IJPPR
INTERNATIONAL JOURNAL OF PHARMACY & PHARMACEUTICAL RESEARCH
An official Publication of Human Journals
ISSN 2349-7203
HUMAN

Human Journals
Research Article
August 2018 Vol.:13, Issue:1

Formulation and Evaluation of Fast Disintegrating Tablet of Carvedilol

IJPPR
INTERNATIONAL JOURNAL OF PHARMACY & PHARMACEUTICAL RESEARCH
An official Publication of Human Journals
ISSN 2349-7203
HUMAN

Kharde Sagar N[1*], Satpute Vivek M [2], Dhobale Avinash V [3], Wani Rakesh M[4]

Department of Quality Assurance at Pravara Rural College of Pharmacy, Pravaranagar Maharashtra, India.

Submission: 20 July 2018
Accepted: 27 July 2018
Published: 30 August 2018

Keywords: FDT, Carvedilol, Disintegration, Lyophilization, Dimethylsulphoxide

ABSTRACT

The oral route of administration is considered as the most widely accepted route because of its convenience of self-administration, compactness and easy manufacturing. Fast disintegrating tablets (FDT) has enormously increased as it has significant impact on the patient compliance some novel FDT technology allows high drug loading, have an acceptable taste, offer a pleasant mouth felling, leaving minimal residue in the mouth after oral administration. FDT have been investigated for their potential in improving bioavailability of poorly soluble drug through enhancing the dissolution profile of the drug and hepatic metabolism drugs. The present study was carried out to design and evaluation of fast disintegrating tablets of carvedilol for the effective management of angina pectoris, hypertension etc. In view of substantial first pass effect and its shorter plasma half-life. The fast disintegrating tablets of carvedilol were prepared by enhancing the solubility of carvedilol using β-cyclodextrin solid dispersion technology. Solubility of carvedilol is enhanced by preparing solid dispersion with β-cyclodextrin 1:4 ratio. DSC and IR spectroscopy data showed the characterization of drug, excipient, compatibility of drug and solid dispersion with excipients, gave evidence of solid dispersion formation and UV absorption spectra shows enhancement of solubility. Various preformulation batches (f1-f10) formulated by direct compression method using different concentration of polymer such as ac-di-sol and pearlitol and it was studied for pre and post compression evaluation. formulation with AC-DI-SOL and pearlitol batch no. F9 shows excellent result with disintegration time of 105 sec, drug content of 99.35%, and greater dissolution rate 98.32%at 40 min.

INTRODUCTION

The oral route of administration is considered as the most widely accepted route because of its convenience of self-administration, compactness and easy manufacturing.[1,2]But the most evident drawback of the commonly used oral dosage forms like tablets and capsules is difficulty in swallowing, leading to patients in compliance particularly in case of pediatric and geriatric patients, but it also applies to people who are ill in bed and to those actively working patients who are busy or traveling, especially those who have no access to water.[2] Over a decade, the demand for development of Fast disintegrating tablets (FDTs) has enormously increased as it has significant impact on the patient compliance. Fast disintegrating tablets are appreciated by a significant segment of populations, particularly who have difficulty in swallowing. It has been reported that Dysphagia[3](difficulty in swallowing) is common among all age groups and more specific with pediatric, geriatric population along with institutionalized patients, psychiatric patients and patients with nausea, vomiting, and motion sickness complications.[1]FDTs with good taste and flavor increase the acceptability of bitter drugs by various groups of population. This dosage form combines the advantages of the dry and liquid formulation. Some novel FDT technology allows high drug loading, have an acceptable taste, offer a pleasant mouth felling, leaving minimal residue in the mouth after oral administration.FDT has been investigated for their potential in improving the bioavailability of poorly soluble drug through enhancing the dissolution profile of the drug and hepatic metabolism drugs.[1-3]

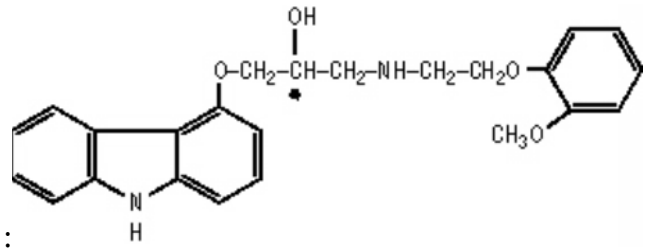
Fast disintegrating tablets are also called as or dispersible tablets, quick disintegrating tablets, mouth dissolving tablets, fast disintegrating tablets, fast dissolving tablets, rapid-dissolving tablets, porous tablets.

Carvedilol

IUPAC Name: 1-(9H-carbazol-4-yloxy)-3-{[2-(2-methoxyphenoxy)ethyl]amino}propan-2-ol

Chemical Formula: $C_{24}H_{26}N_2O_4$

Chemical Structure



:

Description: This compound belongs to the class of organic compounds known as carbazoles. These are compounds containing a three ring system containing a pyrrole ring fused on either side to a benzene ring.

MATERIALS AND METHODS

Following drug substance, resin, excipients, and chemicals were used for the formulation and evaluation studies. Carvedilol was gift sample of Ajanta Pharma Ltd, Mumbai, Maharashtra Hydroxy propyl methyl cellulose E15 (HPMC E15), β-CD were provided by Research-lab fine chem. Industries, Mumbai, Polyvinyl alcohol, Dimethylsulphoxide were purchased from Thomas baker Pvt. Ltd, Ac-Di-Sol S. D. Fine Chem. Ltd. Mumbai Mumbai. All other chemicals were of analytical grade and were used without further purification.

Technologies Used For Manufacturing of Orally Disintegrating Tablets.

Various processes employed in formulating FDTs including conventional technologies and patented technologies.

