IJPSR (2014), Vol. 5, Issue 4 **(Research Article)**

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 09 November, 2013; received in revised form, 26 December, 2013; accepted, 23 March, 2014; published 01 April, 2014

IMPROVEMENT OF SOLUBILITY AND DISSOLUTION RATE OF CANDESARTAN CILEXETIL BY SOLID DISPERSION IN POLYVINYL PYRROLIDONE

Vishal S. Katti, Atul M. Kadam*, Sandip M. Honmane, Shitalkumar Patil, Sachin Patil and Kiran Bhamare

Department of Pharmaceutics, Ashokrao Mane College of Pharmacy, Peth-Vadgaon, Kolhapur– 416112, Maharashtra, India

Keywords:

Solid dispersion, Carrier, Candesartan cilexetil, Solubility, X-ray diffraction

Correspondence to Author:

Atul M. Kadam

Assistant Professor, Department of Pharmaceutics, Ashokrao Mane College of Pharmacy, Peth-Vadgaon, Kolhapur, Maharashtra, India

E-mail- atulpharma@gmail.com

ABSTRACT: The aim of the present study was to characterize solid dispersion (SD) of Candesartan cilexetil (CC) prepared with polyvinyl pyrrolidone K30 (PVP) for enhancing its solubility and bioavailability. The SDs of Candesartan was prepared by solvent evaporation method. The prepared SDs were evaluated for saturation solubility, practical yield, drug content, and in vitro dissolution study, IR-Spectroscopy, X-ray powder diffractometry (XRD) and differential scanning calorimetry (DSC). The dissolution rates of SDs prepared with PVP was much faster than the pure CC and physical mixtures (PM). The data from the XRD showed that drug was crystalline in bulk and in PM. Significant change in melting peak in DSC thermograms of SDs revealed amorphization. SDs showed marked increase in the solubility of CC with increasing carrier concentration. At the highest ratio of carriers the drug solubility was enhanced about 6-folds for SD in PVP. The dissolution rate was increased with increasing carrier concentration at pH 6.5. XRD data revealed a remarkable interaction between the CC and the carrier that enhanced drug dissolution. The 1:4 ratios were sufficient for conversion of Candesartan to amorphous form.

INTRODUCTION: In pharmaceutical Candesartan cilexetil (CC) is marketed as the angiotensin II receptor antagonist; CC is indicated for the treatment of hypertension and congestive heart failure. Thus, while ACE inhibitors are still considered first-line therapy in research and development an increasing number of drug candidates are poorly water soluble. The solubility and dissolution may become rate limiting factors for effective bioavailability of such drugs upon oral administration [1].

QUICK RESPONSE CODE

DOI: 10.13040/IJPSR.0975-8232.5(4).1550-56

Article can be accessed online on: www.ijpsr.com

DOI link: http://dx.doi.org/10.13040/IJPSR.0975-8232.5(4).1550-56

In congestive heart failure, CC can be used in combination with an ACE inhibitor to achieve improved mortality and morbidity. It is quickly and fully bioactivated by ester hydrolysis to form the active Candesartan during absorption from the gastrointestinal (GI) tract [2, 3, 4].

The use of a prodrug form increases the bioavailability of CC. Despite this, absolute bioavailability is relatively low at 15% (CC tablets) to 40% (CC solution). IC_{50} of this drug is 15 µg/kg. It is described as BCS Class II drug [5]. Water-insoluble drugs show low absorption and poor bioavailability thus there is a need of an improvement in solubility of Class II drug formulations [6]. CC show low and erratic oral bioavailability due to poor dissolution of the drug in the fluids of the gastrointestinal tract (GIT). An enhancement of the dissolution rate of water-

insoluble drug remains one of the most challenging tasks of drug development, because it can increase drug oral bioavailability. It is well established that, the solubility and the bioavailability of poorly water soluble drugs can be improved by converting these drugs into an amorphous state [7].

Several methods such as freeze-drying [8] spray drying [9, 10], melting and quench-cooling [11], melt extrusion and mechanical activation (milling) [12] have been reported to successfully prepare amorphous forms of drugs. Formulation of SDs is another strategy used to increase the solubility and dissolution rate of drugs [13].

