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# DESIGN, DEVELOPMENT & CHARACTERIZATION OF FAST DISSOLVING TABLET OF CARVEDILOL

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**Abstract**
Fast dissolving tablets are developed as an alternative to tablet, capsule and syrup for the paediatric and geriatric patient suffering from disease who feels difficulty in swallowing the oral solid dosage form. Carvedilol is practically insoluble in water, slightly soluble in an alcohol, practically insoluble in dilute acids. Carvedilol is a non-cardioselective beta blocker. It has vasodilating properties, which are attributed mainly to its blocking activity at alpha1 receptors; at higher doses calcium-channel blocking activity may contribute. Carvedilol competitively blocks receptors. The elimination half-life is about 6 to 10 hours. The main objective of this research work was to formulate and evaluate fast dissolving tablet of carvedilol using excipients like Croscarmellose sodium, Crospovidone, Microcrystalline Cellulose, magnesium stearate, PVP etc. Formulation of fast dissolving tablets of Carvedilol by direct compression method using different types of polymer in different percentages. The tablets with drug were also evaluated for uniformity of drug content, in-vitro drug release and stability studies. The drug content in the fast dissolving tablets was found to be uniform and with low correlation of variation. The tablets prepared with solid dispersion in combination with super disintegrate showed better release profile as compared to only incorporation of super disintegrates. The tablets prepared by effervescent and pore forming technology provides satisfactory drug release. The release of drug followed first order kinetics and mechanism of drug release was found to be diffusion controlled.
The stability data at different temperature and humidity showed no significant degradation of Carvedilol and shelf life found to be more than 520 days. Fast dissolving tablets prepared by the Ac – Di – Sol in 4% concentration are promising for rapid release of Carvedilol. Incorporation of solid dispersion (PEG 4000 : CARVEDILOL) (4:1) into Ac – Di – Sol in 2 % concentration enhanced the release rate of Carvedilol and thus therapeutic levels of the drug could be achieved through fast dissolving tablets. Tablets prepared by effervescent and pore forming technologies are also very promising for stable and rapid release of Carvedilol.
**Keywords:** Carvedilol, FDDS, solid dispersion, tablets, Sodium, Crospovidone, Microcrystalline Cellulose, magnesium stearate, PVP.

## Introduction

Fast dissolving tablet means tablet that disintegrates and dissolves rapidly in the saliva, within a few seconds without the need of drinking water or chewing. They should readily dissolve or disintegrate in the saliva generally within <60 seconds. Some drugs are absorbed from the mouth, pharynx and oesophagus as the saliva passes down into the stomach. The significance of or dispersible dosage forms are progressively being recognized in both industry and academics. Most of the MDTs include certain super disintigrents and taste masking agents. There are several synonyms in use of MDTs like or dispersible, orally disintegrating tablets, quick dissolving tablet, fast melt tablets, rapid disintegrating tablets and freeze dried wafers. USFDA defines “A solid dosage form containing medicinal substances disintegrates rapidly within a matter of seconds when placed upon the tongue” [1-5]

Carvedilol is practically insoluble in water, slightly soluble in a alcohol, practically insoluble in dilute acids. Carvedilol competitively blocks receptors. It lacks sympathomimetic activity and has a vasodilating property which is exerted mainly through blockade. It reduces both systolic and diastolic blood pressure without reflex tachycardia. Carvedilol is well absorbed from the gastrointestinal tract but is subject to considerable first-pass metabolism in the liver; the absolute bioavailability is about 25%. Peak plasma concentrations occur 1 to 2 hours after an oral dose. It has high lipid solubility. The elimination half-life is about 6 to 10 hours. Carvedilol has been shown to accumulate in breast milk in animals [6].

Carvedilol is a non-cardioselective beta blocker. It has vasodilating properties, which are attributed mainly to its blocking activity at alpha1 receptors; at higher doses calcium-channel blocking activity may contribute. It also has antoxidant properties. Carvedilol is used in the

management of hypertension and angina pectoris, and as an adjunct to standard therapy in symptomatic heart failure [7-9].