1. Freeze drying or lyophilization

A process, in which water is sublimated from the product after freezing, is called freeze drying. Freeze- dried forms offer more rapid dissolution than other available solid products. The lyophilization processes impart glossy amorphous structure to the bulking agent and sometimes to the drug, thereby enhancing the dissolution characteristic of the formulation. The entire freeze-drying process is done at no elevated temperature to eliminate adverse thermal effects that may affect drug stability. The major disadvantages of lyophilization technique are that it is expensive and time-consuming; fragility makes conventional packaging unsuitable for the products and poor stability under stressed conditions and their limited ability to accommodate adequate concentration of drugs.

2. Direct compression

The easiest way to manufacture tablets is by direct compression. Low manufacturing cost, conventional equipment's and a limited number of processing steps led this technique to be a preferable one. However, disintegration and dissolution of directly compressed tablets depend on the single or combined effect of disintegrating, water soluble excipients and effervescing agents. It is essential to choose a suitable and an optimum concentration of disintegrant to ensure quick disintegration and dissolution. Superdisintegrants are newer substances which are more effective at lower concentrations with greater disintegrating efficiency and mechanical strength. On contact with water the superdisintegrants swell, hydrate, change volume or form and produce a disruptive change in the tablet. Effective superdisintegrants provide improved compressibility, compatibility and have a nonnegative impact on the mechanical strength of formulations containing high dose drugs. The type of disintegrants and its proportion are of prime importance. Also, factors to be considered are particle size distribution, contact angle, pore size distribution and water absorption capacity. Studies revealed that the water-insoluble superdisintegrants like sodium starch glycolate and Croscarmellose sodium show better disintegration property than the slightly water-soluble agents like Crospovidone since they do not have a tendency to swell. Superdisintegrants that tend to swell show slight retardation of the disintegration property due to the formation of the viscous barrier. There is no particular upper limit regarding the amount of superdisintegrant as long as the mechanical properties of the tablet are compatible with its intended use. The superdisintegrant may be used alone or in combination with other superdisintegrants.

3. Molding

Molded tablets, usually prepared from soluble ingredients, by compressing a powder mixture which is moistened with a solvent, into mold plates to form a wetted mass. Recently, molded forms have been prepared directly from a molten matrix, in which the drug is dissolved or dispersed or by evaporating the solvent from a drug solution or suspension at a standard pressure. Usually molded tablets are compressed at a lower pressure than are conventional are conventional tablets and possess a porous structure that hastens dissolution. To improve the dissolution rate, the powder blend usually has to be passed through a very fine screen. The tablet produced by molding are solid dispersion. Molded tablets disintegrate more rapidly and offer improved taste because the dispersion matrix is in general made from water-soluble sugars. The active ingredients in most cases are absorbed through the mucosal lining of the

mouth. Unfortunately, molded tablets typically do not possess great mechanical strength. Erosion and breakage of the molded tablets often occur during tablet handling and when blister pockets are opened. Hardness agents can be added to the formulation, but then the rate of tablet solubility usually decreases.

4. Mass extrusion

This technology involves softening the active blend using the solvent mixture of water-soluble polyethylene glycol, using methanol and expulsion of softened mass through the extruder or syringe to get a cylinder-shaped extrude which are finally cut into even segments using the heated blade to form tablets. This process can also be used to coat granules of bitter drugs to mask their taste. Mass extrusion was the technique used for preparing taste masked granules. The tablet was prepared with different super to disintegrate e.g. sodium starch glycolate, croscarmellose sodium, and crospovidone etc.

5. Melt granulation

Melt granulation technique is a process by which pharmaceutical powders are efficiently agglomerated by a meltable binder. The advantage of this technique compared to a conventional granulation is that no water or organic solvents are needed. For accomplishing this process, high shear mixers are utilized, where the product temperature is raised above the melting point of the binder by a heating jacket or by the heat of friction generated by impeller blades. This approach to preparing FDT with sufficient mechanical integrity involves the use of a hydrophilic waxy binder (Superpolystate©, PEG-6-stearate). Super polystate is a waxy material with a melting point of 33–37°C and an HLB value of 9. So it will not only act as a binder and increase the physical resistance of tablets but will also help the disintegration of the tablets as it melts in the mouth and solubilize rapidly leaving no residues.

6. Phase transition process

Proposed a novel method prepare FDTs with sufficient hardness by involving the phase transition of sugar alcohol. In this technique, FDT were produced by compressing powder containing erythritol (melting point: 122 °C) and xylitol (melting point: 93 - 95 °C), and then heating at about 93 °C for 15 min. After heating, the median pore size of the tablets was increased and tablet hardness was also increased. The heating process enhances the bonding

among particles leading to sufficient hardness of tablets which was otherwise lacking owing to low/little compatibility.

7. Sublimation

The slow dissolution of the compressed tablet containing even highly water-soluble ingredients is due to the fact that the low porosity of the tablets reduces water penetration into the matrix. When inert volatile solid ingredient like ammonium bicarbonate, ammonium carbonate, benzoic acid, camphor, hexamethylenetetramine, naphthalene, phthalic anhydride, urea, and urethane was added to along with other tablet excipients and the blend was compressed into a table, which is finally subjected to a process of sublimation resulting in highly porous structures. Sublimation has been used to produce MDTs with high porosity. These compressed tablets exhibit good mechanical strength and have high porosity (approximately 30%) rapidly dissolved within 15 seconds in saliva.

