AMERICAN JOURNAL OF PHARMTECH RESEARCH
Journal home page: http://www.ajptr.com/

Effect of Natural Superdisintegrants on the Fast Dissolving Tablet of Carvedilol by Sublimation Method

Dhaval Mayursinh Raulji*[1], Shwetha S. Kamath K[1], Shashank Nayak N[1], Arpit S Pandya[2], A.R.Shabaraya[3]
1. Srinivas College Of Pharmacy, Valachil, Post Parengipete, Mangalore-574143

ABSTRACT

Fast dissolving tablets are the tablets which dissolves rapidly and shows higher bioavailability than conventional tablets. The concept of formulating Fast dissolving tablets of Carvedilol (antihypertensive drug) offer suitable and practical approach in serving the desired objective of faster disintegration and dissolution characteristic with increase bioavailability and to know the effects of two natural superdisintegrants (Hibiscus Rosa, Linseed Mucilage). In the present work solid dispersion were prepared by solvent evaporation method for improving the bioavailability with beta cyclodextrin as a carrier to increase the solubility of the drug. And after compressing the tablet , heat is applied to create pores in tablet as it contain camphor as subliming agent which increase the porosity and cause faster release of drug from the tablet. Comparison between these two natural superdisintegrants was done by taking different ratios individually and in combination. Combination of these two superdisintegrants shows synergistic effect when it is compared to individually. Prepared tablets were subjected to different evaluation parameters such as hardness, friability, weight variation, drug content uniformity, *in vitro* disintegration time, wetting time, *in vitro* dissolution studies and stability studies are carried out by using the best formulation. From all the formulations prepared and tested, F11 was found to be the best formulation.

Keywords: Fast dissolving tablets, Solid dispersion, sublimation, Hibiscus Rosa, Linseed Mucilage.

*Corresponding Author Email: dhaval_raulji@yahoo.com
Received 01 August 2013, Accepted 10 August 2013

Please cite this article in press as: Raulji *et al* Effect of Natural Superdisintegrants on the Fast Dissolving Tablet of Carvedilol by Sublimation Method. American Journal of PharmTech Research 2013.

INTRODUCTION

The conventional dosage forms like tablet and capsule have wide acceptance up to 50-60% of total dosage forms. Fast dissolving drug delivery systems (FDDDS) are a new generation of formulations which combine the advantages of both liquid and conventional tablet formulations. Fast dissolving tablets are also known as mouth-dissolving tablets, Oro-dispersible tablets, rapid melts and porous tablets. Most fast dissolving tablets must include substances to mask the bitter taste of the active ingredient. These tablets usually dissolve within 15 sec to 3 min. The faster the drug goes into solution, quicker the absorption and onset of clinical effect.[1,2]

Carvedilol is in a group of drugs called beta-blockers. Beta-blockers affect the heart and blood circulation. Carvedilol is a racemic lipophilic aryoxypropanolamine that blocks α1- and ß-adrenergic receptors. Carvedilol significantly decreases systemic blood pressure, pulmonary artery pressure, and pulmonary capillary wedge pressure because of the vasodilatation that occurs with blocking of 1-receptors. Blocking of ß-receptors reduces the heart rate and increases diastolic filling time.[3]

The polymers obtained from the natural origin are more effective and safe. They are easily available in natural regions around the world therefore they are preferred over synthetic polymers. Natural polymers are used in most of the preparation and are more advantageous over synthetic polymers as they are economical they have low cost and are easily available in the sufficient quantity, natural polymers are nontoxic they do not have any harmful effects on the body, Natural polymers are environmental friendly as they are biodegradable in nature they do not cause any pollution, natural polymers are devoid of side effects as they are obtained from the natural source, natural polymers are mainly preferred by the patients as they are more safe and effective as compared to the synthetic polymers and have more patient compliance.[4,5]

A solid dispersion is the dispersion of one or more active ingredients in an inert carrier at solid-state prepared by solvent evaporation method. Sublimation method is one of the technique which is used in preparation of fast dissolving tablets. In this method a subliming (volatile) material is removed by sublimation from compressed tablets and high porosity is achieved due to the formation of many pores where subliming material (particles) previously existed in the compressed tablets. The sublimable materials include camphor, urea, ammonium bicarbonate, ammonium carbonate, menthol, hexa methylene tetramine and thymol.[6,7,8]

Advantages of Fast Dissolving Tablets[9]

- Stability for longer duration of time, since the drug remains in solid dosage form till it is

consumed. So, it combines advantage of solid dosage form in terms of stability and liquid dosage form in terms of bioavailability.