The SD technique for water-insoluble drugs provides an efficient solution to improve the dissolution rate of a drug [14]. According to Chiou and Riegelman, SD of one or more active ingredients in an inert carrier or matrix, where the active ingredients could exist in finely crystalline, solubilized or amorphous state. Reported literatures indicate that polymeric carriers have been employed for enhancing the aqueous solubility of insoluble drugs [1]. Drugs when molecularly dispersed in polymeric carriers, may achieve the highest levels of particle size reduction and surface area enhancement, which result in improved dissolution rates [15].

Polymers such as polyethylene glycol (PEG) and Polyvinyl Pyrrolidone (PVP) have been extensively used as carriers for dispersions due to their low melting point and hydrophilic nature [16]. Methods used to produce SDs include melting method, solvent method and solvent wetting method. However, the melting method has limitations that occur incomplete miscibility between drug and carrier due to the high viscosity of a polymeric carrier in the molten state. Thermally unstable drugs can be degraded due to the requirement of relatively high preparation temperatures [17].

In literature first reported application of solvent evaporation method was preparation of SDs of β-carotene with carrier PVP using chloroform as common solvent [18]. Basically, solvent evaporation method involves two steps (i) preparation of a solution containing both matrix material or carrier and drug and (ii) the removal of the solvent resulting in the formation of the solid mass [17].

Nature of the solvent used and the rate and temperature of evaporation are critical factors that can affect the formed mass [19]. One of the unique features of this method is that thermal decomposition of the drugs can be prevented as low temperature is required for the removal of the organic solvents [20]. Till date solvent evaporation method has been reported for valdecoxib [21], carbamazepine [22], fexofenadine hydrochloride [23], and glibenclamide [24], etc.

The literature reported reveals the successful application of this method for improvement in dissolution of poorly water soluble drugs. Manimaran *et al*., in 2010, prepared the SD of glibenclamide by the solvent evaporation method using PVP, PEG and POLO as hydrophilic carrier. In this study, hydrophilic carriers enhanced the solubility of glibenclamide to a varying degree. All SDs increased dissolution rate compared to pure glibenclamide [25].

Although use of SD has been reported frequently in the field of pharmaceuticals, only few SD systems are used commercially [17]. CC is rapidly absorbed after oral administration but since it has poor aqueous solubility its dissolution rate is very low [6].

In this study, we used solvent evaporation method to prepare the SDs of CC using different concentrations of PVP. Methanol was used because it is common solvent for CC and carriers. The physicochemical properties of different systems were determined from DSC and XRD studies.

In addition, the effect of carrier concentration on dissolution properties of CC in SDs was investigated.

MATERIALS AND METHOD: A gift sample of Candesartan cilexetil (CC) was supplied by Alembic Research Centre, Baroda, India. PVP K-30 and Methanol were purchased from S.D. Fine Chemicals, India. All other chemicals used were of analytical grade.

Solubility: The solubility tests of drug sample were carried out in different solvents (aqueous and organic) according to United States Pharmacopeia. The results were then compared with standard.

Estimation of Candesartan Cilexetil: Contents of CC were estimated by UV Spectrophotometric method by measuring the absorbance at 256 nm in water: methanol (1:1). The method was validated for linearity, accuracy, precision and interference. The method obeyed Beers law in the concentration range of 2-10 µg/mL (r = 0.9995).

Preparation of PMs and SDs: Physical mixtures of CC with PVP at 1:2, 1:4 weight ratio of CC: carrier were prepared by blending with trituration for 10 min followed by sieving (500 µm). The prepared mixtures were then filled in glass bottles, sealed and stored in a dessicator until further use.

SD Compositions were selected based on literature reviewed. SDs of CC was prepared at various weight ratios by solvent evaporation method. Amount of carrier was varied keeping amount of CC constant (1:2, 1:4). Accurately weighed amount of CC & PVP are dissolved in the methanol and water respectively. The clear solution was obtained when both the solutions were mixed; Tween 20was added the as a surfactant to same. Then this solution was placed on the hot plate at 60 °C with magnetic stirring until the solvent evaporates. The solid dispersion prepared above was scrapped, dried, and was passed through sieve no.60 and stored in the dessicator until further use.