FORMULATION

Preparation of the Fast disintegrating tablet of Carvedilol:

Prepare tablet by direct compression method using the 10-station rotary punch tablet compression machine using 7 mm biconvex plain on both side die-punches set. By using drug: β-Cyclodextrin complex, super disintegrant like Ac-di-sol, Avicel pH102 (diluent), talk (lubricant), Magnesium stearate (lubricant), Lactose (filler), Dextrose (Binder/Diluent), sorbitol (Wetting agent), Xylitol (sweetener), Aerosil (glidant), Strawberry (flavor). Weigh all ingredient and passed through mesh no. 60 excepting lubricants. Lubricants were passed through mesh no.80. Lubricants were added at the time of compression. The blend is mixed uniformly by manually for 30 minutes.

Table no. 1: Ingredients used in the preparation of Carvedilol

INGREDIENTS	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
Carvedilol : β-CD complex (mg)	62.5	62.5	62.5	62.5	62.5	62.5	62.5	62.5	62.5	62.5
Ac-Di-Sol (mg)	-	-	-	-	3	15	30	15	15	15
Pearlitol	-	21	30	45	-	-	-	21	30	45
Talk (mg)	6	6	6	6	6	6	6	6	6	6
Mg stearate (mg)	3	3	3	3	3	3	3	3	3	3
Lactose	227.5	206.5	197.5	182.5	224.5	212.5	197.5	191.5	182.5	168.5
Flavour (Strawberry)	1	1	1	1	1	1	1	1	1	1
Total	300	300	300	300	300	300	300	300	300	300

RESULTS AND DISCUSSION

1. Preformulation study:

Drug identification study:

A. The melting point of carvedilol:

The melting point of pure Carvedilol was determined by the open capillary method and it is found to be 114.06^{0}C. As maintained in table no.2.

Table. No.2 Melting point of carvedilol

Sr. no.	Drug	Observed Melting point (^{0}C)	Reference Melting point (^{0}C)
1	Carvedilol	114	114-115
2	Carvedilol	114.2	114-115
3	Carvedilol	114	114-115

B. FTIR of Carvedilol:

FTIR of carvedilol of carvedilol was measured by using Jasco FT/IR-4100 with diffuse reflectance principle. To carry out the identification of drug. The spectrum was scanned over a frequency range 400-4000 cm-1.

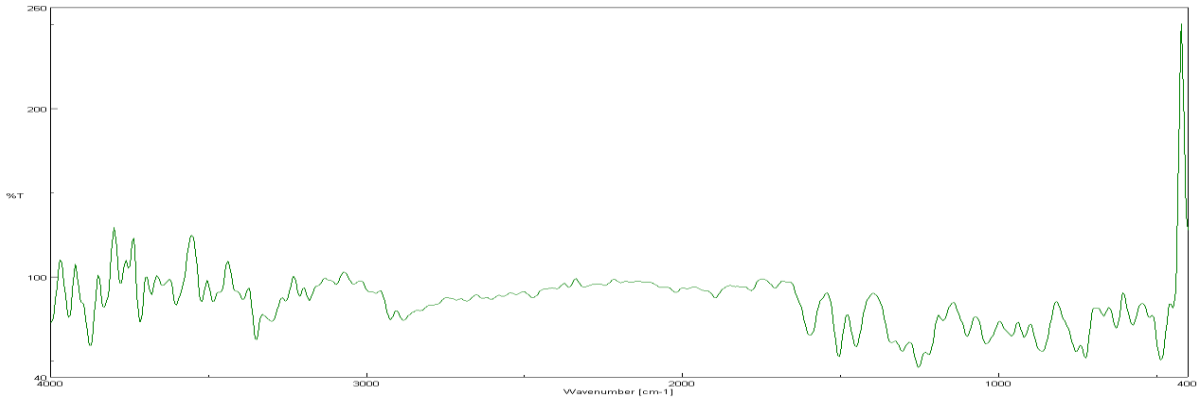


Fig. no.1: FTIR spectra of carvedilol

Carvedilol showed characteristic peaks at 3346.27 cm^{-1} (O-H and N-H stretching vibration peaks merged together), 2925.81 cm^{-1} ((C-H stretching vibrations), 1598.88 cm–1 (N-H bending vibrations) and 1253.64 cm^{-1} (O-H bending and C-O stretching vibrations).

C.DSC of carvedilol:

DSC of carvedilol was measured by DSC 60, Shimadzu) to confirm the identity and purity of carvedilol.

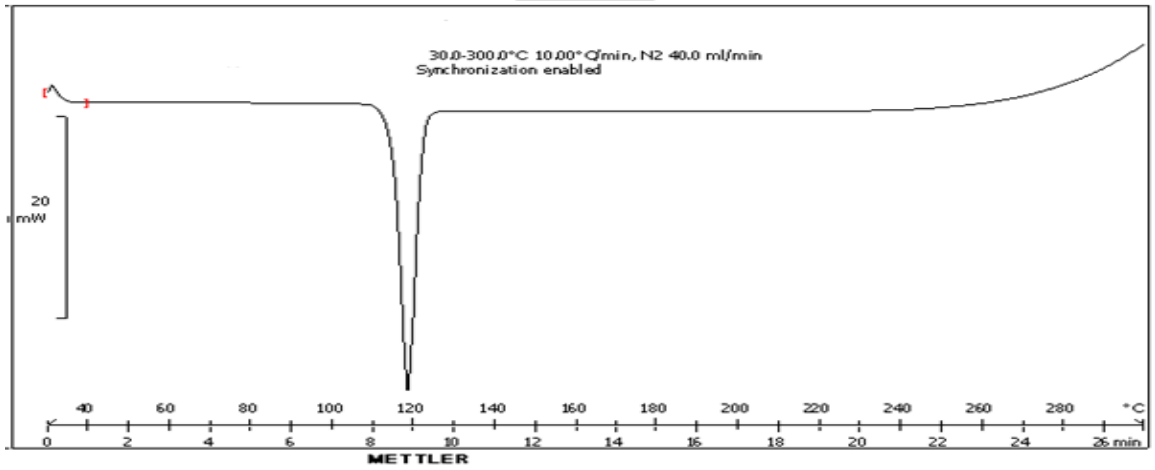


Fig. no.2: DSC Thermogram of carvedilol

Above Figure shows the DSC thermograms of carvedilol. DSC studies revealed that endothermic peaks for pure Carvedilol were obtained at 118.38°C.