- An increased bioavailability, particularly in cases of insoluble and hydrophobic drugs, due to rapid disintegration and dissolution of these tablets.
- FDTs are less sensitive to environmental condition hence they are very stable.
- FDTs provide new business avenues as product differentiation, product promotion, line extension, uniqueness, and life cycle management.
- FDTs are cost effective it does not require costly ingredients, natural polymers when used as excipient are available easily and at low cost and also it does not require special packaging material it can be packed in simple blister packs.

In the current studies attempt has been made to formulate carvedilol fast dissolving tablets using hibiscusrosa mucilage powder and linseed mucilage powder as natural super disintegrants. Camphor is used as as subliming agent and Aspartame is used as sweetening agent

MATERIAL AND METHODS

Carvedilol is obtained as gift sample from Yarrowchem laboratories. ß-Cyclodextrin andcamphor from Hi Media laboratories.All the other ingredients are of analytical grade.

Preparation of Solid Dispersion of Carvedilol[6]

Solid dispersions of Carvedilol were prepared by solvent evaporation method. Drug was weighed and taken in a china dish, dissolved in Ethanol and then carrier (beta cyclodextrine) was added in ratio of 1:1, 1:2, 1:3 and 1:4. The solvent was evaporated at room temperature and dried in hot air oven at 50°C for 4 hr. The resultant mass was passed through sieve no. 60 and stored in desiccator. The solid dispersion obtained was evaluated for drug content and dissolution studies.

Drug content of solid dispersion

Accurately weigh solid dispersions equivalent to 12.5 mg of Carvedilol were weighed and transfer to 100 ml volumetric flask. Dissolve in 0.1N HCl buffer and the volume was made up with the same. An aliquot of the filtrate was analyzed spectrophotometrically at 240 nm.

Extraction Process of Natural Superdisintegrants

Extraction of Hibiscus Rosa Mucilage[10]

The fresh leaves of Hibiscus rosasinensis Linn were collected, washed with water to remove dirt and debris, and dried. The powdered leaves were soaked in water for 5–6 h, boiled for 30 min, and kept aside for 1 h for complete release of the mucilage into water. The material was squeezed from an eight-fold muslin cloth bag to remove the marc from the solution. Acetone was

added to the filtrate to precipitate the mucilage in a quantity of three times the volume of the total filtrate. The mucilage was separated, dried in an oven at a temperature < 50 °C, collected, dried-powdered, passed through a sieve (number 80), and stored for further use in desiccators and evaluation of mucilage powder was performed which is shown in Table.1

Table 1 Evaluation Parameters of mucilage powder

Sr. No.	Parameter	Hibiscus Rosa Mucilage Powder	Linseed mucilage powder
1	Angle of Repose	21.20^{o}	26.98^{o}
2	Bulk density	0.356	0.325
3	Tapped Density	0.418	0.402
4	Hausner's Ratio	1.17	1.23
5	Carr's Index	14.83	19.15

Table 2 Formulation chart for fast dissolving tablets of Carvedilol

Ingredients (mg)	Formulation code											
	F1	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**	**F10**	**F11**	**F12**
Solid dispersion equivalent to 12.5 mg of drug	50	50	50	50	50	50	50	50	50	50	50	50
Hibiscus Rosa mucilage powder	**3.5**	**7**	**10.5**	**14**	-	-	-	-	**7**	**4.62**	**9.38**	**9.38**
Linseed mucilage powder	-	-	-	-	**3.5**	**7**	**10.5**	**14**	**7**	**9.38**	**4.62**	**4.62**
Camphor	10	10	10	10	10	10	10	10	10	10	10	-
Microcrystalline cellulose	76.5	73	69.5	66	76.5	73	69.5	66	66	66	66	76
Talc	4	4	4	4	4	4	4	4	4	4	4	4
Mg-stearate	2	2	2	2	2	2	2	2	2	2	2	2
Aspartame	4	4	4	4	4	4	4	4	4	4	4	4
Total	**150**	**150**	**150**	**150**	**150**	**150**	**150**	**150**	**150**	**150**	**150**	**150**

