IJPSR (2012), Vol. 3, Issue 10 **(Research Article)**

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 05 June, 2012; received in revised form 25 July, 2012; accepted 20 September, 2012

DESIGN AND EVALUATION OF FAST DISSOLVING TABLETS OF CARVEDILOL USING SUBLIMATION TECHNIQUE

Mohd Azharuddin*, Krishnananda Kamath and A.R. Shabaraya

Department of Pharmaceutics, Srinivas College of Pharmacy, Valachil, Mangalore, Karnataka, India

Keywords:
Carvedilol, β-Cyclodextrin, *in-vitro* and sublimation technique

Correspondence to Author:

Mohd Azharuddin

Department of Pharmaceutics, Srinivas College of Pharmacy, Valachil, Mangalore, Karnataka, India

E-mail: azhar.12345@rediffmail.com

QUICK RESPONSE CODE

IJPSR: ICV- 4.57

Website: www.ijpsr.com

ABSTRACT

The purpose of the study was to design and evaluate fast dissolving carvedilol tablets using β-Cyclodextrin and superdisintegrants adopting sublimation technique. Tablets were prepared by direct compression method. Tablets were evaluated for their physico chemical properties, wetting time, disintegration, *in-vitro* release and stability studies. SEM analysis was carried out to determine the surface characteristics of solid dispersions. Precompressional studies revealed good micromeritic properties of powder blend for direct compression. The hardness (3.9-4.3 kg/cm^2), friability (0.35-0.51), drug content (96.58-99.43 %) and disintegration time (44.05-66.21 sec) of fast dissolving tablets were found uniform and reproducible. Dissolution of tablets was directly proportional to the superdisintegrants concentration. Selected tablet (F1) was found superior than any other formulations with respect to disintegration and dissolution time.

INTRODUCTION: The concept of fast dissolving drug delivery system emerged from the desire to provide patient with conventional mean of taking their medication. Difficulty in swallowing (Dysphagia) is a common problem of all age groups, especially elderly and paediatrics, because of physiological changes associated with these groups of patients.

Solid dosage forms that can be disintegrated, dissolved, or suspended by saliva in the mouth resulting in easy swallowing can provide significant benefits to the paediatric and geriatric population, as well as other patients who prefer convenience of easily swallowable dosage form.

Fast dissolving tablets disintegrates instantaneously when placed on tongue, releasing the drug that dissolves or disperses in the saliva leading faster release of the drugs in the oral cavity [1]. Cyclodextrins (cyclic linked oligosaccharides) have been shown to improve the bitter taste masking of the drug by trapping the drug within the cyclic structure long enough to render initial dissolution. The other taste masking methods are namely, coating methods including electrochemical, hot melt and super critical fluids [2, 3].

In sublimation technology, the high porosity necessary for fast disintegration is achieved by using volatile materials. Inert solid ingredients, such as urea, ammonium carbonate, ammonium bicarbonate, hexamethylene tetramine, and camphor, can volatilize readily. When these volatile materials are compressed into tablets, they can be removed via sublimation, which generates porous structures. In addition, several solvents (e.g., cyclohexane, benzene) can also be used as pore forming agents [4, 5].

Carvedilol is a novel multiple-action cardiovascular drug that is currently approved in many countries for the treatment of hypertension and used in treatment of coronary artery disease, left ventricular dysfunction

following myocardial infarction and congestive heart failure [6]. Carvedilol reduces the risk of death as well as the risk of hospitalization for cardiovascular causes in patients with heart failure who are receiving treatment with digoxin, diuretics and an angiotensin-converting-enzyme inhibitor. Its bioavailability is 25-35% only indicating extensive first pass metabolism in liver which is an ideal feature for rapid release drug delivery system [7].

MATERIALS AND METHODS:

Materials: Carvedilol B.P was obtained from M/s Vijashree chemicals Pvt. Ltd., Hyderabad, India. Beta cyclodextrin was obtained from Stride Organics Pvt. Ltd., Uttarkhand, India. Indion 414 was obtained from Ion Exchange India Ltd., Mumbai, India. Croscaramellose sodium and Sodium starch glycolate were obtained from Maruti Chemicals., Ahmedabad, India. All other ingredients used throughout the study were of analytical grade and were used as received.

