Journal of Applied Pharmaceutical Science Vol. 4 (11), pp. 081-086, November, 2014
Available online at http://www.japsonline.com
DOI: 10.7324/JAPS.2014.41114
ISSN 2231-3354

Enhancing Solubility and Dissolution of Olanzapine by Spray Drying Using β- Cyclodextrin Polymer

Mudit Dixit, R. Narayana Charyulu, Anupama Shetty, Narayana Charyalu, Meghana Rao, Pallavi Bengre, Sharin Thomas

Department of Pharmaceutics, NGSM Institute of Pharmaceutical sciences, Nitte University, Mangalore-575018, Karnataka, India.

ARTICLE INFO

Article history:
Received on: 15/09/2014
Revised on: 04/10/2014
Accepted on: 22/10/2014
Available online: 27/11/2014

Key words:
Spray drying, microspheres, Olanzapine, β-cyclodextrin, solubility, dissolution.

ABSTRACT

Olanzapine, an antipsychotic agent, exhibits poor water solubility, dissolution and flow properties. Thus, the aim of the present study was to improve the solubility and dissolution rate of Olanzapine by preparing microspheres by spray drying technique using β-cyclodextrin. Olanzapine Microspheres containing different ratios of β-cyclodextrin were produced by spray drying using Propanol and water (50:50) as solvent system to enhance solubility and dissolution rate. The prepared formulations containing different ratios of drug and β-cyclodextrin were evaluated for solubility and in-vitro dissolution. The prepared formulations were characterized by DSC, FT-IR, XRD and SEM. Dissolution profile of the prepared spray dried microspheres was compared with its physical mixture and pure sample. Spray dried microspheres exhibited decreased crystallinity. The solubility of microspheres containing Olanzapine and β-cyclodextrin (1:3w/w) exhibited tenfold increases than the commercial Olanzapine and dissolution of same ratio microsphere showed 99 % release in 20 min. while same composition in physical mixture showed 37% release in 20 min. Consequently, from the above result it can be concluded that spray dried microspheres of Olanzapine is a useful technique to improve the solubility and dissolution of poor water soluble drug like Olanzapine.

INTRODUCTION

Olanzapine, 2-methyl-4-(4-methyl-1-piperazinyl)-10*H*-thieno-[2, 3b], [1, 5] benzodiazepine is a potent antipsychotic agent. As a free base or its hydrochloride salt, olanzapine is an active ingredient of pharmaceutical preparations used in the treatment of disorders of the central nervous system. Olanzapine belong to class II category under the biopharmaceutical classification system (BCS), i.e., it is inherently highly permeable through biological membranes, but exhibits low aqueous solubility.

Rate of absorption and/or extent of bioavailability for such insoluble hydrophobic drug are controlled by rate of dissolution in gastro-intestinal fluids. However, its oral bioavailability is very low, probably due to poor solubility in water and insufficient dissolution rate (Aarsland *et al.*, 1999; Adams and Mutasim, 1999; Almeida, 1998). Consideration of the modified Noyes-Whitney equation provides some hints about the dissolution rate of poorly soluble compounds might be improved to minimize the limitations to their oral availability. There have been numerous efforts to improve drug dissolution rates.

These include (a) reducing the particle size to increase the surface area; (b) using water-soluble carriers to form inclusion complexes; (c) solubilization in surfactant systems; (d) using pro-drugs and drug derivatization; and (e) manipulation of the solid state of drug substances to improve the drug dissolution i.e. by reducing the crystallinity of drug substances through formation of solid dispersions.

However, there are practical limitations to these techniques (Shivakumar and James, 2001). Although particle size reduction is commonly used to increase the dissolution rate, there is a practical limit to the size reduction that can be achieved by such commonly used methods as controlled crystallization and grinding. The use of very fine powders in a dosage form may also be problematic because of handling difficulties and poor wettability. Salt formation is not feasible for neutral compounds and the synthesis of appropriate salt forms of drugs which are weakly acidic or weakly basic may often not be practical.

* *Corresponding Author*
Mudit Dixit, Department of Pharmaceutics, NGSM Institute of Pharmaceutical sciences, Nitte University, Mangalore-575018, Karnataka, India. Email: muditdixit911@yahoo.com

Even when salts can be prepared, an increased dissolution rate in the gastrointestinal tract may not be achieved in many cases because of the reconversion of salts into aggregates of their respective acid or base forms.