Practical Yield and Drug Content: Generally, percentage practical yield (% PY) is calculated to know about the efficiency of any method, thus it helps in selection of appropriate method of production. SDs were weighed to determine practical yield and % PY was calculated. SDs equivalent to 10mg of CC were accurately weighed and dissolved in 10 mL of methanol. The solution was filtered, diluted suitably and drug content was determined from absorbance at λ max 256 nm by spectrophotometric method from the following equation**.**

$$PY\ (\%) = \frac{\text{Practical mass (Solid Dispersion)}}{\text{Theoretical mass (Drug +carrier)}} X\ 100$$

Saturation Solubility: An excess amount of drug sample (CC) was added to 1.5 mL of both Water and phosphate buffer pH 6.5 containing 0.7% Tween 20 separately. The samples were shaken for 48 hrs at 37°C in a horizontal orbital shaker. The supernatant was filtered through a Millipore filter (pore size 0.45 µm). Accurately measured 0.5 mL of the filtrate was immediately diluted and analyzed spectrophotometrically using UV-visible spectrophotometer (UV-1700, Shimadzu AS, Japan) at 256 nm after suitable dilution. For determination of saturation solubility of prepared SD, excess quantity of SD was added separately to 1.5 mL of both water and phosphate buffer (pH 6.5) containing 0.7% Tween 20 and then saturation solubility was also measured in the same way. All experiments were conducted in triplicate.

FT-IR Studies: Structural changes and lack of a crystal structure can lead to changes in bonding between functional groups which can be detected by infrared spectroscopy. The FT-IR spectrum was obtained by using FT-IR Spectrophotometer-Jasco. The samples were previously grinded and mixed with Potassium Bromide at 1:100 ratio respectively. The scanning range was 4000-400 cm^{-1}.

DSC Analysis: Differential scanning calorimetry (DSC) studies were carried out using Mettle-Toledo DSC 821 instrument. Indium and zinc standards were used to calibrate the DSC temperature and enthalpy scale. The powdered samples (5 mg) are hermetically sealed in aluminum crucibles and heated at a constant rate of 10°C/min over a temperature range of 25–250°C. Inert atmosphere was maintained by purging nitrogen gas at flow rate of 30 mL/min. Results were obtained in triplicates for each sample.

XRD Analysis: XRD studies have been widely used to understand crystallinity of solids. The XRD patterns were recorded on X-ray diffractometer (PW 1729, Philips. Netherlands). Samples were irradiated with monochromatized Cu-Ka radiation (1.542 A˚) and analyzed from 5^0 to 50^0 2θ. The voltage and current used were 30 kV and 30 mA, respectively. The X-ray diffraction procedure to estimate the degree of crystallinity was based upon the measurement of the total scattering and the scattering from the crystalline region of formulations

***In vitro* Dissolution Studies:** The USP dissolution test type II apparatus (Electrolab TDT- 06 N, India) was used. Amount of samples equivalent to 10 mg of drug were dispersed into the dissolution vessel

containing 900 mL of phosphate buffer pH 6.5 containing 0.75% of Tween 20 at 37°C. and stirred at 50 rpm. Samples were withdrawn periodically, filtered and replaced with a fresh dissolution medium. After filtration through 0.45 µm microfilter, concentration of CC was determined spectrophotometrically at λ max 256 nm. All experiments were carried out in triplicate.

Stability studies: Stability studies of the prepared SDs were carried out at two different storage conditions, Room temperature (RT) and Refrigerated (RF i.e. 2–8°C) for 3 months. Three batches for both formulations were used for each condition. Assay was carried out one month time interval to determine the chemical stability of CC. To determine the drug content of formulation with amount equivalent to 2.5 mg of CC was dissolved in methanol, diluted appropriately, filtered and absorbance of resulting solution was measured spectroscopically at 256 nm.

RESULTS AND DISCUSSION: Percent practical yield and drug content in prepared SDs of (1:2), (1:4) ratio was in the range of 83.44% - 91.64% and 94.82% - 96.33%, respectively. Composition containing CC: PVP at ratio 1:4 showed highest percentage yield and drug content.

