., New Delhi, also supplied HPLC-grade methanol, while Changshu Hongsheng Fine Chemical Co.Ltd., Changshu City, provides ethanol. Microencapsulation was performed using ultrapure water obtained from a Milli-Q® ultrapure water purification system manufactured by Millipore in Bedford, USA. We obtained n-octanol, sodium hydroxide pellets, hydrochloric acid, and chloroform from Fisher Scientific India Pvt. Ltd. in New Delhi. The supplier of potassium dihydrogen orthophosphates is Thomas Baker in New Delhi. Meghmani Finechem Ltd. in India provides methylene chloride. The solvents and reagents were all of analytical grade.

Preparations of Risperidone loaded with Eudragit L 100 Microparticles by Spray Drying Technique

The spray-drying process was used to prepare the microparticles. Table 1 presents the six distinct formulations that were obtained based on the compositional amount of risperidone. After removing the Eudragit L100's percentage age weight, the animals were categorized as F1, F2, F3, F4, F5, and F6. In summary, clean water was added after risperidone and Eudragit® L100 was dissolved in ethanol with magnetic stirring. An Indian spray dryer manufactured by Techno Search Process in Mumbai was used to dry this liquid composition. The operational parameters that were employed were as follows: a 0.82 mm diameter nozzle, 3 kgf·cm−2 atomizing air pressure, 50 L·min^{-1}, 0.20 L·h^{-1}, feed flow rate, 150 ± 5°C intake air temperature, and 60 ± 5°C outlet air temperature. The dried powders were carefully extracted, weighed, and kept in a glass vessel that was tightly sealed and kept at room temperature under ideal circumstances. Three duplicates of each formulation were acquired from separate batches. As a negative control, unloaded microparticles were also created. A physical mixture including Eudragit® L100 and risperidone in a weight ratio of 1:1 was created in order to perform a comparative examination.[9]

Evaluation of Microparticles of Risperidone

Particle size and zeta potential

Laser diffraction is a method that quantifies particle size distributions by measuring the angular change in light intensity scattered when a laser beam passes through a dispersed particulate sample. Regarding the laser beam, sizable particles disperse light at narrow angles, whereas diminutive particles disperse light at wide angles. During this process, a 10 mg sample of our completed formulation is dissolved in 10 mL of distilled water, thoroughly mixed, and subsequently analyzed for particle size and zeta potential utilizing a particle analyzer device.[10]

Table 1: Composition of different risperidone loaded with Eudragit L 100 microparticles

S. No	*Formulation code*	*Risperidone (mg)*	*Eudragit L 100 (mg)*	*Ethanol (mL)*	*Water (mL)*
1	F1	0	4000	200	200
2	F2	200	3800	200	200
3	F3	400	3600	200	200
4	F4	600	3400	200	200
5	F5	800	3200	200	200
6	F6	1000	3000	200	200

Percentage yield

Following preparation, the microparticles were gathered and weighed. The weight that was measured was divided by the total weight of the medication and excipients. The formula below was used to determine the yield percentage:

$$\text{percentage yield} = \frac{\text{actual yield}}{\text{theoretical yield}} \times 100$$

Drug loading and encapsulation efficiency

The precise mass of the microparticles, equivalent to 20 mg, was measured to estimate the risperidone content in the microparticles (mg•g^{-1}) and the encapsulation efficiency (%) using UV spectroscopy. After dispersing this substance in 7 mL of methanol, it was agitated using a magnetic stirrer at a speed of 1000 revolutions per minute for a duration of 12 hours. Subsequently, the volume was augmented to 10 mL using a volumetric flask and then filtered via a polyvinylidene fluoride membrane filter (Durapore® membrane, with a pore size of 0.22 μm, manufactured by Millipore, located in Bedford, MA, USA). The concentration of risperidone was determined in triplicate using UV detection at a wavelength of 234 nm after diluting it appropriately in methanol. An equation was utilized to determine the encapsulation efficiency (EE).[11]

$$\text{EE\%} = \frac{\text{actual drug loading}}{\text{theoretical drug loading}} \times 100\%$$

Scanning Electron Microscopy

Scanning electron microscopy (SEM) was used to analyze the external surface morphology. Using an SEM, the precise structural characterizations and morphologies of the particles, both pure drug and polymer, were examined. The samples were created by utilizing graphite glue to mount powder onto a brass stub, and then vacuum-coating the stub with gold before using it. Using an SEM, images were captured at the necessary magnification at an acceleration voltage of 10 KV.[12]

FTIR of Final Formulation

Any substance's or drug's fourier transform infrared (FTIR) spectrum provides information on the groups that are present in that specific compound. For the structure study, FTIR spectroscopy was employed. To identify the final structure and functional group contained in the formulation, an FTIR spectra was acquired. 5 to 10 mg of the finished product were FTIR scanned, and the 4000 to 400 cm^{-1} portion of the infrared spectrum was recorded.