The solubilization of drugs in organic solvents or in aqueous media by the use of surfactants and co-solvents leads to liquid formation that is usually undesirable from the viewpoints of patient acceptability and marketing (Christian and Jennifer, 2000). Solid dispersions have been widely used to enhance the solubility, dissolution rate, and bioavailability of poorly soluble drugs (Anne *et al.,* 2003; Abu, 1999; Sekiguchi and Obi, 1961; Win and Sidney, 1971). There are different types solid dispersion systems categorized according to the physical states of the drug and the carrier in the systems. It may be a molecular solid solution, a dispersion of amorphous or crystalline drug particles in an amorphous carrier matrix, or a combination of a solution and dispersion of solids.

The enhancement in the dissolution rate is obtained by one or a combination of the following mechanisms: eutectic formation, increased surface area of the drug due to precipitation in the carrier, formation of true solid solution, improved wetability and drug precipitation as a metastable crystalline form or a decrease in substance crystallinity. The type of solid dispersion formed depends on both the carrier-drug combination and the method of manufacture.

Olanzapine was previously formulated as a solid dispersion in pre-gelatinized starch and sodium glycollate, obtaining a marked increase in aqueous solubility, dissolution rate and an improved drug release profile with respect to the pure drug (Venkateskumar, *et al.,* 2011).

The drug was also associated with hydrophilic polymers with the aim of improving the dissolution parameters in different formulations, such as freeze-dried tablets with micronized gelatin (Mudit *et al.,* 2011), controlled release tablets in the presence of methocel and ethocel (Amir et al.,2010), long acting microspheres formed by different polylactic/polyglycolic acid (PLGA) co-polymers (Nahata and Saini, 2008), or in the form of inclusion complexes with cyclodextrins (José *et al,* 2012; Ajit *et al.,* 2012) and Lutrol solid dispersion (Adamo *et al,* 2010).

Spray drying is one of the techniques of preparing solid dispersion and is widely used as an alternative to milling to reduce particle size (Michael *et al.,* 2013; Amal and Ebtessam, 2005; Yuh-Fun *et al.,* 2010). The large surface area of the resulting particle should result in an enhanced solubility and dissolution rate, consequently, improved bioavailability. β-cyclodextrin are a family of compounds made up of sugar molecules bound together in a ring and contain 7-membered sugar ring molecule. Cyclodextrins are hydrophobic inside and hydrophilic outside, they can form complexes with hydrophobic compounds. Thus they can enhance the solubility and bioavailability of such compounds. The aim of the present study was to improve the solubility and dissolution rate of olanzapine by spray drying technique using different ratio of β-cyclodextrin.

MATERIALS AND METHODS

Materials

All chemicals and buffers used were of analytical grade.

Methods

Preparation of microspheres

The microspheres were prepared by spray-drying technique. The spray drying was performed by Mini Spray Dryer LSD -48; (Jay instrument & systems Pvt. Ltd. Mumbai). The different drug–polymer ratios used for various microsphere formulations were prepared described in Table 1. The polymer solution was prepared by adding given quantity of polymer to the propanol as solvent. The given quantity of Olanzapine was added to the polymer solution and the resulting mixture was spray-dried. The spray drying parameters are described in Table 2.

Table 1: Spray-Dried microspheres formulation.

Numbers	Formulation Code	Different ratio of polymer and drug (w/w)
Spray drying formulations		
1	SD 1	1:1
2	SD 2	1:2
3	SD 3	1:3
	Physical mixture	
1	PM 1	1:1
2	PM 2	1:2
3	PM 3	1:3

Table 2: Spray-Drying Parameters.

Inlet temperature (°C)	Feed pump speed %	Vacuum (mm Wc)	Aspirator level (kg/cm^2)
43	15	-70	2

Preparation of Physical Mixtures

The different drug–polymer ratios used for various physical mixtures formulations were prepared as described in Table 1 and were prepared by mixing different ratio of Olanzapine and β-cyclodextrin in the mortar for 5 min and then sieving.

Evaluation of Microspheres

Determination of percentage yield and drug content

The percentage yield of each formulation was determined according to the total recoverable final weight of microspheres and the total original weight of Olanzapine and β-cyclodextrin.