Methods:

Preparation of complex of Carvedilol with Beta cyclodextrin: A mixture of carvedilol and β cyclodextrin in 1:2 ratio was grounded in motar by adding hydro alcoholic solution (ethanol: water = 15:85) and kneaded thoroughly with a pestle to obtain a paste which was dried under vacuum at room temperature passed through sieve no.60 and stored in a desiccator.

Solubility studies of Carvedilol and Solid Dispersion: The solubility of carvedilol and its solid dispersion prepared was determined in phosphate buffer of pH 6.8. The solubility study was conducted by taking excess amount of the drug and solid dispersions in 10 ml of buffer solution. Then the samples were kept in the water bath shaker and agitated for 24 h at 37 ± 0.5°C. The samples were filtered and diluted suitably with buffer solution. The samples were analyzed spectrophotometrically at 242 nm. The concentration of drug was determined.

Scanning Electron Microscopy (SEM): The morphologies of solid dispersions was examined by using SEM. Dried samples were attached to specimen stubs using double-sided copper tape and sputter coated with gold palladium in the presence of argon gas using a Hummer I sputter coater (Anatech Ltd., Denver, NC). The samples were imaged with scanning electron microscope (JEOL USA Inc., Peabody, MA) using a 5 kv accelerating voltage.

***In-vitro* dissolution of Solid Dispersion:** *In-vitro* drug release for prepared solid dispersion were carried out using USP XXIV (Type II) dissolution apparatus at 37±0.5°C and 100 rpm speed using 900 ml of phosphate buffer pH 6.8 as dissolution medium. At a predetermined interval of time 5 ml of sample was withdrawn and replaced with fresh medium. After filtration and appropriate dilution, the samples were analysed at 242 nm for carvedilol by UV-visible spectrophotometer against blank. The amounts of drug present in samples were calculated. The test was done in triplicate.

Micromeritic properties of Solid Dispersion:

1. **Angle of Repose** [7]: A funnel was fixed at a particular height on a burette stand. A graph paper was placed below the funnel on the Table. The blended powder was passed through the funnel until it forms a pile. The radius of the pile was noted down. Angle of repose of the powder material was calculated using the formula.

$$\text{Angle of repose } (\theta) = \tan^{-1} h/r$$

Where, h is height of the pile and r is radius of the pile. The test was repeated thrice.

2. **Apparent Bulk Density** [8]: The bulk density, as a measure used to describe packing materials or granules, was determined by transferring the accurately weighed amount of blend to the graduated cylinder (10 ml) with the aid of a funnel. The volume was noted. The ratio of weight of the sample to the volume occupied was calculated. The test was repeated thrice.

3. **Tapped Density** [8]: Weighed quantity of blend, was transferred to a 10 ml graduated cylinder and tapped manually at specific height for a fixed number of taps (100). Average of three determinations was taken. The tapped density was determined as the ratio of weight of sample to tapped volume.

$$\text{Density} = \frac{\text{Mass}}{\text{Volume}}$$

Carr's Index [9]: The compressibility of sample blend was determined from their apparent bulk density and the tapped densities by using the following formula. The test was carried out in triplicate.

$$\%\text{Compressibility} = \frac{\text{Tapped density} - \text{Bulk density}}{\text{Tapped density}} \times 100$$

Hausner's Ratio [9]: Hausner's ratio is an indication of the flowability of powder and the ratio is greater than 1.25 is considered to be an indication of poor flowability. Hausner's ratio was determined by the ratio of tapped density/bulk density. The test was done in triplicate.

Preparation of Tablets by Sublimation Technique: The solid dispersions equivalent to 12.5 mg of carvedilol, diluents, superdisintegrants, sublimating agent and sweetening agent were passed through sieve no.60 and mixed together. Magnesium stearate and aerosil passed from mesh no.80 were mixed and blended with above mixture. Then the tablets were prepared by direct compression method using 4 mm flat punches on a 10 station rotary compression machine. After compression the tablets were heated by vacuum drying technique at 45^{o}C until a constant weight was obtained to ensure the complete removal of sublimable component. The sublimable component was removed to make the tablet porous. The various tablets were formulated as per **Table 3**.