Extraction of Linseed Mucilage[11]

Linseeds seeds were soaked in distilled water for 2 days. Then it boiled for few minutes. Then the mucilage was completely released into the water. The material collected was squeezed through muslin cloth. The mucilage squeezed out and the marc separated. Then the mucilage (filtrate) treated with equal volume of Acetone to precipitate. The separated mucilage dried in oven t a temperature less than 60^{0}C. After proper drying it powdered and pass through sieve no.80 and stored in desiccator until use and evaluation of mucilage powder was performed which is shown in Table.1

Drug-Excipient Compatibility studies

Compatibility of the drug with excipients was determined by FT-IR spectral analysis, the study was carried out at 400 – 4000 nm to detect any changes on chemical constitution of the drug after

combined it with the excipients. The samples were taken for FT-IR study.

PREPARATION OF FAST DISSOLVING TABLETS OF CARVEDILOL BY SUBLIMATION METHOD[12,13]

The solid dispersions equivalent to 12.5 mg of drug was taken and other ingredients were passed through sieve #60 and mixed geometrically. The mixture was then compressed into tablets using 9.0 mm round shape flat punch in 16 station tablet compression machine. After compression tablets were heated in a hot air oven at 60°C until constant weight was obtained to ensure the complete removal of volatile component. The tablets were evaluated for *in vitro* dispersion time in pH 1.2, 0.1 N HCl buffer and mean tablet weight before and after sublimation. The formula used for the preparation of tablets were shown in Table 2.

EVALUATION[,14]

Evaluation of pre-compression parameters of powder

Prior to compression, granules were evaluated for their flow and compressibility parameters. Flow properties of granules were determined by angle of repose method, bulk density, tapped density. Compressibility index of granules were determine by Carr's index and Hauser ratio

Angle of Repose (θ):

The friction forces in a loose powder can be measured by the angle of repose (θ). It is an indicative of the flow properties of the powder. It is defined as maximum angle possible between the surface of the pile of powder and the horizontal plane.

$$\tan(\theta) = h / r$$

$$\theta = \tan^{-1}(h/r)$$

Where, θ is the angle of repose

h is the height in cm.

r is the radius in cm.

Bulk Density (D_b):

It is the ratio of total mass of powder to the bulk volume of powder. It was measured by pouring the weight powder (passed through standard sieve # 20) into a measuring cylinder and initial weight was noted. This initial volume is called the bulk volume. From this the bulk density is calculated according to the formula mentioned below. It is expressed in g/ml and is given by

$$D_b = M / V_b$$

Where, M is the mass of powder

V_b is the bulk volume of the powder.

Tapped Density (D_t)

It is the ratio of total mass of the powder to the tapped volume of the powder.

$$D_t = M / V_t$$

Where, M is the mass of powder

V_t is the tapped volume of the powder.

Hauser's ratio:

Hauser's ratio is an indirect index of ease of powder flow.

$$\text{Hauser's ratio} = D_t / D_b$$

Where, Dt is the tapped density.

D_b is the bulk density.

Carr's index (or) % compressibility:

It indicates powder flow properties. It is expressed in percentage and is given by

$$I = (D_t - D_b / D_t) \times 100$$

Where, D_t is the tapped density of the powder and D_b is the bulk density of the powder.

Evaluation of post-compression parameters of Tablets[9,14]

Post compression, the tablets were evaluated for their characteristics such as weight variation, hardness, friability, drug content uniformity, disintegration test, wetting time and *in-vitro* dissolution study.

Weight variation

The procedure described in Indian Pharmacopoeia (IP, 1996) was employed to determine the weight variation of the tablets. Ten tablets were randomly selected from each batch and weighed on an electronic balance and mean weight was taken. Each tablet was then weighed individually and standard deviation in weight was calculated for each batch.

Hardness

Five tablets were randomly selected from each batch and hardness of tablets was determined by using Monsanto hardness tester. The mean values and standard deviation for each batch were calculated.