Microspheres (50 mg) were triturated with 10 ml of water. Allowed to stand for 10 min with occasional swirling and methanol was added to produce 100 ml. After suitable dilution, samples were measured at 250 nm. Drug content was determined from standard plot.

Differential scanning calorimetry (DSC)

A DSC study was carried out to detect possible polymorphic transition during the crystallization process. DSC measurements were performed on a DSC DuPont 9900, differential scanning calorimeter with a thermal analyzer.

Fourier transform infrared spectroscopy (FTIR)

The FTIR spectral measurements were taken at ambient temperature using a Shimadzu, Model 8033 (USA). Samples were dispersed in KBr powder and the pellets were made by applying 5 ton pressure. FTIR spectra were obtained by powder diffuse reflectance on FTIR spectrophotometer.

X-ray diffraction analysis (XRD)

X-Ray powder diffraction patterns were obtained at room temperature using a Philips X' Pert MPD diffractometer, with Cu as anode material and graphite monochromator, operated at a voltage of 40 mA, 45 kV. The process parameters used were set as scan step size of 0.0170 (2θ).

Scanning electron microscopy (SEM)

Scanning electron microscopic (Joel- LV-5600, USA, with magnification of 250x) photographs were obtained to identify and confirm spherical nature and surface topography of the crystals.

Mechanical properties

Tensile strength of microspheres was determined by compressing 500 mg of crystals using hydraulic press at different ton/cm^2 for 1 min. The compacts were stored in desiccator overnight to allow elastic recovery.

The thickness and diameter were measured for each compact. The hardness of each compact was then measured using Pfizer hardness tester. The tensile strength (σ) of the compact (ton/cm^2) was calculated using following equation.

$\sigma = 2F/\pi Dt$

Where, F, D and t are hardness (ton), compact diameter (cm) and thickness (cm), respectively.

Determination of solubility

Drug solubility was determined by adding excess amounts of pure Olanzapine, their physical mixture and microspheres in distilled water at 37 ± 0.5°C, respectively. The solution formed were equilibrated under continuous agitation for 24 h and passed through a 0.8 μm membrane filter to obtain a clear solution.

The absorbance of the samples was measured using UV spectrophotometer method (UV 1601 A Shimadzu, Japan) at 229 nm and the concentrations in μg/ml were determined. Each sample was determined in triplicate.

Dissolution studies of microspheres

The dissolution of pure Olanzapine, their physical mixture and microspheres was determined by using USP dissolution apparatus XXIV-Type II (Electro Lab, Mumbai). Dissolution medium was 900 ml of pH 7.4 phosphate buffer. The amount of dissolved drug was determined using UV spectrophotometer method (UV 1601 A Shimadzu, Japan) at 229 nm. Each sample was determined in triplicate.

Determination of the physical stability

To determine the physical stability of optimized Microspheres, a stability study of prepared Microspheres was carried out at 25°C and 60% relative humidity for 6 months according to the ICH guidelines. The spherical agglomerates were packed in high density polyethylene (HDPE) container and placed in stability chamber. The samples were withdrawn at the interval of 0, 1, 3 and 6 months and evaluated for appearance, characterization by FT-IR and dissolution release and compared with initial results.

RESULT AND DISCUSSION

Cyclodextrins (CDs) are cyclic oligosaccharides consisting of (α-1, 4)-linked α-D-glucopyranose units that contain a lipophilic internal cavity and a hydrophilic outer surface. The hydroxyl functions of the glucose are orientated to the exterior, which gives it hydrophilic character. The inner cavity is lined by skeletal carbons and ethereal oxygen's of the sugar residues, which gives it a lipophilic character. These characteristics favour CDs to form inclusion complexes with a variety of host-guest molecules of suitable polarity and size. This characteristic of cyclodextrin is used to improve the pharmaceutical properties of numerous drugs such solubility, dissolution, bioavailability and stability. (Kaneto *et al.*, 1998; Martin, 2004; Rubén *et al.*, 2010).

The spray dried microspheres formulations were collected and were found to be free-flowing and white in color. The percentage yield of spray dried microspheres of different ratios of drug–polymer was found to be in the range of 65-84 %. This small yield could be increased by addition of solid substance or in large scale production. Drug content for the spray dried microspheres of different ratio of drug–polymer formulation was found to be in the range of 93-99 %±0.013 (Table-3). DSC curves obtained for pure material, physical mixtures and microspheres are showed Fig. 1.