D. UV spectra of carvedilol:

The absorption maxima (λmax) for Carvedilol in 0.1 N HCl was determined by scanning the drug solution within the range of 200-400nm using UV-Visible Spectrophotometer (Thermo scientific; evaluation 201). It was found that the drug exhibited λmax at 242 nm.

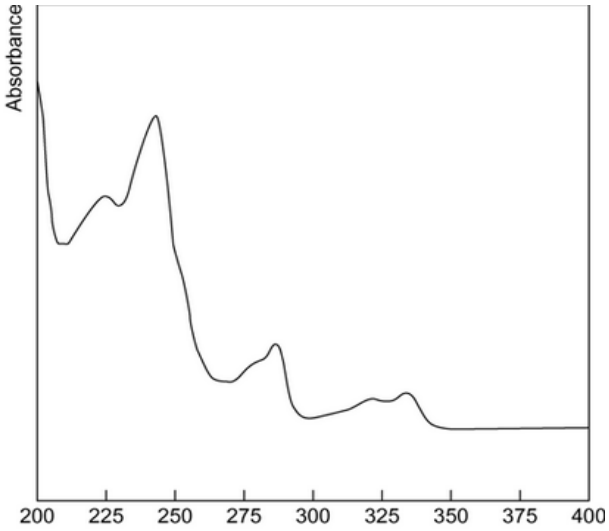


Fig. no.3: UV spectra of carvedilol

E. Calibration curve Carvedilol:

Calibration curve of carvedilol was measured by UV spectrophotometer at 242 nm in 0.1 N HCl, phosphate buffer ph 6.8, phosphate buffer ph 7.4 respectively to determine linearity and wither the drug follow Beer's low. The linearity of the drug in 0.1 N HCl, phosphate buffer ph 6.8, phosphate buffer ph 7.4 was found to be 0.9982, 0.9990, 0.9992 respectively and drug follow Beer's low.

Calibration curve of carvedilol in 0.1 N HCl:

Table. No.3: Calibration curve of carvedilol in 0.1 N HCl

Sr. no	Concentration (µg/ml)	Absorbance (nm)
1	0	0
2	2	0.127
3	4	0.328
4	6	0.643
5	8	0.907
6	10	1.105
7	12	1.364

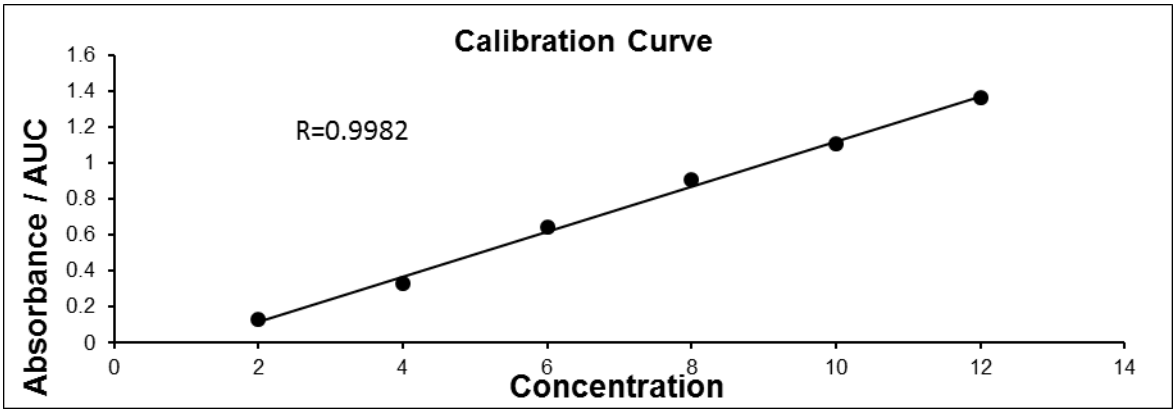


Fig. no. 4: Calibration curve of carvedilol in 0.1 N HCl

Calibration curve of carvedilol in phosphate buffer ph 6.8:

Table. No. 4: Calibration curve of carvedilol in phosphate buffer pH 6.8

Sr. no	Concentration (µg/ml)	Absorbance (nm)
1	0	0
2	2	0.089
3	4	0.290
4	6	0.553
5	8	0.765
6	10	0.968
7	12	1.15

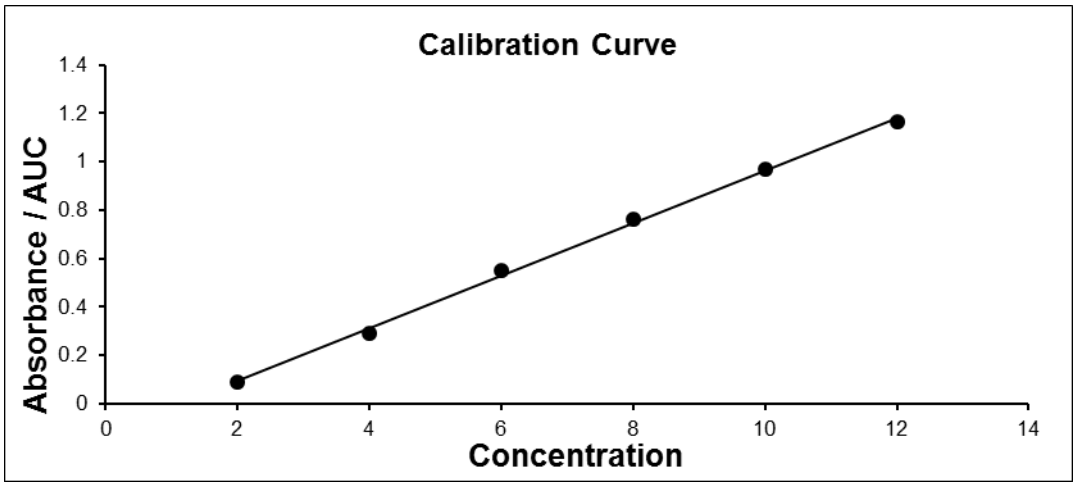


Fig. no. 5: Calibration curve of carvedilol in phosphate buffer pH 6.8

Calibration curve of carvedilol in phosphate buffer ph 7.4:

Table no. 5: Calibration curve of carvedilol in phosphate buffer pH 7.4

Sr. no.	Concentration (µg/ml)	Absorbance
1	0	0
2	2	0.096
3	4	0.294
4	6	0.561
5	8	0.783
6	10	0.985
7	12	1.199

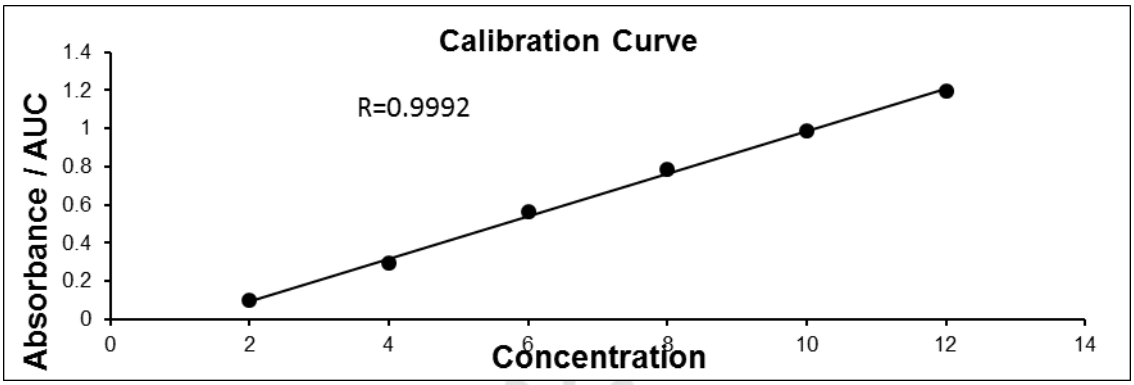


Fig. no.6: Calibration curve of carvedilol in phosphate buffer pH 7.4

Evaluation of fast disintegrating tablet of carvedilol:

Evaluation of blend:

Table no. 6: Evaluation of blend

Formulation Series	Bulk Density	Tapped Density	Compressibility Index	Hausner Ratio	Angle of Repose
F1	0.510gm/ml	0.641gm/ml	20.40%	1.256	32.82
F2	0.507gm/ml	0.595gm/ml	14.72%	1.1726	28.07
F3	0.534gm/ml	0.714gm/ml	25.13%	1.3357	34.59
F4	0.5076gm/ml	0.597gm/ml	14.97%	1.176	28.07
F5	0.515gm/ml	0.602gm/ml	14.43%	1.168	29.02
F6	0.505gm/ml	0.591gm/ml	14.64%	1.17	27.758
F7	0.510gm/ml	0.641gm/ml	20.40%	1.256	32.82
F8	0.507gm/ml	0.595gm/ml	14.72%	1.1726	28.07
F9	0.512gm/ml	0.60gm/ml	14.87%	1.17	27.14
F10	0.530gm/ml	0.714gm/ml	28.60%	1.3472	35.01

The precompression properties of the blend were studied for of repose, %compressibility, Hausner's ratio and it is reported in table no.6. The batch no.F3, F10 Poor flowability while the batch no. F9 shows greater flowability.

Evaluation of Tablet:

Table no. 7: Evaluation of tablet

Batch no.	Weight variation	Hardness kg/cm2	Friability (%)	Disintegration time (sec)	Wetting time (sec)	Water absorption Ratio
F-1	Passes	3.7	0.08	254	142	60
F-2	Passes	3.5	0.32	187	92	75
F-3	Passes	3.4	0.30	170	87	80
F4	Passes	3.2	0.29	178	89	78
F5	Passes	3.2	0.26	166	78	90
F6	Passes	3.1	0.23	131	72	92
F7	Passes	3.2	0.24	152	82	87
F8	Passes	3.3	0.27	118	69	89
F9	Passes	3.0	0.21	105	63	95
F10	Passes	3.1	0.24	127	71	86

Drug content of tablet:

Table no. 8: drug content of the tablet

Batch No.	The theoretical amount of drug in Tablet	Theoretical % amount of drug in Tablet	Assayed Drug content (mg)	% Drug content
F-1	12.5	100%	10.90	87.27
F-2	12.5	100%	11.69	93.54
F-3	12.5	100%	12.04	96.35
F4	12.5	100%	11.85	94.87
F5	12.5	100%	11.82	94.58
F6	12.5	100%	12.20	97.65
F7	12.5	100%	11.91	95.32
F8	12.5	100%	11.61	94.78
F9	12.5	100%	12.41	99.35
F10	12.5	100%	12.20	97.58

The drug content of tablet was carried out by using UV spectrometry method at 242 nm by thermal scientific; evaluation 201 and result is mentioned in table no.8 it was found to be in the range of 87.27-99.35%. Maximum % drug content was found in the formulation of F9 and was found to be 99.35%.