Post compression properties of solid dispersion:

1. **Thickness and Diameter** [10]: Thickness and diameter of prepared tablets were tested by using vernier calipers. The test was done in triplicates and average was determined.

2. **Hardness** [10]: The hardness of prepared tablets were determined by using Monsanto hardness tester and measured in terms of kg/cm^2. Test was done in triplicate.

3. **Friability** [11]: The test was performed to assess the effect of friction and shocks, which may often cause tablet to chip, cap or break. Roche friabilator was used for testing the friability of prepared fast dissolving tablets. 20 tablets were accurately weighed and placed in the friabilator and operated for 100 revolutions. The tablets were de-dusted and reweighed. Friability (F) was calculated using the following formula.

$$F = (1 - W_0/W) \times 100$$

Where, W_0 and W are the weight of the tablets before after the test respectively. The test was done in triplicate.

The tablets that loose less than 1% weight were considered to be compliant.

4. **Weight Variation:** The weight variation test was done by (Shimadzu digital balance) weighing 20 tablets individually, calculating the average weight and comparing the individual tablet weights to the average. The percentage weight deviation was calculated and then compared with USP specifications.

5. **Drug Content** [12]: Weighed tablets (5) were powdered using a glass mortar and pestle. An accurately weighed quantity of powder equivalent to 12.5 mg of carvedilol was taken into 50 ml volumetric flask, dissolved in phosphate buffer of pH 6.8 and the solution was filtered through Whatman filter paper no.41. The filtrate was collected and suitably diluted with phosphate buffer of pH 6.8. The drug content was determined at 242 nm by UV-spectrophotometer (UV-1700 Shimadzu Corporation, Japan) against blank. The test was done in triplicate.

6. **Disintegration test** [12]: Six tablets along disc were introduced in each tube of basket of disintegration test apparatus (Lab care instruments). The basket was positioned into a beaker containing 900 ml of distilled water and operated at 37 $\pm$ 0.5^{o} C. The time of disintegration of tablet was recorded. The average time and standard deviation were calculated. Three trails were performed.

7. **Wetting time** [13]: A piece of tissue paper folded twice was placed in a small Petri dish (internal diameter = 6.5cm) containing 5 ml of distilled water. A tablet was placed on the paper, and the time for complete wetting of the tablet was measured. Test was repeated thrice.

8. **Water Absorption Ratio** [13]: A piece of tissue paper folded twice was placed in a small Petri dish (internal diameter = 6.5cm) containing 5 ml of distilled water. A tablet was placed on the tissue paper. The wetted tablet was weighed. The test was done in triplicate. The water absorption ratio (R) was determined according to the following equation,

$$R = \frac{W_a - W_b}{W_b} \times 100$$

Where, W_a is the weight of the tablets before the test and W_b is the weight of the tablet after water absorption.

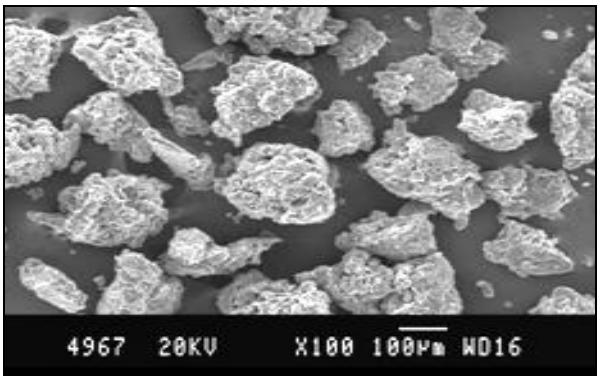
9. ***In-vitro* drug release studies**: Dissolution test was carried out using USP type II dissolution test apparatus. One tablet containing 12.5 mg of carvedilol was taken and the test was carried out as per method described earlier for solid dispersions.