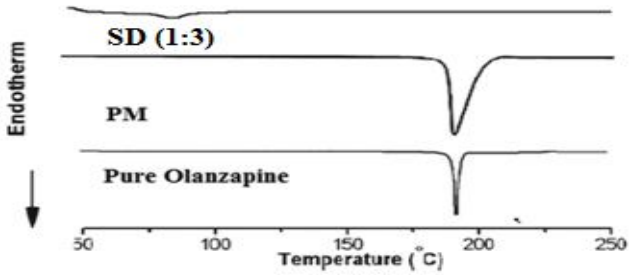

Fig. 1: DSC Spectrum of pure drug, physical mixture (1:3) and microspheres (1:3).

In DSC curve, pure celecoxib had a sharp endothermic peak at 160°C that corresponded to the melting point of Olanzapine. In the thermogram of β-cyclodextrin, a sharp peak (261.3°C) was observed, which was associated with the endothermic melting of β-cyclodextrin. In DSC spectra of physical mixture showed peaks at 257 to 261°C for Olanzapine. However, the melting endotherm was absent on the DSC thermogram for the Microspheres,

suggesting absence of crystallinity and presence of an amorphous state of the drug. This could be because Olanzapine was molecularly or amorphously dispersed in the Microspheres.

The FTIR spectra of pure Olanzapine, β-cyclodextrin, their physical mixture and microspheres of different ratios are shown in Fig 2. FTIR spectroscopy has been successfully used for exploring the differences in molecular conformations, crystal packing and hydrogen bonding arrangements for different solid-state forms of an organic compound. Spectral variations originate due to alteration in bonds that exhibit characteristic vibrational frequencies, leading to frequency shifts and splitting in absorption peaks. The FTIR spectra of Olanzapine (Fig. 2) showed a characteristic peak for amino group of the ring containing two nitrogen atoms (3100–3400 cm−1). All the FTIR spectra's are showing similar peaks, hence its confirmed that both drug and polymer were comparable with each other.

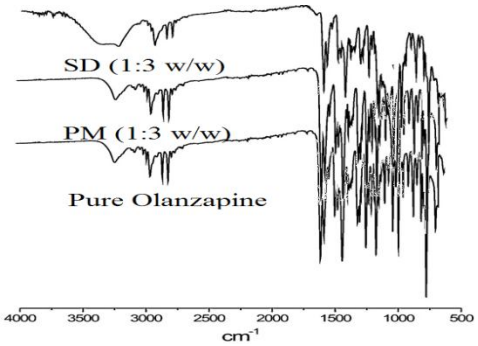

Fig. 2: FT-IR Spectrum of pure drug, physical mixture (1:3) and microspheres (1:3).

X- Ray diffraction was used to analyze potential changes in the inner structure of Olanzapine nanocrystals during the formulation of the Microspheres. The extent of such changes depends on the chemical nature and physical hardness of the active ingredient. The powder X-ray dif-fraction patterns of the pure drug, PM, and Microspheres are shown in Figure 2. The results of the DSC were further conformed by X-ray diffraction studies (Figure 3).

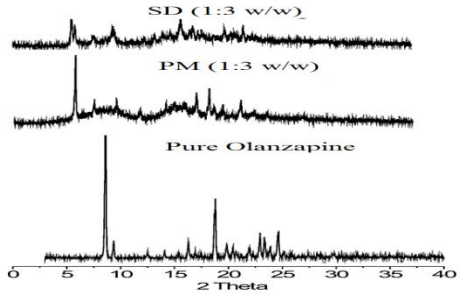

Fig. 3: X- Ray diffractogram of pure drug, physical mixture (1:3) and microspheres (1:3).

The characteristic peak of the olanzapine appeared in the 2θ range of 10–30o, thus indicating that the unprocessed Olanzapine was a crystalline material (José *et al.,* 2012). The pure drug exhibits its characteristic diffraction peaks at various diffraction angles, thus indicating the presence of crystallinity. The X-ray diffraction study of the drug and excipients PM showed the peak corresponding to the crystalline drug molecules present in the mixture, although their intensity was lower due to the high excipients-drug ratio employed. The diffraction pattern of the drug Microspheres showed absence, broadening and reduction of major Olanzapine diffraction peaks, thus indicating that the Microspheres contained mostly an amorphous form (disordered state). These results could explain the observed enhancement of solubility and rapid dissolution of Olanzapine in Microspheres. The SEM image of the pure drug, physical mixture and microspheres are shown in Fig. 4.