Friability (F)

Friability of the tablet determined using Roche friabilator. This device subjects the tablet to the combined effect of abrasion and shock in a plastic chamber revolving at 25 rpm and dropping a tablet at a height of 6 inches in each revolution. Pre weighed sample of tablets was placed in the friabilator and were subjected to the 100 revolutions. Tablets were dusted using a soft muslin cloth and reweighed. The friability (F) is given by the formula.

$$F = (W_{initial} - W_{final} / W_{initial}) \times 100$$

Drug content uniformity

Three tablets were powdered and weigh accurately equivalent to 12.5 mg of Carvedilol and transferred into a 100 ml volumetric flask. Then it was diluted to 100 ml with 0.1 N HCl buffer and absorbance was measured at 240 nm (shimadzu 1700) and drug content was determined

Disintegration test

The disintegration time was determined by using USP Tablet disintegration test apparatus using 900 ml of distilled water without disk. The time in seconds taken for complete disintegration of the tablets until no mass remaining in the apparatus was measured.

Wetting time

The wetting time and capillarity of the oral dispersible tablets were measured by a conventional method. The tablet was placed in a petridish of 6.5 cm diameter containing 10 ml water at room temperature and the times for complete wetting of tablets were recorded.

***In-vitro* drug release studies**

USP II Paddle apparatus was used and paddle was allowed to rotate at 75 rpm.0.1 N HCl buffer (900 ml) was used as a dissolution medium. Determination of amount of drug dissolved form tablets was carried by UV spectrophotometer at 240 nm.

In-vitro drug release studies details

Apparatus used	:	USP XXIII dissolution test apparatus
Dissolution medium	:	0.1 N HCl buffer
Dissolution medium volume	:	900 ml
Temperature	:	37±0.5 ^{o}C
Speed of basket paddle	:	75 rpm
Sample withdraw	:	5 ml
Absorbance measured	:	240 nm

Stability study:

Selected formulations were subjected to stability studies as per I.C.H. Guidelines.

Following conditions were used for stability studies

- ✶ 30°C/65 % RH analyzed at a time interval of 30 days till a period of 60 days
- ✶ 40°C/75 % RH analyzed at a time interval of 30 days till a period of 60 days

RESULTS AND DISCUSSION

In this work initially solid dispersion of carvedilol were prepared by solvent evaporation

technique by using beta cyclodextrin. Standard graph of carvedilol was taken in 0.1 N HCl buffer, the absorption maxima was found at 240 nm.

Percentage cumulative drug release from SD1 to SD4 was ranged between 82.07% to 99.26% at 7 min and the pure drug (Carvedilol) was released 32.90% at 7 min. The rapid drug dissolution was observed in SD3 (1:3), which releases 99.26% at 7 min. So the SD3 was found to be the best formulation ratio and was selected for the formulation of FDT. Which is shown in Table 4 and Figure4.

The average weight of twenty tablets were calculated for each formulation which is in the ranged from 149.3±2.53 mg to 150.7±1.9 mg .The hardness for all the formulations were ranged from 2.7±0.081 kg/cm^2 to 3±0.081 kg/cm^2. The percentage friability of all the formulations was found to be not more than 0.83±0.094%. The drug content of all the formulations was found to be between 98.25±0.20% to 100.23±0.03%. The disintegration time for all formulations was ranged from 23.46±1.22 sec to 82.66±3.09 sec. The wetting time for all the formulations was found between 27.13±0.83 sec to 92.96±2.05sec.The rapid drug dissolution was observed in F11, which releases 99.69% at the end of 2.5min which contain 9.38mg Hibiscus Rosa mucilage powder and 4.62mg Linseed mucilage powder per tablet, which confirms that the combination of Hibiscus Rosa mucilage powder and Linseed mucilage powder gives synergistic effect when it's compared with the individual super disintegrating agent. which is shown in Table 4, 6,7,8 and 9 and Figure. 3, 5.