***In-vitro* Drug Release Study**

Experiments on the dissolution of pure drugs and drugs in their final formulation (microparticles) were conducted *in-vitro*. The dissolution assays were conducted in triplicate in 900 mL

of degassed phosphate buffer solution pH = 6.8 for 24 hours using a dissolution apparatus (Lab India Ltd., Mumbai, India) equipped with a basket (apparatus I). The system was maintained at 37 ± 0.5°C with a thermostat and agitated at 50 rev·min^{-1}. Every experiment was carried out. Samples (10 mL) were collected at prearranged intervals, filtered (0.45 µm pore size), and subjected to spectrophotometric evaluation using a UV-vis Spectrophotometer at 234 nm. The calibration curve, which ranged from 3 to 18 µg·mL^{-1} (y = 0.054x + 0.0379, r = 0.999), was previously determined. The amount of medication released at each time period was used to calculate the dissolution values. The cumulative dilution brought on by replacing the sample with an equivalent volume of new medium was corrected by using a correction factor.[13]

RESULT

Preparation of Risperidone Loaded with Eudragit L 100 Microparticles

A large amount of microparticles were obtained by spray drying technique (Table 2).

Visual Appearance

The visual appearance of all formulations is given in Table 3.

Percentage Drug Entrapment

The percentage of drug entrapment in all formulations is given in Table 4 and represented in Figure 2.

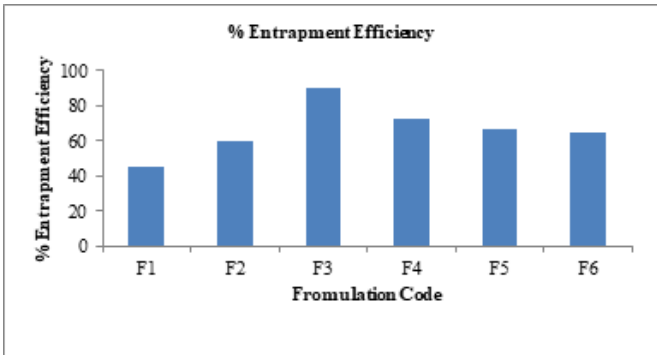

Figure 2: Percentage drug entrapment of risperidone loaded Eudragit L 100 microparticles

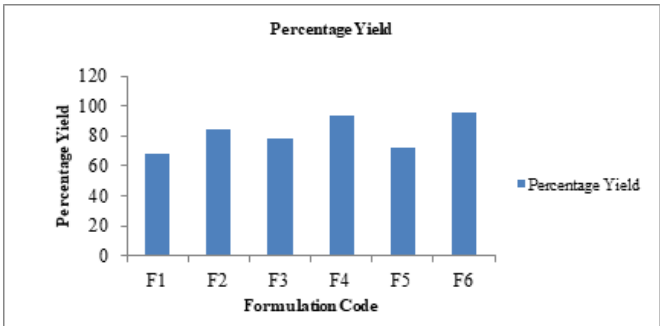

Figure 3: Percentage yield of risperidone loaded with Eudragit l 100 microparticles

Table 2: Quantity of risperidone microparticles

S. No	*Formulation code*	*Quantity of microparticles (mg)*
1	F1	2700.85
2	F2	3375.25
3	F3	3118.75
4	F4	3700.25
5	F5	2871.56
6	F6	3799.25

Table 3: Visual appearance of risperidone microparticles

S. No.	*Formulation code*	*Visual appearance*
1	F1	A white color uniform microparticles are formed.
2	F2	A white color uniform microparticles are formed.
3	F3	A white color uniform microparticles are formed.
4	F4	A white color uniform microparticles are formed.
5	F5	A white color uniform microparticles are formed.
6	F6	A white color uniform microparticles are formed.

Table 4: Percentage drug entrapment of risperidone loaded Eudragit L 100

S. No.	*Formulation code*	*%Entrapment efficiency*
1	F1	45.51 ± 0.588
2	F2	59.55 ± 0.294
3	F3	89.94 ± 0.728
4	F4	72.50 ± 0.192
5	F5	66.31 ± 0.073
6	F6	64.59 ± 0.524

Table 5: Percentage yield of risperidone loaded Eudragit L 100

S. No.	*Formulation code*	*Percentage yield*
1	F1	68.22 ± 0.829
2	F2	84.01 ± 0.769
3	F3	78.40 ± 0.845
4	F4	93.35 ± 0.747
5	F5	72.05 ± 0.393
6	F6	95.46 ± 0.816

Percentage Yield

The percentage yield of all formulations was given in Table 5 and shown in Figure 3.