10. **Stability studies** [14]: The selected formulations were also subjected for temperature dependent stability studies as per ICH guidelines. The formulations were stored at 40±0.2°C 75% RH in stability chamber for a period of one month. The formulations were studied for drug content, disintegration time and *in-vitro* drug release.

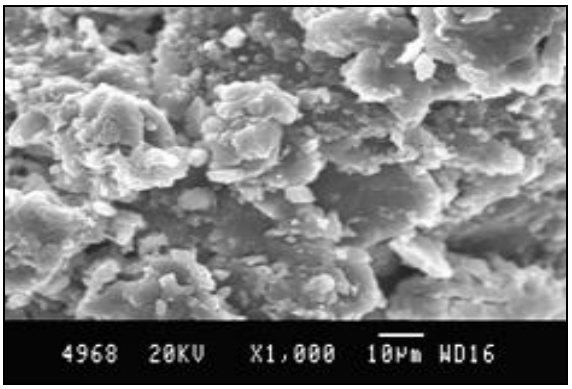
RESULTS:

TABLE 1: SOLUBILITY STUDIES OF CARVEDILOL AND SOLID DISPERSION

Sl. No	Components	Concentration (mg/ml)
1.	Carvedilol	0.358 ± 0.005
2.	Solid dispersion	32.05 ± 0.034



A



B

FIG. 1: SCANNING ELECTRON MICROSCOPY (SEM) OF SOLID DISPERSION (A) AND ITS SURFACE (B)

Table 2: *In-vitro* dissolution of solid dispersion.

Time (min)	Cumulative % Drug Release	
	Pure Drug	Solid Dispersion
0	0	0
5	5.947	29.113
10	8.172	43.048
15	13.069	51.269
30	22.376	65.169
45	28.917	76.640
60	34.554	90.365

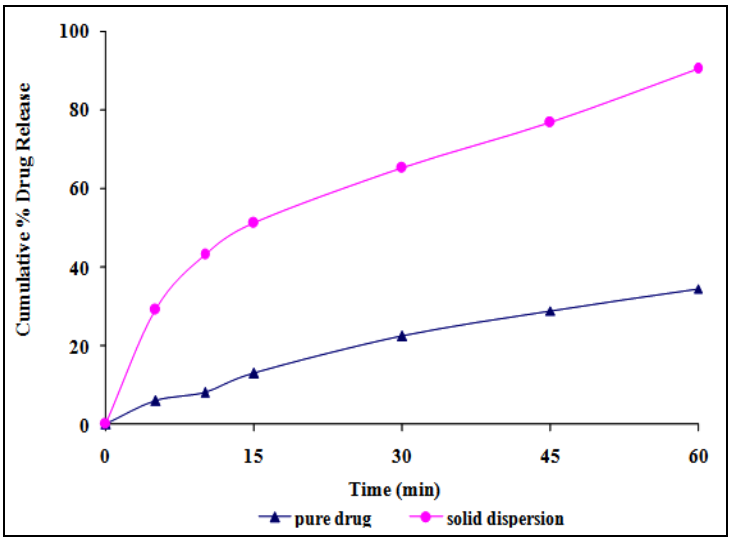


FIGURE 2: *IN VITRO* DISSOLUTION OF SOLID DISPERSION

TABLE 3: COMPOSITION OF CARVEDILOL FAST DISSOLVING TABLETS PREPARED BY SUBLIMATION TECHNIQUE

Ingredients (mg)	Formulation code								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
Quantity of complex equivalent to 12.5 mg of carvedilol	87.5	87.5	87.5	87.5	87.5	87.5	87.5	87.5	87.5
Cross caramellose sodium	9	6	3	---	---	---	---	---	---
Sodium starch glycolate	---	---	---	9	6	3	---	---	---
Indion-414	---	---	---	---	---	---	9	6	3
Sucralose	1	1	1	1	1	1	1	1	1
Menthol	15	15	15	15	15	15	15	15	15
Directly compressible mannitol	40	40	40	40	40	40	40	40	40
Microcrystalline cellulose	44.5	47.5	50.5	44.5	47.5	50.5	44.5	47.5	50.5
Magnesium stearate	2	2	2	2	2	2	2	2	2
Aerosil	1	1	1	1	1	1	1	1	1
Total weight	200	200	200	200	200	200	200	200	200