Table 3 FTIR frequencies observed with excipients (BCD: Betacyclodextrin, SD: Solid dispersion, HR: Hibiscus Rosa)

Sr. no	Functional Group	Reported Frequency cm^{-1}	Observed Frequency cm^{-1}					
			Pure drug (cm^{-1})	Drug +BCD (cm^{-1})	SD + HR (cm^{-1})	SD+Linseed (cm^{-1})	SD+HR +Linseed(cm^{-1})	F11 (cm^{-1})
1	N-H	3400-3250	3345.89	3345.89	3345.89	3345.89	3345.89	3345.89
2	=C-H	3100-3000	2995.87	2995.87	2995.87	2995.87	2995.87	2918.73
3	O-H	3300-2500	2923.56	2923.56	2923.56	2923.56	2923.56	2849.31
4	O-CH_3	1320-1100	1101.15	1105.05	1101.15	1102.12	1102.12	1104.05

Table 4 *In-vitro* release of Carvedilol Pure Drug and Solid dispersion

Time (min)	*Cumulative Drug Release (%)				
	Pure Drug	SD1	SD2	SD3	SD4
1	07.58	27.09	29.30	35.81	30.36
2	12.41	35.89	37.66	43.87	43.57
3	17.81	45.15	43.90	56.03	50.42
4	22.86	57.10	56.11	64.85	60.57
5	27.66	64.32	70.65	74.14	72.13

6	29.87	76.78	81.33	89.09	85.82
7	32.90	82.07	93.23	99.26	91.60

Table 5Micromeritic properties of pre-compressional powder blend.

Batch no.	Angle of repose (Ɵ)± SD	Bulk Density (gm/cc)± SD	Tapped Density (gm/cc)± SD	Hausner's Ratio± SD	Carr's Index (%)± SD
F1	29.20±0.54	0.393±0.0124	0.433±0.0077	1.12±0.0262	14.35±0.6125
F2	29.24±0.52	0.393±0.0066	0.434±0.0107	1.143±0.0286	15.46±0.3681
F3	29.55±0.52	0.385±0.0074	0.441±0.0103	1.14±0.0408	13.5±0.7257
F4	27.85±0.29	0.386±0.0056	0.447±0.0095	1.11±0.0489	14.16±0.6944
F5	28.78±0.19	0.398±0.0106	0.447±0.0116	1.17±0.0355	15.7±0.5354
F6	29.29±0.38	0.383±0.0062	0.437±0.0105	1.14±0.0571	16.1±0.2943
F7	29.80±0.47	0.394±0.0131	0.430±0.0119	1.16±0.0571	16.17±0.5317
F8	28.58±0.39	0.394±0.0139	0.433±0.0143	1.13±0.0286	14.63±0.5312
F9	28.7±0.32	0.396±0.0171	0.437±0.0110	1.13±0.0492	15.6±0.5354
F10	29.59±0.40	0.398±0.0094	0.439±0.0123	1.12±0.0449	15.81±0.1915
F11	**26.98±0.35**	**0.387±0.0069**	**0.431±0.0132**	**1.11±0.0489**	**15.16±0.8433**
F12	28.64±0.80	0.396±0.0171	0.437±0.0105	1.14±0.0411	14.71±0.5198

All values are expressed as mean ± SD, n=3

Table 6 Evaluation of different fast dissolving tablets of Carvedilol

Batch	Weight variation*(mg) ±SD	Hardness^{+} (kg/cm^2)±SD
F1	149.95±1.58	2.86±0.047
F2	150.1±1.81	2.76±0.094
F3	149.9±2.21	2.8±0.081
F4	149.3±2.53	2.73±0.094
F5	149.6±2.28	2.8±0.081
F6	149.4±2.24	2.73±0.047
F7	150.7±1.9	2.83±0.047
F8	150.4±2.72	2.76±0.094
F9	151.2±3.09	2.83±0.047
F10	150.5±1.96	2.83±0.094
F11	150.2±2.18	2.7±0.081
F12	150.1±1.92	2.86±0.047

All values are expressed as mean ± SD, n = 6^{+}, 10*.