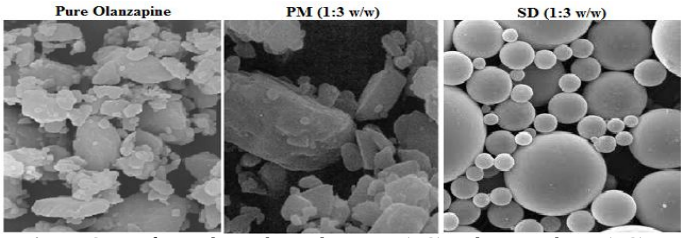

Fig . 4: SEM of pure drug, physical mixture (1:3) and microspheres (1:3).

The Olanzapine particles in the physical mixture were broken into much smaller ones and irregular size (17-29 µm) and the shape of prepared microspheres are uniform and spherical in shape with small in size (8-16 µm) (Table-3).The spherical shape of microspheres does not lead to cake formation during storage because of less point of contact thereby increasing the stability of the microsphere formulation, which is an advantage over other shapes. This could be therefore, indicate that Olanzapine particle size has been reduced, which also accelerates solubility and dissolution.

Table 3: Solubility, Percentage yield, Drug content and Particle size microspheres.

Formulations code polymer: Drug ratio(w/w)	Concentration of Olanzapine microparticle in water (µg/ ml) SD±3	Percentage yield%	Drug content SD ±3	Particle size determination (µm) SD±3
Pure drug	0.033	--	--	
SD 1	0.124	79.85	94.11±0.02	7-12
SD 2	0.167	65.64	95.94±0.23	8-15
SD 3	0.188	84.13	99.73±-0.21	7-16
PM 1	0.047	-	97.88±0.22	17-25
PM 2	0.051	-	93.34±0.01	18-28
PM 3	0.064	-	98.63±0.03	17-29

Microspheres exhibited superior compressibility characteristics compared to physical mixture and pure sample of Olanzapine drug crystals (Fig. 5). It could be due to the fact that during the process of compression fresh surfaces are formed by fracturing crystals. Surface freshly prepared by fracture enhanced the plastic inter particle bonding, resulting in a lower compression force required for compressing the microspheres under plastic deformation compared to that of single crystal. Tensile strength of the same ratio of microspheres and physical mixture (1:3) showed that tensile strength of microspheres higher than physical mixture as well as pure sample. This could be due to the increasing in the plastic inter particle bonding of microspheres.

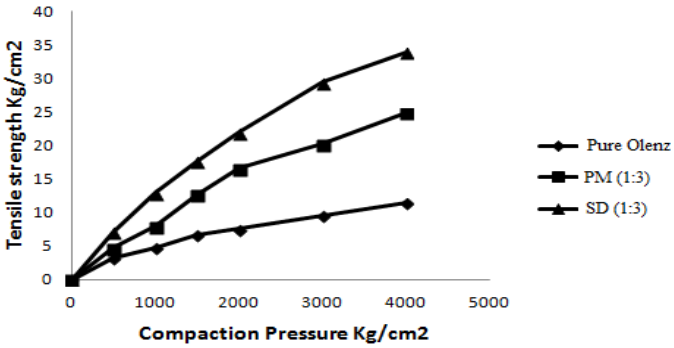

Fig. 5: Tensile strength of pure drug, physical mixture (1:3) and microspheres (1:3).

Increase in the solubility of Olanzapine from microspheres (0.188 mg/mL) was found to be nearly six times higher than the solubility of the pure drug (0.033 mg/mL), suggesting the presence of a high amount of an amorphous form of Olanzapine in the Microspheres, indicating super-saturation obtained from the SDT. Increase in the solubility of Olanzapine from the PM (0.064 mg/mL) was nearly two times higher than pure drug. This could be due to the solubilising effect of highly water-soluble β-cyclodextrin used in the formulation. The solubility results for the different formulations are shown in Table 3. The higher solubility of Olanzapine from Microspheres may be due to the increased surface area, wettability and solubilising effect of highly water-soluble β-cyclodextrin used in the formulations.