TABLE 4: MICROMERITIC PROPERTIES OF SOLID DISPERSION

Formulation code	Bulk density* (gm/cm^3)	Tapped density* (gm/cm^3)	Angle of repose* (θ)	Carr's Index* (%)	Hausner's Ratio*
F1	0.43 ± 0.11	0.48 ± 0.24	13.32 ± 0.15	10.41 ± 0.03	1.11 ± 0.01
F2	0.54 ± 0.11	0.59 ± 0.63	14.36 ± 0.51	10.16 ± 0.02	1.09 ± 0.01
F3	0.46 ± 0.10	0.52 ± 0.42	15.81 ± 0.21	11.53 ± 0.03	1.13 ± 0.03
F4	0.51 ± 0.09	0.58 ± 0.52	13.98 ± 0.13	12.06 ± 0.05	1.10 ± 0.02
F5	0.46 ± 0.14	0.52 ± 0.35	14.21 ± 0.53	13.20 ± 0.01	1.12 ± 0.01
F6	0.40 ± 0.13	0.47 ± 0.43	15.72 ± 0.32	14.89 ± 0.03	1.01 ± 0.03
F7	0.42 ± 0.11	0.48 ± 0.33	14.38 ± 0.15	12.50 ± 0.05	1.14 ± 0.05
F8	0.40 ± 0.12	0.49 ± 0.36	15.70 ± 0.18	13.04 ± 0.01	1.22 ± 0.03
F9	0.42 ± 0.23	0.49 ± 0.42	16.54 ± 0.12	14.28 ± 0.03	1.16 ± 0.02

*****Average of 3 determinations ± SD

TABLE 5: POST COMPRESSION PROPERTIES OF SOLID FAST DISSOLVING TABLETS

Formulation code	Thickness** (mm)	Hardness test* (kg/cm^2)	Weight variation*** (%)	Friability**	Drug content* (%)
F1	4.28 ± 0.01	4.0 ± 0.36	199.64 ± 1.71	0.42 ± 0.03	99.23 ± 0.71
F2	4.30 ± 0.05	4.1 ± 0.28	198.55 ± 1.35	0.51 ± 0.01	98.63 ± 0.45
F3	4.28.± 0.01	3.8 ± 0.32	200.66 ± 1.48	0.49 ± 0.02	96.58 ± 0.73
F4	4.31 ± 0.03	4.1 ± 0.34	201.51 ± 1.56	0.37 ± 0.03	99.04 ± 0.65
F5	4.28 ± 0.02	4.2 ± 0.43	196.64 ± 1.63	0.39 ± 0.01	98.37 ± 0.42
F6	4.32 ± 0.01	4.0 ± 0.63	200.78 ± 1.45	0.42 ± 0.03	99.43 ± 0.65
F7	4.31 ± 0.03	3.9 ± 0.26	200.42 ± 1.68	0.35 ± 0.05	98.08 ± 0.45
F8	4.33 ± 0.05	4.1 ± 0.58	199.58 ± 1.32	0.49 ± 0.03	99.28 ± 0.35
F9	4.31 ± 0.03	4.3 ± 0.34	201.61 ± 1.58	0.51 ± 0.01	97.02 ± 0.62

All values are expressed as mean ± SD, n=5/10**/20***

TABLE 6: COMPARISON OF WETTING TIME, DISINTEGRATION TIME AND WATER ABSORPTION RATIO

Formulation code	Wetting time* (sec)	Disintegration time* (sec)	Water absorption ratio*
F1	38.28 ± 1.3	44.05 ± 1.6	72.08 ± 1.3
F2	46.63 ± 1.1	52.12 ± 1.5	70.50 ± 1.2
F3	54.12 ± 1.5	58.08 ± 1.0	67.34 ± 1.6
F4	43.08 ± 1.4	50.12 ± 1.1	70.28 ± 1.7
F5	50.12 ± 1.3	58.13 ± 1.3	68.50 ± 1.5
F6	60.28 ± 1.8	66.21 ± 1.2	65.06 ± 1.4
F7	40.15 ± 1.2	45.35 ± 1.4	68.32 ± 0.8
F8	48.23 ± 1.5	54.21 ± 1.2	65.56 ± 1.2
F9	58.16 ± 1.1	63.16 ± 1.6	62.63 ± 1.3