Croscarmellose sodium is used in oral pharmaceutical formulations as a disintegrant for capsules, tablets, and granules. In tablet formulations, croscarmellose sodium may be used in both direct-compression and wet-granulation processes [10-12].

Crospovidone is a water-insoluble tablet disintegrant and dissolution agent used at 2–5% concentration in tablets prepared by direct-compression or wet- and dry-granulation methods. It rapidly exhibits high capillary activity and pronounced hydration capacity, with little tendency to form gels. Studies suggest that the particle size of crospovidone strongly influences disintegration of analgesic tablets larger particles provide a faster disintegration than smaller particles. Crospovidone can also be used as a solubility enhancer. With the technique of co-evaporation, crospovidone can be used to enhance the solubility of poorly soluble drugs. The drug is adsorbed on to crospovidone in the presence of a suitable solvent and the solvent is then evaporated. This technique results in faster dissolution rate [13-16].

The main objective of this research work was to formulate and evaluate fast dissolving tablet of carvedilol using excipients like Croscarmellose sodium, Crospovidone, Microcrystalline Cellulose, magnesium stearate, PVP etc. Formulation of fast dissolving tablets of Carvedilol by direct compression method using different types of polymer in different percentages.

**Materials & Method**

Carvedilol was received as a gift sample from Sun Pharmaceutical Industries Ltd., Silvassa, Gujarat. Crosspovidone was purchased from Signet Chemicals Pvt. Ltd., Mumbai and Polyethylene Glycol 4000 was purchased from Merck ltd, Mumbai. All others chemicals, reagents and solvents used in the present investigation were analytical grades.

**Methods**

**Analysis of Carvedilol**

**Differential Scanning Calorimetry**

Differential Scanning Calorimetry (DSC) was employed to determine the melting point of Carvedilol sample used in present investigation. The DSC analysis was carried out over 50-250$^0$C at 5$^0$C/minute, using duplicate samples of 5mg in crimped aluminum samples pans. Indium was used to calibrate the DSC instruments.

**Infra Red Spectroscopy**

The IR analysis of the sample was carried out for qualitative compound identification. The pellet of approximately 01 mm diameter of the drug was prepared grinding 3-5 mg of sample with 100-150 mg of Potassium Bromide in pressure compression machine. The sample pellet was mounted in IR compartment and scanned at wavelength 4000 cm$^{-1}$ -400 cm$^{-1}$.

**Ultraviolet absorption**

Ultraviolet absorption in the rage 200 to 400 nm of a 5ug/ml solution in 5% (v/v) methanolic Sorensons Buffer (pH 6.8) was measured [17].

**Solubility**

The solubility of Carvedilol was determined in different solvents. An excess quantity of the drug was added in 10 ml of each solvent in screw capped glass test tubes and shaken or 12 hours at room temperature. The solution was filtered, diluted and the solubility was determined by spectrophotometrically [18].

**PREPARATIONS & EVALUATION OF FORMULATIONS:**

**Preparation of Drug Free tablets**

Drug free fast dissolving tablets were prepared by direct compression method using single punch Cadmach tablet machine. The formulations were developed by using different techniques in various ratios.

**By addition of super disintegrates**

The super disintegrant (Ac – Di- Sol, Crosspovidone) in varying concentration (01 – 05%) were used to develop the tablets. All the ingredients are were passed through mesh no. 60. All the ingredients were co ground in a pestle motor. Finally talc and magnesium stereate were added and mixed for 5 minutes. The mixed blend of excipients was compressed using a single punch machine to produce convex faced tablets weighing 125 mg each with 2.85 mm thickness and 7.8 mm in diameter. A minimum fifty tablets were prepared [19].

**By using Solid dispersion**

For the means of fast release of the drug, solid dispersion were prepared with PEG 4000 in various ratio (1:1 to 1:8) by using melt fusion method. The fused mixtures were prepared by heating the corresponding ground mixture in a porcelain dish to about 5$^0$C above the melting point of PEG 4000 with continuous stirring for a minute. The samples were immediately quenched to 4$^0$C, the resulting solid was scraped out and stored in a descicator at room temperature [20].