Table 7 Evaluation of different fast dissolving tablets of Carvedilol

Batch no.	%Friability†± SD	Disintegration Time*(sec)± SD	Wetting Time*(sec)± SD	Drug Content (%)±SD
F1	0.733±0.124	80.33±1.24	89.33±3.29	100.07±0.10
F2	0.766±0.124	63.33±3.39	73.66±2.05	98.65±0.48
F3	0.83±0.094	52.66±3.09	58±2.44	99.72±0.18
F4	0.66±0.094	29±0.81	35.1±0.69	100.14±0.04
F5	0.77±0.131	82.66±3.09	92.96±2.05	98.25±0.20
F6	0.74±0.122	70.66±2.49	78±3.26	98.28±0.26
F7	0.7±0.141	53.66±3.85	63.33±1.69	99.87±0.02

F8	0.66±0.047	38.33±1.24	44.16±0.62	99.37±0.02
F9	0.63±0.124	45±2.44	88.5±1.08	100.09±0.04
F10	0.63±0.124	52.66±1.69	57.66±1.24	98.85±0.08
F11	0.62±0.088	23.46±1.22	27.13±0.83	100.23±0.03
F12	0.63±0.124	27.66±0.94	32.93±0.73	99.37±0.02

All values are expressed as mean ± SD, n = 10†, 6*

Table 8 *In-vitro* release of Carvedilol Fast Dissolving Tablets from formulations F1 to F6

Time (min)	Cumulative Drug Release (%)					
	F1	F2	F3	F4	F5	F6
0.5	13.02	14.81	19.63	22.02	12.88	14.48
1	19.28	28.96	38.37	41.83	16.21	21.08
1.5	35.57	42.90	47.21	57.89	28.96	36.57
2	48.53	56.39	58.33	70.87	39.13	47.14
2.5	58.22	71.76	72.4	82.30	47.19	57.92
3	70.25	75.88	82.31	97.79	60.84	67.41
3.5	78.49	85.05	91.58	_	72.41	81.46

Table 9: *In-vitro* release of Carvedilol Fast Dissolving Tablets from formulations F7 to F12

Time(min)	Cumulative Drug Release (%)					
	F7	F8	F9	F10	F11	F12
0.5	19.18	23.19	32.31	27	41.99	31.85
1	29.86	38.41	55.38	39.28	57.25	49.98
1.5	41.28	46.35	68.34	52.90	70.31	57.28
2	53.64	59.39	84.28	66.07	81.55	64.45
2.5	71.70	76.04	93.03	72.4	99.69	72.40
3	80.55	86.88	96.79	84.89	-	80.62
3.5	87.21	93	-	91.97	-	88.97