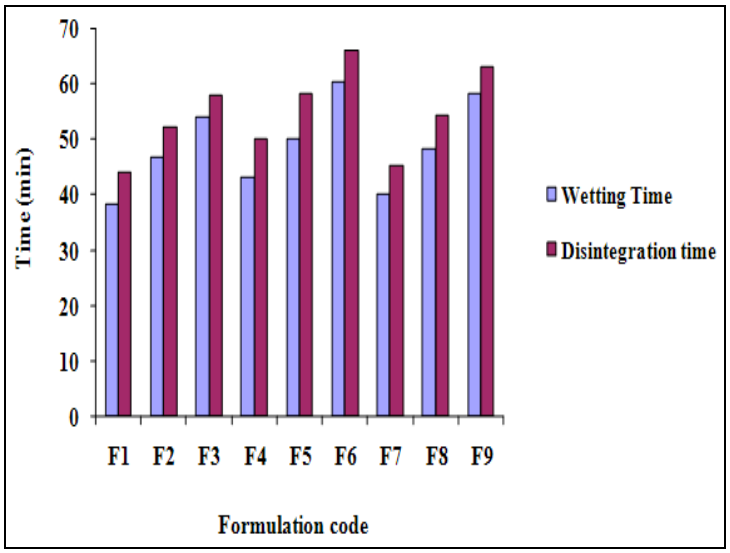


FIGURE 3: COMPARISON BETWEEN WETTING AND DISINTEGRATION TIME

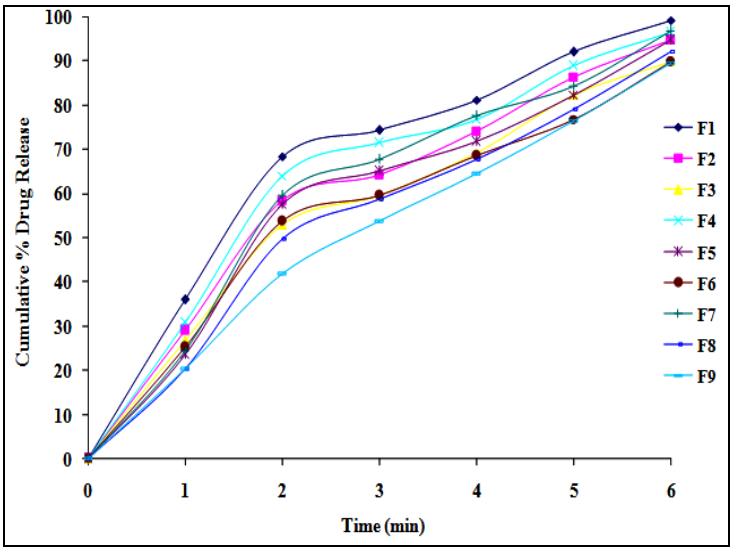


FIGURE 4: *IN VITRO* RELEASE DATA OF CARVEDILOL FROM TABLET CONTAINING SUBLIMATING AGENT AND SUPERDISINTEGRANTS (CCS, SSG AND INDION-414)

TABLE 7: *IN-VITRO* RELEASE DATA OF CARVEDILOL FROM TABLETS CONTAINING SUBLIMATING AGENT AND SUPERDISINTEGRANTS (CCS, SSG AND INDION-414)

Time (min)	Cumulative % Drug Release								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
1	36.08	29.16	26.78	30.74	23.62	25.20	24.53	20.47	20.46
2	68.35	58.49	52.92	64.02	57.62	53.70	59.49	49.73	41.82
3	74.34	64.33	59.51	71.47	65.03	59.51	67.74	58.67	53.86
4	81.17	74.15	69.29	76.59	71.69	68.50	77.61	67.66	64.39
5	92.04	86.38	82.27	88.83	82.33	76.75	84.37	79.06	76.55
6	99.09	94.73	89.81	96.42	94.59	89.77	96.70	92.09	89.56

TABLE 8: STABILITY DATA OF F1 AFTER ONE MONTH STUDY.