The prepared solid dispersion was evaluated for Saturation Solubility, X- Ray Powder Diffraction Studies and Drug content.

All the ingredients were taken in the pestle mortar. Super disintegrating agents were mixed in various proportions. The mixed blend of solid dispersion and other excipients was compressed using single punch machine to produce convex faced tablets.

**By Effervescence Technology**

For the development of mouth dissolving tablet various formulations using different ratio of Sodium Bi Carbonate and Citric Acid in combination with other excipients were grounded in pestle mortar. Finally talc and magnesium stereate were added and mixed for 5 minutes. The mixed blends of excipients were compressed using a single punch machine to produce convex faced tablets weighing 125 mg each with 2.85 mm and 7.8 mm in diameter. A minimum fifty tablets were prepared. For the fast release of the drug the tablets were also prepared with the solid dispersion in the addition of the effervescence technology [21].

**By vacuum drying**

The tablets were prepared by vacuum drying technique the various concentrations (5, 10, 15, 20%) of subliming agent (camphor) were used. All the ingredients were taken in the pestle mortar. The mixed blend of super disintegrants and other excipients were compressed using single punch machine to produce convex faced tablets. The tablets were vacuum dried at $60^0$C for 24 hour to sublime camphor [22].

**PREPARATION OF FAST DISSOLVING TABLET OF CARVEDILOL**

The critical parameters to formulate a fast dissolving tablet are choice of super disintegrates and optimization of concentration of superdisintigrant. The main criteria for fast dissolving tablets is to disintegrate or dissolve rapidly in oral cavity in 15-60 seconds, without need of water and should have pleasant mouth feel. The fast dissolving tablets of Carvedilol were prepared by different technologies in different ratios as described earlier. On the characterization of the drug free tablet the best formulations were selected and the drug Carvedilol was incorporated in these formulation. The ingredients depicted in Table 1-4 (Except talc and magnesium stearate) were mixed homogenously and co ground in a mortar and pestle. Finally talc and magnesium stearate were added and mixed for five minutes. The mixed blend of Carvedilol and other excipients were compressed using a single punch machine to produce convex faced tablet weighing 125 mg each with 2.85 mm and 7.8 mm in diameter, a minimum 30 tablets were prepared for each batch [20 & 22].

**Table 1:** Carvedilol Fast Dissolving Tablets by Addition of Super disintegrates

| Ingredients | FDT 1 | FDT 2 | FDT 3 | FDT 4 |
|---|---|---|---|---|
| Carvedilol | 12.5 | 12.5 | 12.5 | 12.5 |
| Ac Di Sol | 3.75 | 5 | -- | - |
| Crosspovidone | - | - | 3.75 | 5 |
| Dextrose | 18 | 18 | 18 | 18 |
| Lactose | 18 | 18 | 18 | 18 |
| Sorbitol | 25 | 25 | 25 | 25 |
| Xylitol | 19 | 17.75 | 19 | 17.75 |
| Avicel pH 102 | 25 | 25 | 25 | 25 |
| Talc | 1.25 | 1.25 | 1.25 | 1.25 |
| Magnesium Stereate | 2.5 | 2.5 | 2.5 | 2.5 |

**Table 2:** Carvedilol Fast Dissolving Tablets by Solid Dispersion technology

| Ingredients | FDT 5 | FDT 6 | FDT 7 | FDT 8 |
|---|---|---|---|---|
| Carvedilol + PEG 4000(1:4) | 62.5 | 62.5 | 62.5 | 62.5 |
| Ac Di Sol | 1.25 | 2.5 | - | - |
| Crosspovidone | - | - | 1.25 | 2.5 |
| Sorbitol | 18.75 | 18.75 | 18.75 | 18.75 |
| Xylitol | 12.5 | 11.25 | 12.5 | 11.25 |
| Avicel pH 102 | 25 | 25 | 25 | 25 |
| Talc | 2.5 | 2.5 | 2.5 | 2.5 |
| Magnesium Stereate | 2.5 | 2.5 | 2.5 | 2.5 |