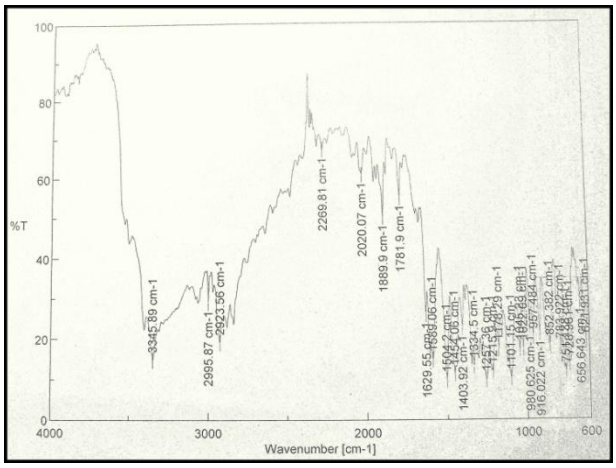

Figure 1: FTIR spectrum of Carvedilol

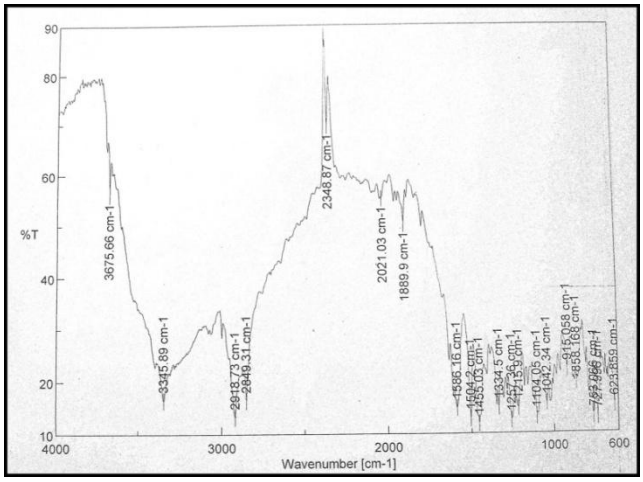

Figure 2: FTIR spectrum of F11(Optimized formula

Figure 3: Wetting time of F11

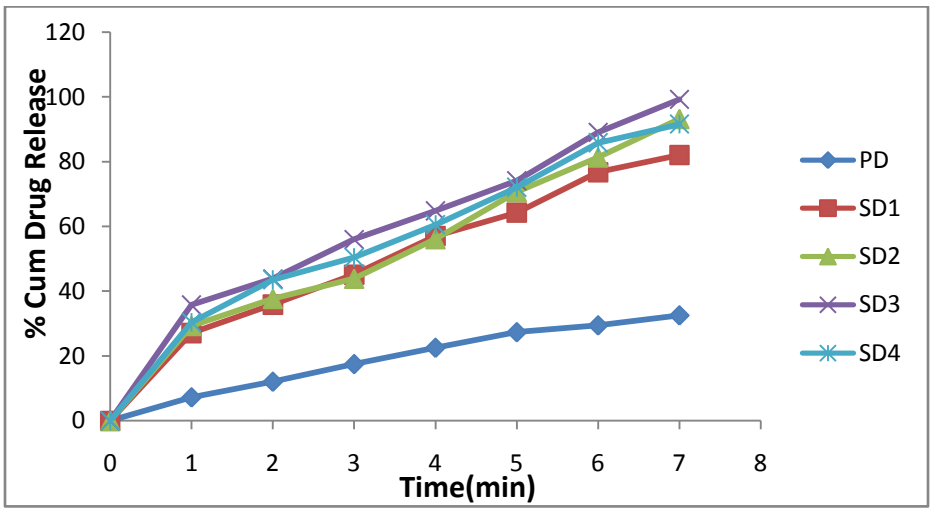

Figure.4 *In-vitro* release of SD1, SD2, SD3, SD4 and PD (SD: Solid dispersion & PD: Pure drug)