Solubility Determination: The aqueous solubility of a drug is a prime determinant of its dissolution rate and absorption. CC is practically insoluble in water and slightly soluble in phosphate buffer pH 6.5 at room temperature. The solubility of CC in phosphate buffer pH 6.5 was markedly increased in presence of PVP. The solubility of CC in phosphate buffer pH 6.5 was found to be 147 µg/mL at 37°C±0.5ºC. Formulated SD 1:2, 1:4 shows 597±0.85 µg/mL and 893 µg/mL in phosphate buffer pH 6.5, respectively. In general, the increase in solubility of CC is 4 fold and 6 fold when SD formulated as 1:2 and 1:4 respectively with PVP.

The results of solubility study revealed that solubility increases with increase in concentration of carrier. Reasons for this might be improved wettability and porosity, decreased primary particle size and partial amorphization of drug in dispersed state compared to raw crystals of CC [26]. Enhanced solubility and dissolution rate of CC in SD prepared using PVP could be attributed to the chemical structure of highly water soluble PVP. PVP has amphiphilic structure and ability to form monomolecular micelles by changing configuration in solution. At higher concentration, these monomolecular micelles associate to form aggregates of varying size, which have the ability to solubilize drug [27]. Results indicated that solubility of Candesartan increases with increase in concentration of PVP.

FT-IR Studies: FT-IR spectroscopic studies conducted for possible drug carrier interaction. FT-IR spectra of pure drug & solid dispersion indicated no significant evidence of chemical interaction between drug and carrier. This confirms the stability of drug with its solid dispersion shown in **figure 1.**

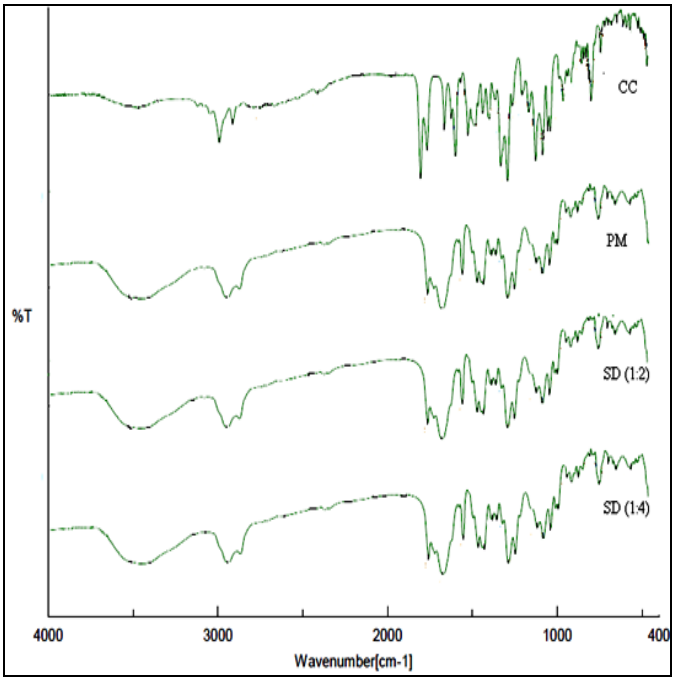

FIGURE 1: IR SPECTRUM OF PURE CC, PM OF CC AND PVP (1:4), SD 1:2, SD 1:4

Differential Scanning Calorimetry: The thermogram of pure CC has shown a sharp endotherm at 169.29°C corresponding to its melting point. This sharp endothermic peak signifies crystalline nature of pure CC. The endothermic peak at 156.3ºC is characteristic melting peak of PVP.

In thermogram of SDs 1:2 and 1:4, endothermic peak was observed at 153.97°C and 153.69°C respectively with the loss of its sharp appearance. The broadening and shifting of peak towards the left side shows the partial conversion of pure crystalline CC into its amorphous form.

The absence of melting peak corresponding to melting of drug was supported by XRD studies. The results suggested that CC is dispersed completely into carrier. Thermograms of CC, PVP and their PM and SDs are shown in **figure 2.** The differences in the thermal behavior of CC in the form of PM and SDs suggested the amorphization of drug dependent of the ratio of the carrier used when prepared as SDs. The thermal analysis indicated decrease in crystallinity of CC in presence of higher proportions of carriers. All PM and SDs in PVP exhibited endothermic peaks due to the fusion of PVP. This revealed the existence of carriers in the crystalline state that was consistent with the appearance of diffraction peaks in the corresponding XRD pattern.