Formulation code	Drug content* (%)	Disintegration time (sec)	Cumulative % Drug Release
F1	99.18± 0.27	38.68	98.26 ± 0.4

DISCUSSION: The solubility of pure carvedilol and solid dispersion was carried out in phosphate buffer of pH 6.8. The solubility of pure drug, solid dispersion was found to be 0.358 and 32.05 mg/ml respectively. The solubility of carvedilol was in accordance with the reported value of 0.323mg/ml by Shailesh *et al*. It showed that the solubility of pure drug in pH 6.8 was enhanced to 100% with its solid dispersions technique. The results are shown in **Table 1**.

In-vitro release of pure drug and solid dispersion in pH 6.8 was found 34.55 and 90.36% respectively at the end of 60 min. Studies showed that solid dispersion have enhanced the drug solubility and dissolution rates. The results are shown in **Table 2 and Fig 2**. **Fig. 1** shows different magnifications of SEM micro-photographs of solid dispersion and their surfaces. Particles appear as irregular shaped agglomerates with rough surface indicating an amorphous nature. The surface topography shows presence of less crystalline drug, uniformly and finely dispersed or adhered to the carrier surface was observed in solid dispersion. Fast dissolving tablets were prepared by using super-disintegrants like CCS, SSG and Indion-414 in three different concentrations 1.5, 3 and 4.5% w/w of tablets.

Directly compressible vehicles like mannitol and MCC were used as diluents. Besides the improvement of flow and compaction properties the directly compressible vehicles may aid optimum release of drug from the tablet.

Magnesium stearate and aerosil were used as lubricants and antadherent to facilitate easy compression and ejection of tablets. Sucralose as sweetening agent was used. Menthol was used as sublimating agent which facilitates faster disintegration of tablets. The compositions of different fast dissolving tablets are shown in the **Table 3**.

The method employed for preparation of FDTs in the study was direct compression for which the drug or the mixture of drug and polymer should posses good flow properties. **Table 4** shows the micromeritic property of precompressional mixture. Studies showed the angle of repose value of 13.32-16.54^{o} indicating good flow property. Bulk density was found in between 0.40-0.54 gm/cm^2 and tapped density between 0.47-0.59% gm/cm^2 for all the formulations.

From density data % compressibility was calculated. It was further supported by good carr's index value of 10.16-14.89% and Hausner's ratio of 1.01-1.22 for all precompressional mixtures. Hence powder mixture was found suitable for direct compression method. Further the tablets were subjected to physico-chemical evaluation. The results of physicochemical evaluation of tablets are given in **Table 5**.

As the material was free flowing, tablets were obtained of uniform weight due to uniform die filling. Hardness of tablets was between 3.8-4.3 kg/cm^2 for all the formulations. The thickness was found in range of 4.28-4.33 mm. Friability was found in between 0.35-0.51. The value below 1% was an indication of good mechanical resistance of the tablet. The drug content was found to be 96.58-99.43 % which was with in the acceptable limits.

Disintegration time is very important for FDTs which is desired to be less than 67 sec. Wetting time is used as an indication from the ease of tablet disintegration in buccal cavity. There is a good relationship between wetting time and disintegration time. The wetting time decreases with increase in the concentration of superdisintegrants. It was observed that as the concentration of superdisintegrants increases water absorption ratio increases and disintegration time decreases. Sublimating agent enhances the wetting of tablet due to formation of pores.

The porous structure is responsible for faster water uptake hence it facilitates wicking and swelling of superdisintegrants in bringing about faster disintegration. The results are shown in **Table 6 and Fig 3**. The *in-vitro* dissolution of carvedilol tablets was studied in phosphate buffer of pH 6.8 using USP XXIV dissolution test apparatus by paddle method.