The dissolution of pure Olanzapine, physical mixture and prepared microspheres in pH 7.4 phosphate buffer shown in Fig. 6, the dissolution profiles were plotted as the % release from the different microspheres, physical mixture and pure Olanzapine versus time in minute.

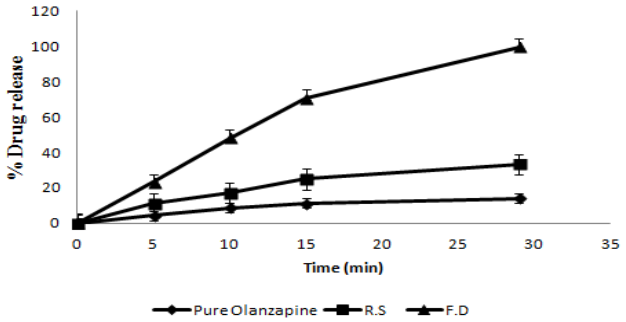

Fig. 6: m Dissolution release of pure drug, physical mixture (1:3) and microspheres (1:3).

The rate of dissolution of pure Olanzapine was slow compared with Olanzapine from its physical mixtures and different microspheres formulation in 60 min. The % release from ratio of (1:3 w/w) drug and polymer showed more release compared to other ratios. In case of microspheres containing (1:3 w/w) showed 99% release in 20 min and at the same ratio of physical mixture showed 68% release in 60 min. There was a significant difference in the drug release between the microspheres and physical mixture. The increase in dissolution from the microspheres and physical mixtures was probably due to the wetting and solubilizing effect of the β-cyclodextrin, which could reduce the interfacial tension between the Olanzapine and the dissolution medium, thus leading to a higher dissolution rate then pure Olanzapine. The large surface area of the resulting microspheres should result in an enhanced dissolution rate and thereby improve the bioavailability.

The best way to guarantee stability is by maintaining their physical state and molecular structure. The results of the stability study of prepared microspheres (1:3 w/w) of Olanzapine stored at 25 ^{0}C and 60% relative humidity for 6 month is presented in table 4. The influence of physical stability on the prepared crystals was investigated. Prepared microspheres of Olanzapine were stable and complied with all the properties when compared to initial results of prepared microspheres of Olanzapine.

Table 4: Stability data of Spray dried microspheres.

Testing interval	Description of Drug	FT-IR Study	XRD Study	Drug content (±SD)	Dissolution Study (±SD)
Sample name: Olanzapine microspheres (1:3 w/w) **Storage condition:** 25^{0}C /60% RH					
Initial	White to off white	As standard	As standard	99.12±0.01	99.60±0.011
1 month	Complies	Complies	Complies	99.28±0.02	98.39±0.040
3 month	Complies	Complies	Complies	99.14±0.01	99.28±0.027
6 month	Complies	Complies	Complies	98.87±0.03	99.89±0.013

CONCLUSION

In this present study, an increased solubility and dissolution rate of olanzapine were achieved by preparing microspheres by spray drying technique using different ratio of β-cyclodextrin. DSC, FT-IR and XRD studies showed that there is no change in the crystal structure of olanzapine during the spray drying process and showed that spray dried microspheres exhibited decreased crystallinity. The solubility and dissolution of the spray dried microspheres was improved significantly compared with its physical mixture and pure sample of olanzapine. The olanzapine microspheres containing 1:3 w/w (olanzapine: β-cyclodextrin) showed highest % of drug release and solubility compare to other ratio, physical mixture and pure sample of olanzapine. Stability results showed that prepared microspheres stable for 6 month as per ICH guidelines. Hence, , from the above result it can be concluded that spray dried microspheres of Olanzapine is a useful technique to improve the solubility and dissolution of poorly water soluble drug like Olanzapine.

ACKNOWLEDGEMENTS

The authors are thankful to IPCA labs, Mumbai, India for the gift sample of Olanzapine and cyclodextrin.

REFFRENCEES

Aarsland D, Larsen JP, Lim NG and Tandberg E. Olanzapine for psychosis in patients with Parkinson's disease with and without dementia. J. Neur. Clin. Neurosci.1999;11:.392-394.

Adamo F, Cristina C, and Giancarlo C. Design of Olanzapine/Lutrol Solid Dispersions of Improved Stability and Performances. Pharmaceutics 2013; 5: 570-590.