**Table 3:** Carvedilol Fast Dissolving Tablets by Effervescent Technology

| Ingredients | FDT 9 | FDT 10 | FDT 11 | FDT 12 |
|---|---|---|---|---|
| Carvedilol | 12.5 | 12.5 | - | - |
| Carvedilol + PEG 4000 (1:4) | - | - | 62.5 | 62.5 |
| Dextrose | 20 | 17 | 7.5 | 7 |
| Lactose | 20 | 16.75 | 7.5 | 7 |
| Sodium bi carbonate | 6.25 | 8.325 | 6.25 | 8.325 |
| Citric acid | 12.5 | 16.675 | 12.5 | 16.675 |
| Avicel pH 102 | 50 | 50 | 25 | 20 |
| Talc | 1.25 | 1.25 | 1.25 | 1.25 |
| Magnesium Stereate | 2.5 | 2.5 | 2.5 | 2.5 |

**Table 4:** Carvedilol Fast Dissolving Tablets by Vacuum Drying Technology

| Ingredients | FDT 13 | FDT 14 | FDT 15 | FDT 16 |
|---|---|---|---|---|
| Carvedilol | 12.5 | 12.5 | 12.5 | 12.5 |
| Camphor | 12.5 | 18.75 | 12.5 | 18.75 |
| Ac Di Sol | 2.5 | 2.5 | - | - |
| Crosspovidone | - | - | 2.5 | 2.5 |
| Sorbitol | 24 | 23 | 24 | 23 |
| Xylitol | 19.75 | 14.5 | 19.75 | 14.5 |
| Avicel pH 102 | 50 | 50 | 50 | 50 |
| Talc | 1.25 | 1.25 | 1.25 | 1.25 |
| Magnesium Stereate | 2.5 | 2.5 | 2.5 | 2.5 |

**EVALUATION OF SOLID DISPERSION**

**Saturation solubility**

An excess amount of drug and solid dispersion was placed in 30 ml glass vials equipped with aluminum seals containing 20ml of Distilled water. The contents in the vials were shaken in a khan type shaker for 24 hours. The aliquots were withdrawn, filtered, diluted to an

appropriate volume with Sorenson's buffer pH 6.8 and analyzed at 285 nm using UVspectrophotometer [21].

**X- Ray diffraction Studies**

The X ray diffraction pattern of a selected preparation, excipients and drug were obtained on powder samples using nickel filtered copper radiation at the scanning speed of $2^0$ per minute in the form of $20^0$ angle [22].

**Drug content**

An accurately weighed quantity of solid dispersion equivalent to 50 mg of drug was taken in 100ml volumetric flask and dissolve in minimum amount of methanol and the volume was made up to mark with Sorenson's buffer pH 6.8 and assayed for drug content using UV double beam spectrophotometer at 285 nm [22].

**Evaluation of blends**

Tablets were made from blends by direct compression method. The quality of tablet, once formulated by rule, is generally dictated by the quality of physicochemical properties of blends. There are many formulation and process variables involved in mixing step and all these can affect the characteristics of blends produced.

The various characteristics of blends tested are as given below:

**Angle of Repose**

The frictional force in a loose powder can be measured by the angle of repose θ. It is defined as, the maximum angle possible between the surface of the pile of the powder and the horizontal plane. If more powder is added to the pile, it slides down the sides of the pile until the mutual friction of the particles producing a surface angle θ, is in equilibrium with the gravitational force.

The angle of repose was determined by the funnel method suggested by Newman. Angle of repose is determined by the following formula [22]-

$\text{Tan } \theta = h/r$

$\text{Therefore } \theta = \text{Tan}^{-1}\, h/r$

Where θ = Angle of repose

h = height of the cone

r = Radius of the cone base

**Bulk Density**

Density is defined as weight per unit volume [22].

Bulk density, $\rho_b$, is defined as the mass of the powder divided by the bulk volume and is expressed as gm/ $cm^3$.

The bulk density of a powder primarily depends on particle size distribution, particle shape and the tendency of particles to adhere together. There are two types of bulk density.

**Low bulk density**

The particles are pack in such a way so as to leave large gaps between their surfaces resulting up in light powder of low bulk density.