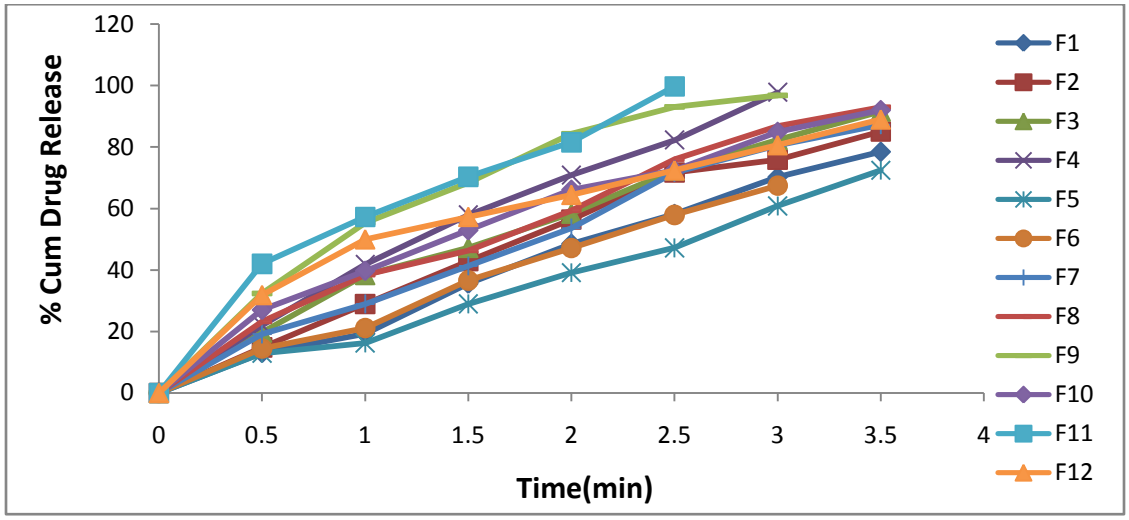

Figure.5: *In Vitro* release of Formulation F1 to F12

CONCLUSION

From the above work it was concluded that the solid dispersion of carvedilol can be complexed with the B-cyclodextrin and also with the other excipients which was used in formulation of fast dissolving tablets of carvedilol and there was no interaction between carvedilol and excipients. Which is shown in table 3 and figure1, 2. Formulation F11 showed maximum drug release within 2.5 minute when it compared to all other formulation and natural superdisintegrants which was used in F11wass combination of hibiscus rosa mucilage powder and linseed mucilage powder which shows good results compare to individual.F12 contains same ratio of natural superdisintegrants as of F11 but F12 does not contain camphor so drug release from F12 is less when it compared to F11, so presence of camphor shows faster release of drug. Hence the present formulation of fast dissolving tablet of carvedilol by sublimation method using natural superdisintegrants can be used for better patient compliance.

ACKNOWLEDGEMENTS

We are thankful to Srinivas college of Pharmacy for providing the opportunity to carry out our research work successfully. I heartly thank Prof Dr A.R Shabaraya for providing us Kind support all the time throughout the work

REFERENCE

1. Rushabh S, Darshan S, Chirag AP, Rajesh AK. A Comprehensive Review On Fast Disintegrating Tablets and Its Manufacturing Techniques. Int J Mod Pharm Res 2013;2(2): 44-65.
2. Chitlange V, Bakliwal S, Rane B, Gujrathi N, Pawar S.Fast Dissolving Tablets: An Overview. Int J of Pharm Sci Review Res2012;12(1):35-41.

3. Theivarasu C, SantanuG Indumathi T, UV Spectrophotometric Determination Of Carvedilol In Pharmaceutical Formulations. Asian J Pharm Clinical Res2010; 3(4): 64-8.
4. Parul S, Nitin S.Natural Polymers used in Fast Disintegrating Tablets: A Review. Int J of Drug Dev Res 2012; 4(4): 18-27.
5. Swathi S, Neeharika V, Lakshmi P. Formulation and Evaluation of Fast Dissolving Tablets of Freely and Poorly Soluble Drug With Synthetic and Natural Disintegrants. Drug Invention Today 2011; 3(10): 250-6.
6. Anuj K, Sangram KS, Kumud P, Prithi PSK,Ajit S and Naveen P. Review On Solubility Enhancement Techniques for hydrophobic Drugs. Int J Compre Pharmacy 2011;3(3): 1-7.
7. Sameer S, Raviraj SB, Lalit Y.A Review on Solid Dispersion. Int J Pharm Life Sci 2011; 2(9): 1078-95.
8. Mohit M, Nishant T, Raman B, Sunil T, Manish G. Fast Dissolving Tablet: An Approach for Emergency Treatment. Int J Res in Ayur & Pharma 2012; 3(3): 377-80
9. Saravana KK, nagaveni P, Chandrasekhar KB, Jayachandra P, Grace R. Fast Dissolving Tablet: Backgrounds, Trends and Future Prospective: A Review. Int J Review In Life Sci 2011;1(3): 88-96.
10. Viral S, RuchaP, Studies On Mucilage From Hibuscus RosaSinensis Linn As Oral Disintegrant. Int J Applied Pharm 2010; 2(1):18-21.
11. Senthil S, Bhama S, Ramya R.R., Chandrasekhar Y, Perumal P. Orodispersible Tablets of Lornoxicam With Natural and Synthetic Super Disintegrants. Int J Pharm Tech 2011;3(3):3130-42.
12. Kaushik D, Saini TR, Dureja H. Development of melt in mouth tablets by sublimation technique. J. Pharm. Res,2004; 3: 35-37.
13. Kalpesh G, Lalit KT, Kori ML, Sharma CS, Nema RK. Formulation and Characterization of Fast Disintegrating Tablet of Aceclofenac by using Sublimation Method. Int J Pharm Sci Drug Res 2011; 3(1): 19-22.
14. Debjit B, ChiranjibB, Krishnakanth , Pankaj, Margret CR. Fast Dissolving Tablet: An Overview.J of Che and Pharm Res 2009;1(1):163-77.
15. Rakesh P, Mona P, Vipin Kumar G, Rekha R, Lamba HS. Formulation and evaluation of orally disintegrating tablets: comparison of natural and synthetic superdisintegrants. Der Pharm Lett 2011; 3(2): 407-18.