***In vitro* drug release:**

The *In-Vitro* drug release studies of the 10 batches of carvedilol fast disintegrating formulations were performed using USP dissolution rate test apparatus. The dissolution medium was 900 ml 0.1N HCl. The dissolution medium was kept in a thermostatically controlled water bath, maintained at 37+/-0.5^{0}C. The tablet was placed into the vessel and the speed of rotation was kept at 50 rpm. At predetermined time intervals, 5 ml of samples were withdrawn and replaced by an equal volume of fresh medium to maintain the sink conditions. Samples collected at 0, 5, 10, 15, 20m 25, 30 and 35 min were filtered and analyzed at each interval for carvedilol content released at λmax of 242 nm using UV-Visible Spectrophotometer. The maximum drug release was shown by F9 (at 40min 98.32%).

Table no. 9: Cumulative % drug release

Time	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
0	0	0	0	0	0	0	0	0	0	0
5	34.78	35.94	38.81	37.65	38.75	39.86	37.91	39.51	41.78	38.59
10	40.97	42.56	47.79	48.97	46.17	48.32	48.96	49.32	52.17	48.58
15	49.85	49.89	52.71	53.18	55.64	57.12	56.02	58.40	60.40	56.90
20	57.87	56.78	68.71	65.38	62.32	68.92	66.75	69.83	71.37	68.46
25	68.36	69.61	75.90	73.50	69.82	79.92	76.35	80.32	83.96	80.05
30	75.46	78.89	82.70	80.25	78.56	85.96	84.72	87.96	89.47	86.52
40	82.50	87.32	89.40	88.42	89.02	93.39	91.32	94.08	98.32	93.07