**High bulk density**

Here the smaller particles shift between the large particles resulting in heavy powder of high bulk density.

Bulk density is very important in the size of containers needed for handling, shipping, and storage of raw material and blend. It is also important in size blending equipment.

A standard procedure used for obtaining bulk density or its reciprocal bulkiness is given below

A sample of about 50 $cm^3$ (blend) is carefully introduced in a 100ml graduated cylinder. The cylinder is dropped onto a hard wood surface three times from a height of 1 inch at two second interval. The bulk density is then obtained by dividing the weight of sample in gms by final volume in $cm^3$.

$\rho_b = M/ V_p$

Where $\rho_b$ = Bulk Density

M = Weight of sample in gm

$V_p$ = Final volume of blend in $cm^3$

**Bulkiness**

Specific bulk volume or reciprocal of bulk density is called bulkiness or bulk. Bulkiness increases with a decrease in particle size. In mixture of material of different sizes, however the smaller particle shifts between the larger particles and tends to reduce the bulkiness.

The bulkiness [22] can be calculated by the following formula

Bulkiness = $1/ \rho_b$

Where, $\rho_b$ = Bulk Density.

Loose bulk density

It is defined as the ratio of weight of blend in gms to the loose bulk volume (untapped volume) in $cm^3$. loose bulk density is given by

Loose bulk density $\rho_u$ = Weight in gms / Vb

Where Vb = Bulk volume (untapped volume)

Void volume

The volume of the spaces is known as the void volume "v" and is given by the formula

V = Vb – Vp

Where Vb = Bulk volume (volume before tapping)

Vp = True volume (volume after tapping)

**Porosity**

The porosity [22] € of powder is defined as the ratio of void volume to the bulk volume of the packaging.

The porosity of the powder is given by

€ = Vb – Vp / Vp = 1- Vp/Vb

Porosity is frequently expressed in percentage and is given as

% € = (1 – Vp / Vb) X 100

The porosity of powder indicates the types of packaging a powder undergoes when subject to vibrations, when stored, or in tablet machine when passed through hopper or feed frame.

**Percent Compressibility**

It is an important measure obtained from bulk density [22] and is defined as,

$C = \rho_b - \rho_u / \rho_b \times 100$

If the bed of particles is more compressible the blend will be less flowable and vice versa. Materials having "C" values less than 20 -21% is termed as free flowing materials.

**EVALUATION OF FAST DISSOLVING TABLET**

Tablets from all the formulation were subjected to following quality control test.

**General Appearance**

The general appearance of a tablet, its visual identity and over all "elegance" is essential for consumer acceptance. Include in are tablet's size, shape, colour, presence or absence of an odour, taste, surface texture, physical flaws and consistency and legibility of any identifying marking.

**Size and Shape**

The size and shape of the tablet can be dimensionally described, monitored and controlled.

**Uniformity of weight**

I.P. procedure for uniformity of weight was followed, twenty tablets were taken and their weight was determined individually and collectively on a digital weighing balance. The average weight of one tablet was determined from the collective weight. The weight variation test would be a satisfactory method of determining the drug content uniformity [22].

**Disintegration time**

The test was carried out on the 6 tablets using the apparatus specified in I.P.-1996 distilled water at $37^0C \pm 2^0C$ was used as a disintegration media and the time in second taken for complete disinigration of the tablet with no palpable mass remaining in the apparatus was measured in seconds.

**Wetting time**

The method reported by Yunixia *et al.*, was followed to measure tablet wetting time. A piece of tissue paper (12 cm X 10.75 cm) folded twice was placed in a small petridish (ID = 6.5 cm) containing 6 ml of Sorenson's buffer pH 6.8. A tablet was put on the paper, and the time for complete wetting was measured. Three trials for each batch were performed and the standard deviation was also determined.

**In vitro dispersion time**

In vitro dispersion time was measured by dropping a tablet in a beaker containing 50 ml of Sorenson's buffer pH 6.8. Three tablets from each formulation were randomly selected and in vitro dispersion time was performed.