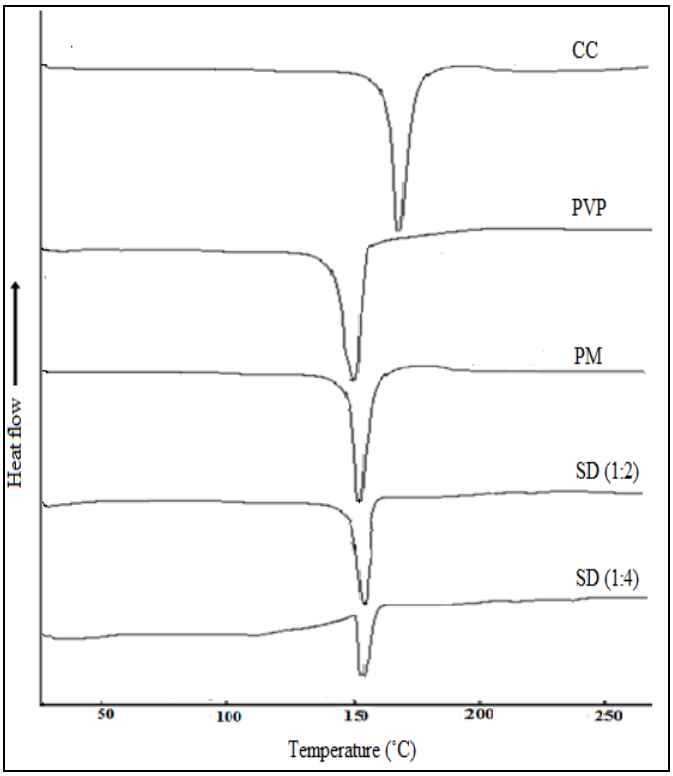

FIGURE 2: DSC THERMOGRAMS OF CANDESARTAN, PVP, PM AND THEIR DIFFERENT SYSTEMS

XRD Analysis: XRD studies were carried out to study transformations in the state of drug in its PMs and SDs. XRD patterns for different systems are shown in **figure 3** for CC-PVP systems, respectively. The diffraction spectrum of pure CC showed that the drug is highly crystalline powder and possesses sharp peaks at 9.86°, 17.04°, and 23.21° at 2° θ. This corresponds to the crystalline form polymorph of CC. Characteristic peaks of PVP appeared at 13.68°, 19.24°, 23.32° and 27.37°2 at 2°θ. PVP showed no prominent peaks.

All the principles peaks from PVP were present in their PMs, but with lower intensities. In the case of the PM, diffractograms were simply the sum of pure components and no interaction could be detected between them particularly at lower ratio (1:2). In case of PM of CC- PVP system at 1:4 ratio, there was a decrease in the intensity of CC but the major peaks remained at the same positions.

The intensity of peaks reflected their mutual concentration. The decrease in the intensity of the diffractogram in case of the SD appeared at 1:2 ratio and the peaks of CC disappeared completely at 1:4 ratio. It could be attributed to the coating of its crystal lattice, because upon evaporation of solvent residual carrier forms a coat around crystals. There was no peak shifting associated to the carriers in PMs indicating formation of an insertion type solid where drug molecules found place inside the structure of the carrier without or with a limited deformation of the original crystal lattice. This is common in mixtures of polymeric carriers with small amounts of low molecular weight drugs. In case of SDs, the intensity of the peaks of CC diminished with the increase in polymer ratio. These observations revealed that the amount of PVP is sufficient to dissolve the CC completely. The amorphization of CC was observed in the SD of CC -PVP at 1:4 ratio, than its PM at same ratio. The results indicated that conversion of crystalline CC into amorphous by different degrees. The reduced peak intensities in XRD patterns clearly indicate that the CC appears amorphous [28].