Sublimation technique was adopted to enhance the dissolution of Solid dispersion FDT using 7.5% w/w menthol as sublimating agent with superdisintegrants like CCS, SSG and Indion 414 (F1-F9). The release profiles indicated the faster and maximum drug release due to easy breakdown of particles due to porous structure formation after sublimation of menthol. At 4.5% superdisintegrants level the drug release at the end of 6 min were found to be 99.09, 96.42 and 96.70% with CCS, SSG and Indion-414 respectively (**Fig. 4**).

The release was also proportionate with superdisintegrant concentration. The results of dissolution profile of FDT were in accordance with that of disintegration data. Hence overall release data of FDT was proportionate with that of disintegration data irrespective of superdisintegrants. The stability studies were carried out for selected tablets (F1) at 40^{o}±2C, 75% RH for one month. The fast dissolving tablets were evaluated by their drug content, disintegration and drug release. The studies indicated that no significant change in disintegration time, drug content and drug release profiles as shown in Table 8. This indicates that the tablets are stable at 40^{o}±2C, 75% RH.

CONCLUSION: The present research work revealed that the sublimation technique along with superdisintegrants in the concentration of 4.5% can be used to enhance the disintegration and dissolution time of poorly soluble drug.

ACKNNOWLEDGEMENT: The authors are thankful to M/s Vijashree chemicals Pvt. Ltd., Hyderabad, India and Srinivas College of Pharmacy Mangalore, India for providing necessary facilities to carry out this research work.

REFERENCES:

1. Kaushik D, Dureja H, Saini TR. Mouth dissolving tablets: A review. Indian Drugs 2004; 41:181-93.
2. Brown D. Orally disintegrating tablets–taste over speed. Drug Deliv Technol 2001; 3 (6):58–61.
3. Hughes L. Ion exchange resinates-Technology behind the mystery. Pharmaceutical Technology Europe. 2005; 17 (4):38-42.
4. Proulx SM, Melchiorre HA. New dosage forms lead to confusion. US Pharm 2001; 26 (2):68-70.
5. Raser BJ, Blair J. US Patent No. 5.762.961.1998.
6. www.accessdata.fda.gov/drugsatfda_docs/label/2005.
7. Milton Packer, The effect of carvedilol on morbidity and mortality in patients with chronic heart failure, NEJM 1996; 334: 1349-1355.
8. Liberman HA, Lachman L, Schwartz JB. Pharmaceutical dosage forms: Tablets. Vol. 2; Marcel Dekker, Newyork; 1990:201-43.
9. Subrahmanyam CVS. Text book of physical pharmaceutics; Delhi: Vallabh prakashan Publications; 1999:152.
10. Aulton EM. Pharmaceutics. The science of dosage form design. 2nd ed. ELBS/Chuchill Livingstone, London: 2002:4.
11. Gupta AK. Introduction to pharmaceutics. Vol.1; 2nd ed. Vol.1.New Delhi: CBS Publications; 1991:270.
12. Banker GS, Anderson NR. Tablets In:Lachman N,Liberman HA, Kanig JL, editors. The theory and practice of industrial pharmacy. 3rd ed. Bombay: Varghese Publication House; 1987:286-300.
13. Aly A, Sermen M, Qato M. Rapidly disintegrating tenoxicam tablets via camphor sublimation. Pharm Technol 2005; 68-78.
14. Jacob S, Shriwaikar AA, Joseph A, Srinivasan KK. Novel co-processed Excipients of Mannitol and Micro crystalline cellulose for preparing Fast Dissolving, Tablets of Glipizide Ind J Pharm Sci 2007: 633-38.
15. Hanawa T, Watanable A, Tsuchiya T, Ikoma R, Hidaka M, Sugaihara M. New oral dosage form for elderly patients: preparation and characterization of silk fibroin gel. Chem Pharm Bull (Tokyo) 1995; 43:284-88.

How to cite this article:
Azharuddin Md, Kamath K and Shabaraya AR: Design and Evaluation of Fast Dissolving Tablets of Carvedilol using Sublimation Technique. *Int J Pharm Sci Res* 2012; Vol. 3(10): 3788-3795.