**Friability**

It is measured of mechanical strength of tablets. Roche fribalator was used to determine the friability by following procedure [22].

A preweighed tablet was placed in the fribalator. Fribalator consist of a plastic chamber that revolves at 25 rpm, dropping those tablets at a distance of 6 inches with each revolution. The tablets were rotated in the friabalator for at least 4 minutes. At the end of test tablets were dusted and reweighed, the loss in the weight of tablet is the measure of friability and is expressed in percentage as

% Friability = loss in weight / Initial weight X 100

**Tablet hardness**

Hardness of tablet is defined as the force applied across the diameter of the tablet in the order to break the tablet. The resistance of the tablet to chipping, abrasion or breakage under condition of storage transformation and handling before usage depends on its hardness [22].

Hardness of the tablet of each formulation was determined using Monsato Hardness tester

**Tablet thickness**

Tablet thickness is an important characteristic in reproducing appearance and also in counting by using filling equipment. Some filling equipment utilizes the uniform thickness of the tablets as a counting mechanism. Ten tablets were taken and their thickness was recorded using micrometer [22].

**Content uniformity**

Ten randomly selected tablets were weighed and average weight was calculated, the tablets were powdered in a glass mortar. The weight equivalent to 12.5 mg Carvedilol was weighed. The weighed amount was dissolved in 5 ml of methanol in separate volumetric flask using magnetic stirrer, the volume was adjusted to 100 ml with Sorenson's buffer pH 6.8 and the solution was filtered. An aliquot of 1.0 ml from these solution were diluted to 10 ml Sorenson's buffer pH 6.8 in separate volumetric flasks. The drug content in each formulation was determined spectrophotometrically at 285 nm.

**In vitro dissolution studies**

In vitro dissolution studies for all the fabricated tablets and marketed formulation was carried out using USP 24 paddle method at 50 rpm in 900 ml of Sorenson's buffer pH 6.8 as dissolution media, maintained at $37\pm0.5^0C$. Five ml aliquots was withdrawn at the specified time intervals, filtered through Whatmann filter paper and assayed spectrophotometrically at 285 nm. An equal volume of fresh medium, which was pre-warmed at $37^0C$ was replaced into the dissolution medium after each sampling to maintain the constant volume throughout the test. Dissolution studies were performed in triplicate.

The various kinetic treatments were given to the dissolution data. The in vitro permeation data obtained were subjected to a zero order and first order kinetics, Korsemeyer's equation, Higuchi model as well as Hixon Crowell Cube Root Law to understand the release profile and release mechanism. When a graph of the cumulative

percentage of the drug released from the tablet against time is plotted, zero order release is linear in such a plot, indicating that the release rate is independent of concentration. The rate of release of the drug can be described mathematically as follows:

**Rate of release = (dCs/t) = k**

Where Cs = concentration of the drug present in the matrix,

k = rate constant and t = time.

Cs is a constant,

x = amount of drug released described as dx / dt = k integration of the equation yields

**x = k t + constant**

A plot of x versus t results in a straight line with the slope = k. The value of k indicates the amount of the drug released per unit of time and the intercept of the line at time zero is equal to the constant in the equation. The curves plotted may have different slopes, and hence it becomes difficult to exactly pinpoint which curve follows perfect zero order release kinetics. Therefore, to confirm the kinetics of drug release, in vitro data were also analyzed using Korsemeyer's equation [22].

Korsemeyer et al., used a simple empirical equation to describe general solute release behavior from controlled release polymer matrices:

$$m_t/m_\infty = k\,t^n$$

Where $m_t/m_\infty$ = fraction of drug released, k = kinetic constant, t = release time and n = the diffusional exponent for drug release.

The slope of the linear curve gives the 'n' value. Peppas stated that the above equation could adequately describe the release of solutes from slabs, spheres, cylinders and discs, regardless of the release mechanism.

The value of 'n' gives an indication of the release mechanism. When n = 1, the release rate is independent of time (zero order) (case II transport); n = 0.5 for Fickian diffusion; and when 0.5 < n < 1, diffusion and non-Fickian transport are implicated. Lastly, when n > 1.0 super case II transport is apparent. 'n' is the slope value of log $m_t/m_\infty$ versus log time curve.