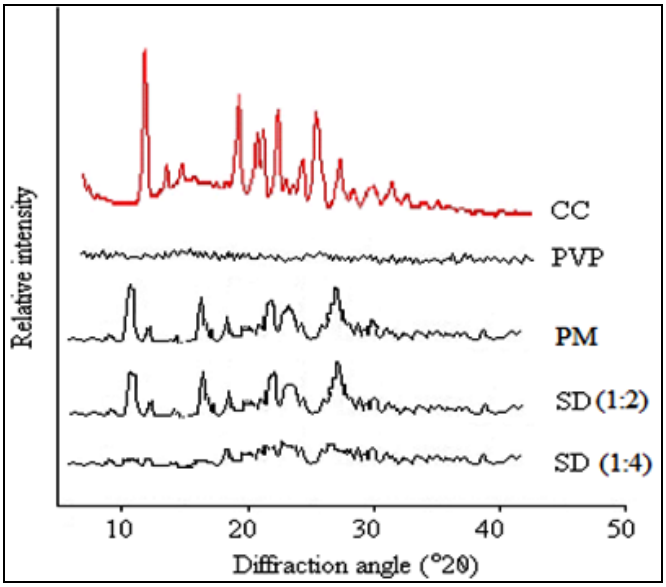

FIGURE 3: XRD DIFFRACTOGRAMS OF CC, PVP, PM AND THEIR DIFFERENT SYSTEMS

***In vitro* Dissolution study:** Drug release studies were carried out in phosphate buffer pH 6.5 shown in **Figure 4.** Blending of CC with carriers in the form of PMs or SDs could enhance the release of CC. The faster dissolution rate of PMs compared to pure drug was observed and it could be attributed to the improvement of wettability of CC particles due to the presence of highly hydrophilic molecular components. Dissolution rates for SDs were greater than those for PMs and CC alone. In the dispersed state CC get entrapped into the hydrophilic coat of carriers and its crystallinity changes with change in its physicochemical properties [29]. PVP changed crystalline CC to amorphous CC enhancing the dissolution rate. This observation is supported by the XRD studies of the SDs. The amount of CC dissolved after 60 min of CC, PMs and its SDs in PVP prepared at different drug: carrier ratios as shown in **Table 1**. The highest amount of drug dissolved after time period was 36.55%, 56.78% form pure CC and PM respectively. In case of SDs of the carriers used the amount of 1:2, 1:4 drug dissolved was 69.25%, 87.12% respectively.

TABLE 1: THE PERCENT DRUG DISSOLUTION AFTER 60 MIN OF CC, PM AND ITS SDS IN PVP PREPARED BY SOLVENT EVAPORATION METHOD AT DIFFERENT DRUG: CARRIER RATIOS

Time (Min)	% Drug Release			
	Pure drug	PM	SD (1:2)	SD (1:4)
0	0.0	0.0	0.0	0.0
10	19.00±0.45	23.37±0.48	30.17±0.64	42.79±0.45
20	25.65±0.68	29.12±0.58	39.48±0.21	51.21±0.75
30	28.73±0.25	35.76±0.56	46.72±0.73	59.71±0.64
40	31.85±0.67	43.68±0.22	54.88±0.42	66.78±0.94
50	33.79±0.71	49.76±0.89	61.64±0.97	75.33±0.38
60	36.55±1.021	56.78±0.74	69.25±0.21	87.12±0.91

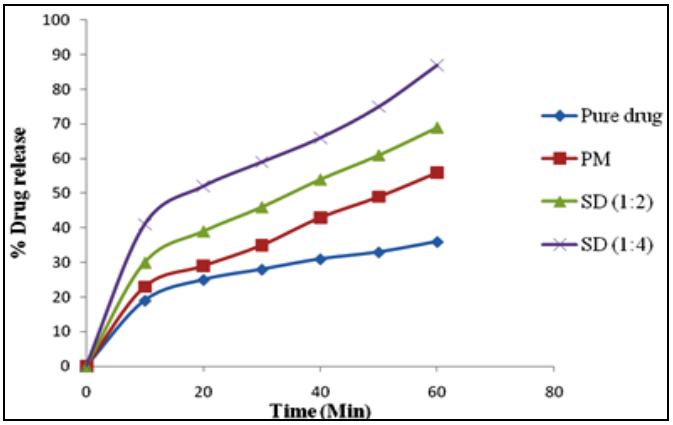

FIGURE 4: DISSOLUTION PROFILES OF CC AND CC - PVP SYSTEMS IN PHOSPHATE BUFFER pH 6.5

Stability studies: The stability of prepared SDs observed was satisfactory at both conditions for 3 months as active content was more than 95% in all cases. Although the active contents are above 95%, it follows a decline order with time so its storage should be maintained at refrigerated condition (**Table 2**).