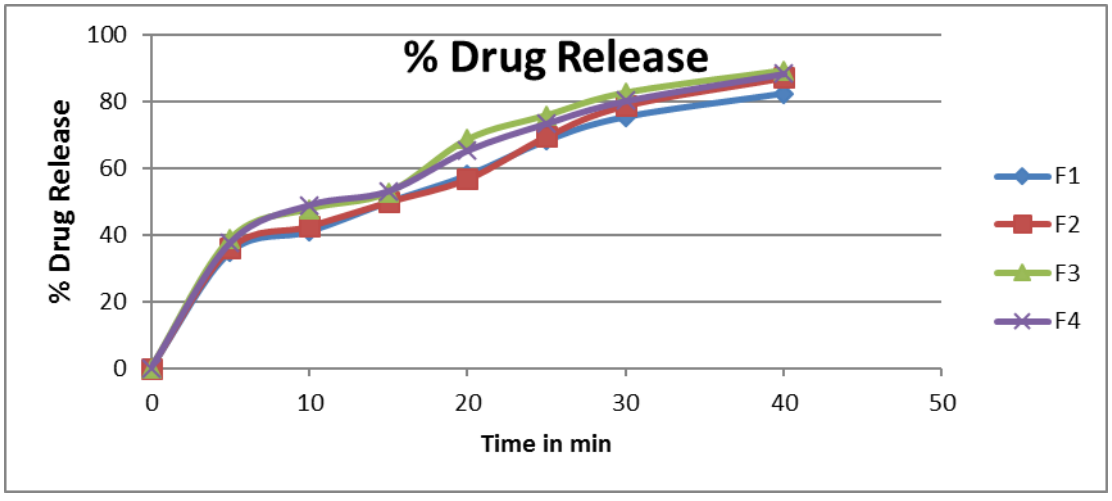


Fig. no. 7: Cumulative % drug release in F1,F2, F3, F4

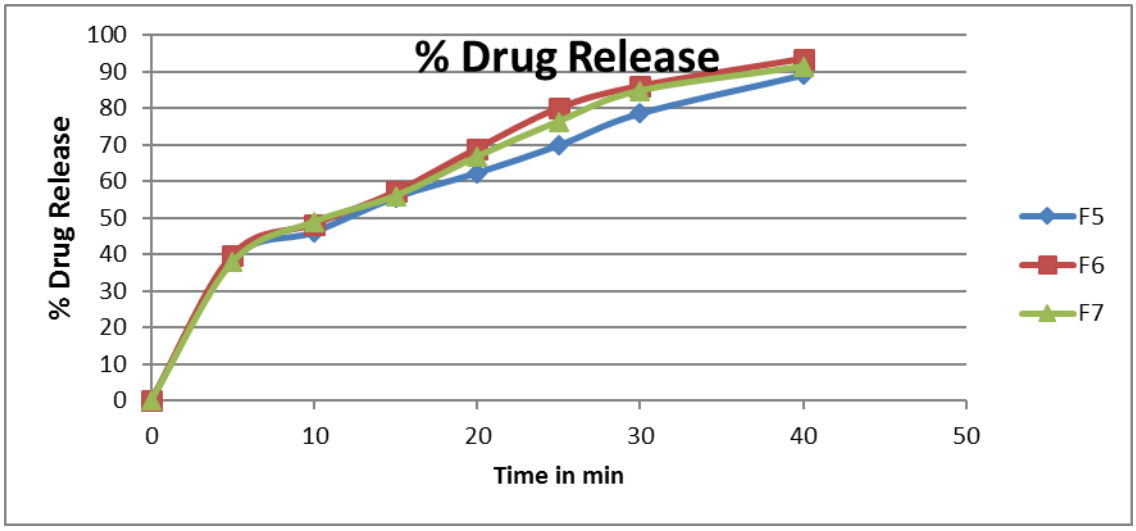


Fig. no.: 8 Cumulative % drug release in F5, F6, F7

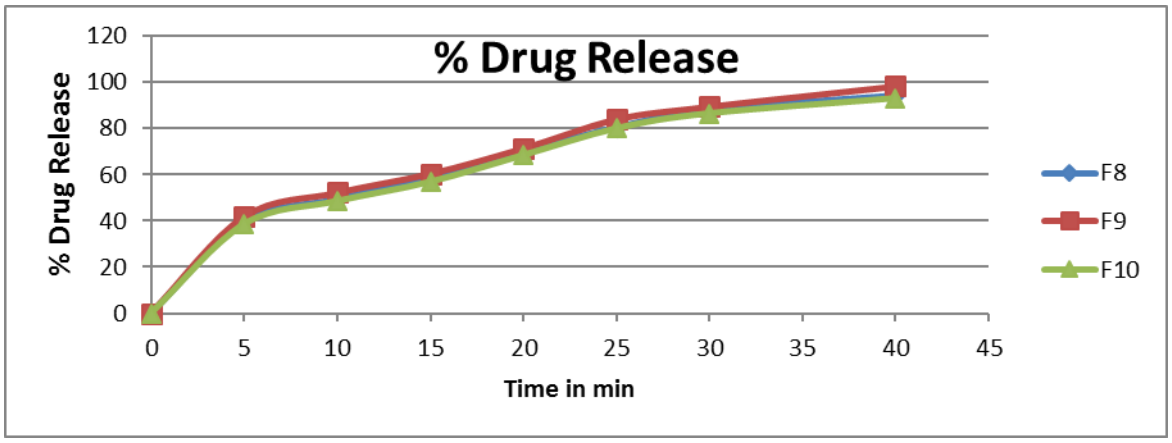


Fig no 9: Cumulative % drug release in F8, F9, F10

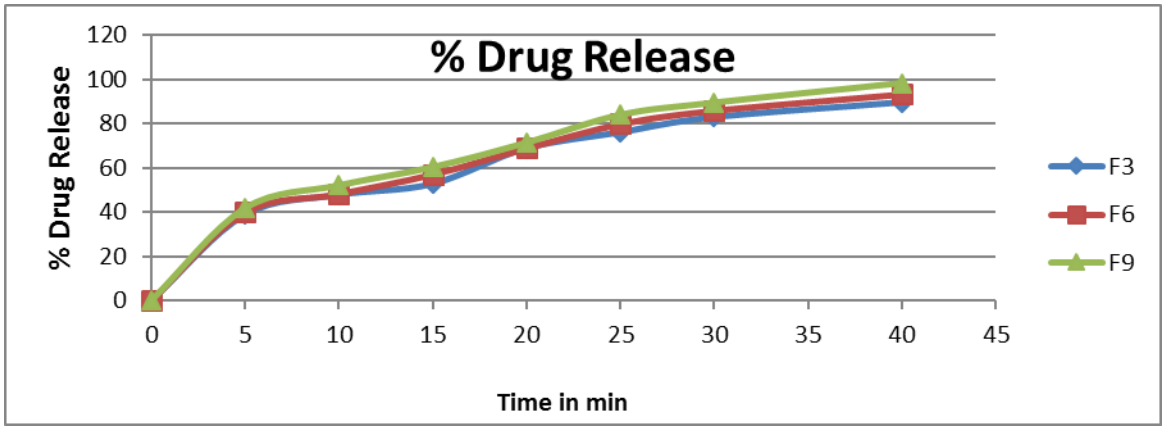


Fig. no.10: Cumulative % drug release in F3, F6, F9 Stability study of the tablet:

Table no.10: Stability study of FDT of Carvedilol

Parameter	Initial	1 Month	2 month
Avg. Weight	297	297	296
Hardness (kg/cm2)	3.7	3.7	3.7
Friability (%)	0.21	0.22	0.22
Disintegration Time (Sec)	105	107	108
Wetting time (sec)	63	65	66
% Drug content	99.35	99.34	99.32

CONCLUSION

The present study was carried out to design and evaluation of Fast disintegrating tablets of Carvedilol for the effective management of angina pectoris, hypertension etc. In view of substantial first pass effect and its shorter plasma half-life. The Fast disintegrating tablets of Carvedilol were prepared by enhancing the solubility of carvedilol using β-cyclodextrin solid dispersion technology. The solubility of carvedilol is enhanced by preparing solid dispersion with β-cyclodextrin 1:4 ratio. DSC and IR spectroscopy data showed the characterization of the drug, excipient, compatibility of drug and solid dispersion with excipients, gave evidence of solid dispersion formation and UV absorption spectra show enhancement of solubility.

Various preformulation batches (F1-F10) formulated by direct compression method using a different concentration of polymers such as Ac-Di-Sol and pearlitol and it was studied for pre and post compression evaluation. Formulation with pearlitol batch no. F3 shows better result but it shows poor drug content (96.35%) and poor flow property. Formulation with Ac-Di-Sol batch no. F6 shows better result but shows low dissolution rate. Formulation with Ac-Di-Sol and pearlitol batch no. An F9 shows the excellent result with disintegration time of 105 sec, drug content of 99.35%, and greater dissolution rate 98.32%at 40 min.

ACKNOWLEDGMENT:

Authors are thankful to Ajanta Parma ltd, Mumbai, Maharashtra for Carvedilol was gift sample. of Authors also Thank Principal Dr. Sunil Nirmal At Pravara Rural College of Pharmacy, Pravaranagar. for support and providing the necessary facilities to carry out this work. And also thanks full Dr. Mrunal.K.Shirsat, Dr. Ravi L Laware, Dr. Siddhashwar, Dr.

Nachiket Dighe. At Loknete Shri Dada Patil Pharate College of Pharmacy Mandavgan Pharata, Pune.