Adams BB, Mutasim DF. Pustular eruption induced by olanzapine, a novel antipsychotic agent. J. Am. Acad. Derma.,1999; 41:851-853, 1999.

Abu TM.S. Solid dispersion of poorly watersoluble drugs: early promises, subsequent problems, and recent breakthroughs. J. Pharm. Sci.1999; 88: 1058-1066

Ajit, SK.; Dhairysheel GM.; Pankaj KB. Formulation and in vitro evaluation of orally disintegrating tablets of olanzapine-2-hydroxypropyl-β-cyclodextrin inclusion complex. Iran. J. Pharm. Res. 2010; 9: 335–347.

Almeida OP. Olanzapine for the treatment of tardive dyskinesia (letter). J. Clin. Psychi., 1998; 49:380-381.

Amal AE, Ebtessam AE. Dissolution of ibuprofen from spray dried and spray cooled particles. pak. j. pharm. sci. 2010; 23: 3: 284-290.

Amir B, Fazal S, and Khalid R. Controlled release matrix tablets of olanzapine: Influence of polymers on the in vitro release and bioavailability. AAPS PharmSciTech 2010, 11, 1397–1404.

Anne MJ ,Catherine B and Cynthia K Evaluation of solid dispersion particles prepared with SEDS. Int. J. Pharm., 2003, 250: 385-401

Christian L and Jennifer D. Improving drug solubility for oral delivery using solid dispersions. Eur. J. Pharm. Biopharm. 2000, 50: 47-60.

José LS, Márcia RF, Larissa A R, Monica FS, Pedro JR, Miracy MA. Inclusion complex of methyl-β-cyclodextrin and olanzapine as potential drug delivery system for schizophrenia. Carbohydr. Polym. 2012; 89: 1095–1100.

Kaneto U, Fumitoshi H and Tetsumi I. Cyclodextrin Drug Carrier Systems. Chem. Rev. 1998; 98:2045–2076

Martin Del Valle E.M. Cyclodextrins and their uses: a review. Process Biochem. 2004; 39:1033–1046.

Michael M, Keith M, Sandeep K, Lei S, Geoffrey L. Effects of process variables on the powder yield of spray-dried trehalose on a laboratory spray-dryer. Eur. J. Pharm. Biopharm., 2005; 59: 565-573.

Mudit D, Ashwini GK and Parthasarthi KK. Enhancing the aqueous solubility and dissolution of olanzapine using freeze-drying. Braz. J. Pharm. Sci. 2011, 47, 743–749.

Nahata T and Saini TR. Optimization of formulation variables for the development of long acting microsphere based depot injection of olanzapine. J. Microencapsul. 2008; 25: 426–433.

Rubén DS, Carlos EJ, Robson AS, Angelo MD, Cynthia FF and Aline NG . Pharmaceutical Composition of Valsartan: β-Cyclodextrin:Physico–Chemical Characterization and Anti-Hypertensive Evaluation. Molecules 2010; 15: 4067-4084.

Sekiguchi K and Obi N. Studies on absorption of eutectic mixture. I. A comparison of the behavior of eutectic mixture of sulfathiazole and that of ordinary sulfathiazole in man. Chem. Pharm. Bull.1961; 9: 866-872

Shivakumar GK and James WA. Processing factors in development of solid solution formation of olanzapine for enhancement of drug dissolution and bioavailability. Int. J. Pharm.2001; 229:193-203

Venkateskumar K, Arunkumar N, Priya RV, Siva P, Neema G and Punitha K. Characterization of olanzapine-solid dispersions. Iran. J. Pharm. Res. 2011, 10, 13–24.

Win LC and Sidney R. Pharmaceutical applications of solid dispersion systems. J Pharm Sci. 1971; 60(9): 1281-1302.

Yuh-Fun M, Phuong-Anh N, Kin S and Chung CH. Spray drying performance of bench-top spray dryer for protein aerosol powder preparation. Biotech. Bioeng. 1998; 60: 301-309.

How to cite this article:

Mudit Dixit, R. Narayana Charyulu. Anupama Shetty, Narayana Charyalu, Meghana Rao, Pallavi Bengre, Sharin Thomas. Enhancing Solubility and Dissolution of Olanzapine by Spray Drying Using β- Cyclodextrin Polymer. J App Pharm Sci, 2014; 4 (11): 081-086.