**Stability Studies:**

**Temperature dependent stability studies:**

The fast dissolving tablets of Carvedilol were packed in wide mouth air tight glass container and stored under the following conditions for a period of 60 days: 40$\pm$ 1$^{o}$C, 50 $\pm$ 1$^{o}$C, 60 $\pm$ 1$^{o}$C and at 37 $\pm$ 1$^{o}$C and RH 75 % $\pm$ 5%.

The tablets were withdrawn after a period of 15 days and analyzed for physical characterization and drug content spectrophotometrically at 285 nm. The data obtained was fitted into first order equations to determine the kinetics of degradation. Accelerated stability data were plotted according Arrhenius equation to determine the shelf life at 25$^{o}$C. In the present study fast dissolving tablets of Carvedilol were prepared and evaluated for their use to obtain fast, controlled release and to prevent first pass metabolism.

**Results and Discussion**

**Analytical Profile of Carvedilol [23-31]:**

The DSC thermogram of Carvedilol is shown in Figure 1. The DSC thermogram of Carvedilol showed sharp peak at 110$^{0}$C. The identity of a compound was confirmed by comparison with that of an authentic sample and verification of the presence of functional groups in an unknown molecule was done by IR spectra**.** The IR spectra obtained was elucidated for important chromophore groups. The IR spectra showed peaks at 3351.1, 2927, 1590.6, 1500.2, 1264.6, 1097.7, 849.7, 748 cm$^{-1}$. The various peaks are depicted in Figure 2.

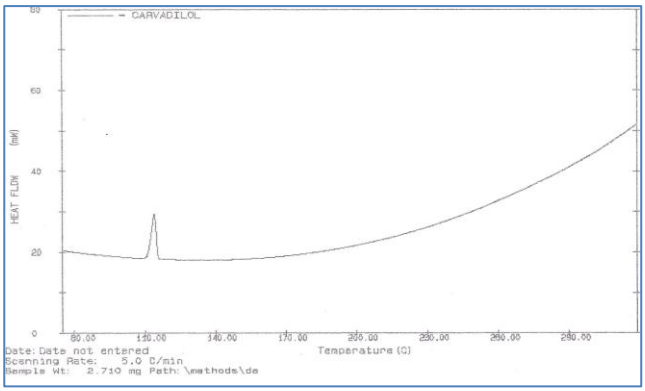


**Figure 1:** DSC Thermogram of Carvedilol

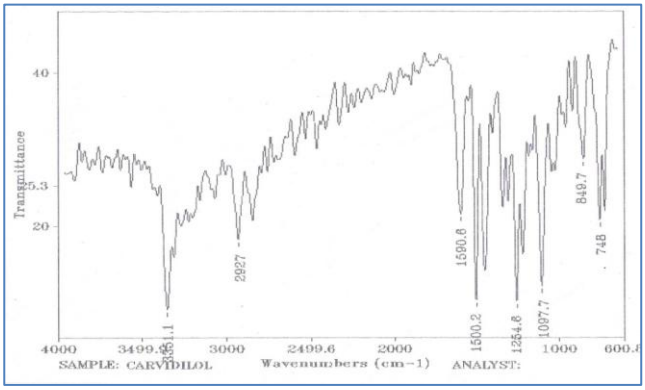


**Figure 2:** IR Spectra of Carvedilol

**EVALUATION OF SOLID DISPERSION [32-40]**

Solid dispersion of Carvedilol: PEG 4000 (1:1 to 1:8) were prepared by fusion method for the fast release of Carvedilol. The prepared solid dispersions were evaluated for Drug content, Saturation solubility and x ray diffraction studies. Drug content from solid dispersion of Carvedilol : PEG 4000 (1:1 to 1:8) was found to be 97.94 % to 99.92%. The results are shown in Table 5.