REFERENCES

1. Sastry SV, Nyshdham JR, Fix JA. Recent technological advances in oral drug delivery: A review. Pharmaceutical Science and Technology Today. 2000; 3:138-45.
2. Seager H. Drug-delivery products and the Zydis fast-dissolving dosage form. Journal of Pharmacy and Pharmacology. 1998; 50(4):375-82.
3. Lindgren S, Janzon L. Dysphagia. Prevalence of swallowing complaints and clinical findings. Medical clinics of North America., 1993; 77: 3-5.
4. Yang S, Jeong SH, Kimura S, Park K. Orally fast disintegrating tablets: Developments, technologies, taste-masking and clinical studies. Critical Review in Therapeutic Drug Carrier System. 2004; 21:433-76
5. Brown D. Orally Disintegrating Tablets- Taste over Speed. Drug Delivery Technology. 2003; 3:58-61.
6. Kumaresan C. Orally Disintegrating Tablet - Rapid Disintegration, Sweet Taste, And Target Release Profile, pharmainfo.net sep9 2008.
7. Makino T, Yamada M. and Kikuta, J. Fast dissolving tablet and its production, 1993, European Patent. 0553777 A2.
8. Reddy L. H, Ghosh B, and Rajneesh. Fast dissolving drug delivery systems: a review of the literature. Indian Journal of Pharmaceutical Science. 2002; 64(4): 331- 336.
9. Seager H. Drug-delivery products and the zydis fast-dissolving dosage form. Journal of Pharmacy and Pharmacology. 1998; 50: 375-382.
10. Modi A and Tayade P. Enhancement of dissolution profile by solid dispersion (kneading) technique. AAPS Pharm. Sci. Tech., 2006; 7(3): 68-75
11. Ujjwal Nautiyal, Satinderjeet Singh, Ramandeep Singh, Gopal, Satinder Kakar. Fast Dissolving Tablets as A Novel Boon: A Review. Journal of Pharmaceutical, Chemical, and Biological Sciences. May 2014; 2(1):05-26
12. Bhandari S, Mittapalli RK, Gannu R, Rao YM, Orodispersible tablet: An overview, Asian Journal of Pharmaceutics 2008; 2:2-11.
13. Sharma S. New Generation of Tablet: Fast Dissolving Tablet. Latest Reviews. Pharmainfo.Net 2008; 6(1).
14. Velmurugan S and Sundar Vinushitha. Oral Disintegrating Tablets: An Overview International Journal of Chemical and Pharmaceutical Sciences Dec 2010; 1(2):1-12
15. Ujjwal Nautiyal, Satinderjeet Singh, Ramandeep Singh, Gopal, Satinder Kakar. Fast Dissolving Tablets as A Novel Boon: A Review. Journal of Pharmaceutical, Chemical, and Biological Sciences. May 2014; 2(1):05-26
16. Takagi H, Kajiyama A, and Yanagisawa M. Rapidly disintegrable Pharmaceutical composition. US Patent. 2005; 6: 899.
17. Tanmoy Ghosh, Amitava Ghosh and Devi Prasad. A Review on new generation orodispersible tablets and its future prospective. International Journal of Pharmacy and Pharmaceutical Sciences 2011; 3(1):1-7.
18. Gupta A, Mishra AK, Gupta V, Bansal P, Singh R and Singh AK. Recent Trends of Fast Dissolving Tablet – An Overview Formulation Technology. International Journal of Pharmaceutical & Biological Archives 2010;1(1):1-10.
19. Kuno Y, Kojima M, Ando S and Nakagami H. Evaluation of rapidly disintegrating tablets manufactured by phase transition of sugar alcohols. Journal of Control Release. 2005; 105: 16-2
20. Bharti Nitan, Bhandari Neeraj, Sharma Pooja, Singh Kulwinder. Fast dissolving tablets: a new era in novel drug delivery system. International Research Journal Of Pharmacy. 2012; 3 (9):59-64
21. Sid diqui MN, Garg G, Sharma PK. Fast Dissolving Tablets: Preparation, Characterization and Evalu atio n: An Overview. Int J Pharm Pharm Sci 2010; 4(2):87-96.
22. Rajni Bal, Sushil Khanna, Pravin Pawar.Polymers In Fast Disintegrating Tablets – A Review. Asian J Of Pharmaceutical And Clinical Research, 5, 2012, 8-14
23. Kamalakkannan V, Puratchikody A, Masilamani K and Senthilnathan B. Solubility enhancement of poorly soluble drugs by solid dispersion technique – A review. Journal of Pharmacy Research 2010;3: 2314-2321.

24. Tiwari R, Tiwari G, Srivastava B and Rai AK: Solid Dispersions: An Overview to Modify Bioavailability of Poorly Water Soluble Drugs. International. Journal of Pharmaceutical Technology and Research 2009;1: 1338-1349.
25. Sharma D, Soni M, Kumar S and GuptaGD. Solubility Enhancement –Eminent Role in Poorly Soluble Drugs. Research Journal of Pharmacy and Technology, 2009;2: 220-224.
26. Vasconcelos TF, Sarmento B and Costa P. Solid dispersion as strategy to improve oral bioavailability of poor water-soluble drugs. Drug Discovery Today, 2007; 12: 1068-1075.
27. Singh MC, Sayyad AB and Sawant SD: Review on various techniques of solubility enhancement of poorly soluble drugs with special emphasis on solid dispersion. Journal of Pharmaceutical Research. 2010; 3(2): 494-501.
28. Verma S, Rawat A, Kaul M and Saini S: Solid Dispersion: A Strategy For Solubility Enhancement. International Journal of Pharmacy & Technology. 2011; 3(2): 1062-1099.
29. Dharna Allawadi, Neelam Singh, Sukhbir Singh and Sandeep Arora. Solid dispersions: a review on drug delivery system and solubility enhancement. IJPSR, 2013; 4(6): 2094-2105.
30. Jatinder Kaur, Geeta Aggarwal, Gurpreet Singh, A.C. Rana. Improvement of Drug Solubility Using Solid Dispersion Int J Pharm Pharm Sci. 2012 4(2): 47-53