Determination of Particle Size and Zeta Potential

Particle size

Demonstrated particle size of F3 formulation was 33.134 µm with Polydispersity Index was found to be 3.5 % as shown in Figure 4.

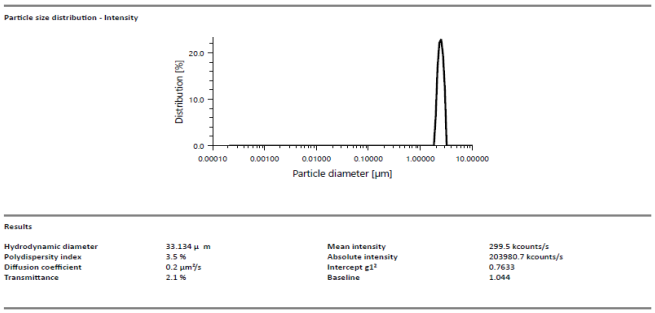

Figure 4: Particle size peak of F3 formulation

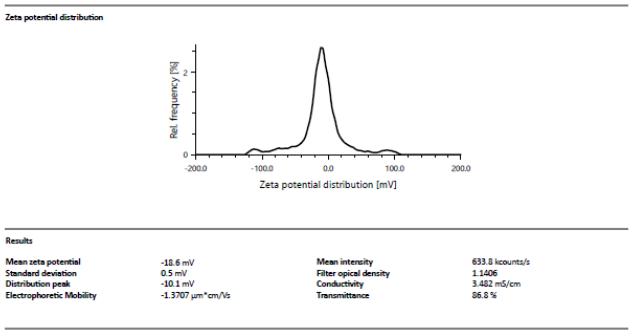

Figure 5: Zeta potential graph of F3 formulation

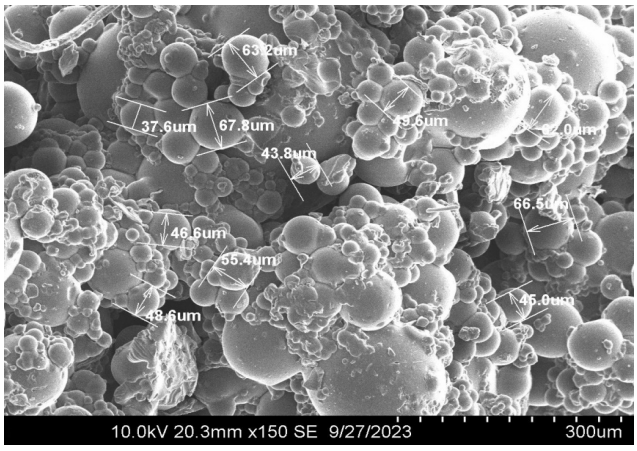

Figure 6: SEM analysis of formulation F3 of microparticles

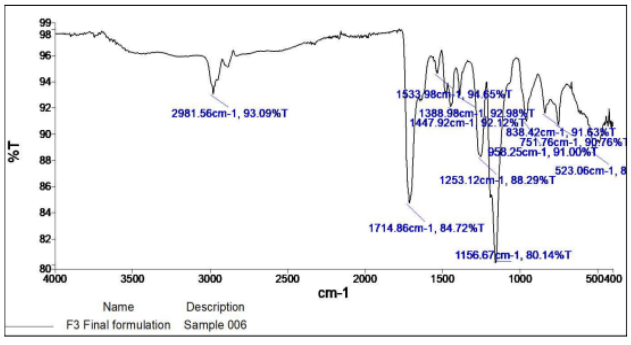

Figure 7: FTIR spectra of final formulation (F3) of risperidone loaded with Eudragit

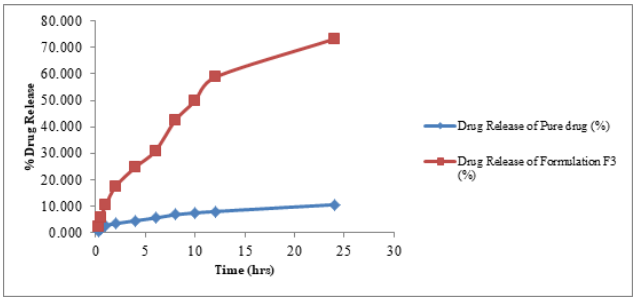

Figure 8: Percentage of drug release of formulation F3 and pure drug formulation

Table 6: *In-vitro* drug release study of microparticles

S. No.	*Time interval (Hr)*	*Drug release of pure drug (%)*	*Drug release of formulation F3 (%)*
1	0	0	0
2	0.25	0.48 ± 0.296	2.15 ± 0.296
3	0.5	1.51 ± 0.194	5.83 ± 0.403
4	1	2.67 ± 0.194	10.35 ± 0.296
5	2	3.45 ± 0.194	17.51 ± 0.296
6	4	4.54 ± 0.296	24.80 ± 0.296
7	6	5.57 ± 0.387	30.93 ± 0.387
8	8	6.80 ± 0.296	42.48 ± 0.403
9	10	7.51 ± 0.512	49.90 ± 0.194
10	12	8.03 ± 0.403	58.74 ± 0.296
11	24	10.61 ± 0.844	73.25 ± 0.403