Thus, it can be concluded that the stability of CC was not affected due to heating and the formulation was stable for 3 months. Further studies are needed to prove long term stability of the formulation and to find out reasons for the decline order.

TABLE 2: % DRUG CONTENT OF SDS AT VARIOUS STABILITY STORAGE CONDITIONS

Stability Condition	Formulation	% Drug content ±SD			
		Initial	1Month	2Month	3Month
Room Temperature	SD (1:2)	99.69±0.73	98.19±0.28	97.26±0.69	96.29±0.25
	SD (1:4)	99.73±0.33	98.67±0.33	97.19±0.88	96.68±0.19
Refrigerator	SD (1:2)	99.69±0.73	98.87±0.39	98.08±0.65	97.11±0.44
	SD (1:4)	99.73±0.33	99.19±0.43	98.37±0.28	97.39±0.56

CONCLUSION: The study demonstrates that dispersions of CC into water-soluble carriers change the crystallinity of CC relative to the type and the amount of the carrier. The formation of CC -PVP SD almost completely destroys the crystallinity of the drug and represents a suitable modification for improving its solubility. Decrease in agglomeration of particles, increase in wettability and decrease in crystallinity of the drug contributes to faster dissolution rate. Preliminary results from this work indicate that preparation of CC SDs by solvent evaporation method using hydrophilic polymer carrier PVP could be a promising approach to improve solubility and dissolution rate of CC. The higher ratio of PVP (1:4) tested in this study was sufficient for conversion of CC to amorphous form.

ACKNOWLEDGEMENT: The authors express their gratitude to Alembic Research Centre, Baroda, India, for providing Candesartan as gift sample for this research work.

REFERENCES:

1. Patel T, Patel L and Makwana S: Formulation and characterizati on of solid dispersions containing glibenclamide.Int J Pharmacy and Pharm Sci 2010; 2(3): 138-141.
2. Mizno K, Niimura S, Tani M, Saito J, Sanada H and Takakashi M: Hypotensive activity of TV-116, a newly developed angiotensin II receptor antagonist in spontaneously hypertensive rats. Life Sci 1992; 51: 183–187.
3. Delacretaz E, Nussberger J, Biollaz J, Waeber B and Brunner H: Characterization of the angiotensin II receptor antagonist TCV-116 in healthy volunteers. Hypertension 1995; 25: 14–21.
4. Detroja C, Chavhan S, and Sawant K: Enhanced Antihypertensive Activity of Candesartan Cilexetil Nanosuspension: Formulation, Characterization and Pharmacodynamic Study. Sci Pharm 2011; 79: 635–651
5. Jyothi S, Reddy K, Mohanty S, Reddy A: Preformulation study of the inclusion complex candesartan cilexetil - hpβcd and its comparision with βcd Int J Current Pharm Res 2013: 5(3); 48-53.
6. Hirasawa N, Ishise S, Miyata H and Danjo K: Physicochemical characterization and drug release studies of nilvadipine solid dispersions using water-insoluble polymer as a carrier. Drug Dev Ind Pharm 2003; 29: 339-44.
7. Hilden L and Morris K: Physics of amorphous solids. J Pharm Sci 2004; 93: 3-12.
8. Cavallari C, Luppi B, Dipietra A, Rodriguez L and Fini A: Enhanced release of indomethacin from PVP/stearic acid microcapsules prepared coupling co-freeze-drying and ultrasound assisted spray-congealing process. Pharm Res 2007; 24:521-29.
9. Paradkar A, Ambike A, Jadhav B and Mahadik K: Characterization of curcumin-PVP solid dispersion obtained by spray drying. Int J Pharm 2004; 271: 281-286.
10. Weuts I, Kempen D, Verreck G and Decorte A: Study of the physicochemical properties and stability of solid dispersions of loperamide and PEG 6000 prepared by spray drying. Eur J Pharm Biopharm 2005; 59: 119-126.
11. Gahoi S, Jain G, Singhal M and Anwar M: Influence of novel dispersed fusion technique on dissolution and pharmacotechnical properties of pharmaceutical solid dispersion. Int J Pharm Sci Rev Res 2011; 8: 170-175.
12. Forster A, Hempenstall J and Rades T: Characterization of glass solutions of poorly water soluble drugs produced by melt extrusion with hydrophilic amorphous polymers. J Pharm Pharmacol 2001; 53: 303-315.
13. Christian L and Jennifer D: Improving drug solubility for oral delivery using solid dispersions. Eur J Pharm Biopharm 2000; 50: 47-60.
14. Abu T: Solid dispersion of poorly water soluble drugs: early promises, subsequent problems and recent breakthroughs. J. Pharm. Sci.1999; 88: 1058-1066.
15. Leuner C and Dressman J: Improving drug solubility for oral delivery using solid dispersions. Eur J Pharm Biopharm 2000; 50: 47-60.
16. Hancock B and Parks M: What is the true solubility advantage for amorphous pharmaceuticals? J Pharm Res 2000; 17: 397-404.
17. Ford J: The current status of solid dispersions. Pharm Acta Helv 1986; 61: 69-88.
18. Ketan Savjani, Anuradha Gajjar and Jignasa Savjani: Drug Solubility: Importance and Enhancement Techniques. International Scholarly Research Network Pharmaceutics 2012; 195727.
19. Yamashita K, Nakate T and Okimoto K: Establishment of new preparation method for solid dispersion formulation of tacrolimus. Int J Pharm 2003; 267: 79-91.
20. Dasi S and Roy S. Solid dispersions: an approach to enhance the bioavailability of poorly water-soluble drugs. Int J Pharmacol Pharm Tech 2008; 3: 227-243.
21. Patel M and Patel D: Fast dissolving valdecoxib tablets containing solid dispersion of valdecoxib. Indian J Pharm Sci 2006; 68: 222-226.
22. Sethia S and Squillante E: Physicochemical characterization of solid dispersions of carbamazepine formulated by supercritical carbon dioxide and conventional solvent evaporation method. J Pharm Sci 2002; 91: 1948-57.
23. Sams M, Anowar S and Reza-ul J: Enhancement of dissolution profile for oral delivery of fexofenadine hydrochloride by solid dispersion (solvent evaporation) technique. Am. J Sci Ind Res 2011; 2: 112-115.
24. Dastmalchi S and Garjani A. Enhancing dissolution, serum concentrations and hypoglycemic effect of glibenclamide using solvent deposition technique**.** J Pharm Sci 2005; 8: 175-181.
25. Manimaran V and Damodharan V: Enhancement of dissolution rate of glibenclamide by solid dispersion technology. Int J Current Pharm Res 2010; 2(3): 975-984.
26. Yadav V and Yadav A: Recrystallized agglomerates of indomethacin by emulsion solvent diffusion technique. Int J Pharm Bio Sci 2010; 1:1-13.
27. Kabanov K, Batrakova E and Alakhov V: Pluronic block copolymers as novel polymer therapeutics for drug and gene delivery. J. Control. Release 2002; 82: 189-212.
28. Shah T and Amin A: Process optimization and characterization of poloxamer solid dispersions of a poorly water-soluble drug. AAPS Pharm Sci Tech 2007; 8: 29-36.
29. Hajare A and Jadhav P: Improvement of Solubility and Dissolution Rate of Indomethacin by Solid Dispersion in Polyvinyl Pyrrolidone K30 and Poloxomer 188. Asian J Pharm Tech 2012; 2(3): 116-122.

How to cite this article:
Katti VS, Kadam AM, Honmane SM, Patil S, Patil S and Bhamare K: Improvement of solubility and dissolution rate of Candesartan cilexetil by Solid Dispersion in Polyvinyl pyrrolidone. *Int J Pharm Sci Res* 2014; 5(4): 1550-56.doi: 10.13040/IJPSR.0975-8232.5(4).1550-56