Zeta Potential

Demonstrated zeta potential of F3 formulation was found to be -18.6 mV which represents stability of formulation as shown in Figure 5.

Scanning Electron Microscopy Analysis

Scanning electron microscopy analysis also verified the optimized formulation F3's shape, which is depicted in Figure 6. The microparticles were primarily spherical in shape and had a porous surface with channels that connected to one another. Size range is between 10 to 100 um.

FTIR of Final Formulation (F3) of Risperidone Loaded with Eudragit Microparticles

The final formulation (F3) FT-IR spectra (Figure 7) show a distinctive signal for risperidone loaded with eudragit L100, indicating that the medication was fully encapsulated in the polymer.

***In-vitro* Drug Release Study**

Table 6 and Figure 8 show the in-vitro drug release of Eudragit L 100 microparticles loaded with risperidone and pure drug formulation. Within 24 hours, the pure drug release shows 10.61 ± 0.844. Conversely, the release of Eudragit L 100 microparticles F3 73.25 ± 0.403 loaded with risperidone occurred during a 24-hour period.

DISCUSSION

It is evident from Table 3 that homogenous microparticles of white color are generated in formulations F1, F2, F3, F4, F5, and F6. Table 4 revealed that the percentage of drugs entrapped in all formulations ranged from 45.51 ± 0.588 to 89.94 ± 0.728. These findings clarify that the concentration of Eudragit L 100 had a noteworthy impact on the percentage of drug entrapment. Formulation F3 had the highest percentage of drug entrapment, 89.94 ± 0.728. Table 5 revealed that the total formulation's percentage yield fell between 68.22 ± 0.829 to 95.46 ± 0.816. These findings clarify the considerable percent yield effect that was reported at a concentration of Eudragit L 100.[14-16] Formulation F6 was determined to have a maximum percentage yield of 95.46 ± 0.816. The F3 formulation's particle size, as shown in Figure 4, was 33.134 µm with a PDI of 3.5%. The F6 formulation's zeta potential, which stands for formulation stability at -18.6 mV, is shown in Figure 5. SEM analysis further validated the improved formulation F3's shape, which is depicted in Figure 6.[17,18] The microsponge was primarily spherical in shape and had a porous surface with channels that connected to one another. The final formulation's (F3) FTIR spectra show a distinctive signal for risperidone loaded with eudragit L100, indicating that the medication was fully encapsulated in the polymer.[19,20] Table 6 and Figure 8 show the *in-vitro* drug release of Eudragit L 100 microparticles loaded with risperidone and pure drug formulation. Within 24 hours, the pure drug release shows 10.61 ± 0.844. Conversely, the release of Eudragit L 100 microparticles F3 73.25 ± 0.403 loaded with risperidone occurred during a 24-hour period.

CONCLUSION

Spray-drying was used to effectively create Eudragit® L 100 microspheres loaded with risperidone. Micrometer-sized formulations with high drug-loading efficiency, which are heat-stable and amorphous/non-crystalline, were successfully developed. Spray-drying worked well to create Eudragit® L100 microspheres loaded with risperidone. The results indicate that the range of percentage drug entrapment for all formulations was 45.51 ± 0.588 to 89.94 ± 0.728, with formulation F3 having the highest percentage of drug entrapment at 89.94 ± 0.728. Additionally, the range of percentage yield for all formulations was determined to be 68.22 ± 0.829 to 95.46 ± 0.816. The microspheres was primarily spherical in shape and had a porous surface with channels that connected to one another. The final formulation's (F3) FTIR spectra show a distinctive signal for risperidone loaded with Eudragit L100, indicating that the medication was fully encapsulated in the polymer. Within 24 hours, the pure drug release shows 10.61 ± 0.844. Conversely, the release of Eudragit L 100 microspheres F3 73.25 ± 0.403 loaded with risperidone occurred during a 24-hour period. These findings provide experimental support for the use of these multiple-unit dosage forms as a potentially useful strategy for extending the duration of medication release. To summarize, these formulations can be employed in various novel oral medicines to relieve irritability associated with autism disorder, bipolar disorder, or schizophrenia. They are also viable carriers for the controlled release of risperidone.

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