The saturation solubility of pure drug as well as solid dispersion was found to be 0.323 mg/ml and 23.341 mg/ml to 32.214 mg/ml. The results are shown in Table 5. It was observed that the saturation solubility of the drug was increased by converting the drug Carvedilol into solid dispersions which may be due to change in physical state of Carvedilol from crystalline to amorphous state, which was confirmed by XRD studies.

**Table 5:** Evaluation of Solid dispersions

| Parameters Ratio | Drug content (%) | Saturation solubility (mg/ml) |
|---|---|---|
| **Pure Drug** | 100 | 0.323±0.0215 |
| **1:1** | 99.91±1.302 | 23.341±1.257 |
| **1:2** | 98.61±1.294 | 24.837±1.072 |
| **1:3** | 97.25±0.416 | 26.359±0.986 |
| **1:4** | 99.92±0.256 | 29.957±0.549 |
| **1:5** | 99.25±0.419 | 29.998±1.024 |
| **1:6** | 97.94±1.253 | 30.001±1.002 |
| **1:7** | 98.26±1.035 | 28.098±0.458 |
| **1:8** | 99.65±0.983 | 32.214±1.914 |

± S.D. means of three readings

On the basis of the obtained results the ratio of Carvedilol: PEG 4000 (1: 4) was optimized for further development of the fast dissolving tablet of Carvedilol.

The X- Ray diffraction pattern of solid dispersion of Carvedilol : PEG 4000 (1:4) showed no defined peak attributes to Carvedilol, this implies the absence of apparent crystallinity in solid dispersion. However in the pure Carvedilol powder typical peak of Carvedilol was present, so confirming the satisfactory sensitivity of the method. The peaks are shown in Figure 3.

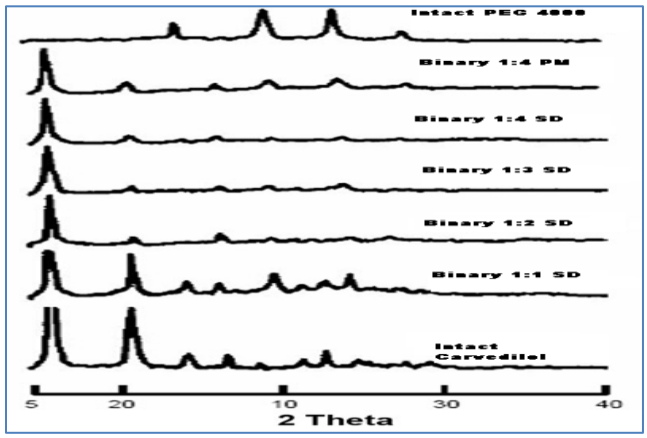


**Figure 3:** X-Ray Diffraction Spectrums

**Characterization of Blends [41-50]**

The characterization of mixed blend done for the flow property of powder that are bulk density, tapped density, angle of repose, Compressibility index, Hausner's ratio were studied.

Bulk density depends on the particle size, shape and tendency of particles to adhere together. It is also important in size hoppers and receivers for milling equipment and for size blending equipment. The bulk density of mixed blend varied between 0.381 to 0.461 gm/cm$^3$. The results were indicating a good packaging capacity of tablets.

The tapped density was found in the range of 0.403 to 0.478 gm/cm$^3$. By using these two density data Hausner's Ratio and compressibility index was calculated. If the bed of the particles is more compressible then the powder will be less flow able and vice versa. Material having value less than 20 % termed as free flow materials. The powder blends of all the formulation had Hausner's ratio of 1.2 or less indicating the good flowability. The compressibility index was found between 1.045 to 1.192. And the compressibility – flowability correlation data indicated a fairly good flowability of the powder blend.

The flowability of the powder was also evidenced by the angle of repose. The angle of repose was below then 30$^0$ showed good to excellent flow properties of powder. Lower the friction occurring within the mass and better flow rate. The angle of repose was found to be 23.54 to 30.15$^0$. This indicates the good flow property of the mixed blends.

**Characterization of Free tablets [51]**

After compression of powder the tablets were evaluated for physical organoleptic characteristics like colour, odour, taste, diameter, Thickness, Hardness, Friability, dispersion time, Disintegration time, wetting time. All the formulations are white in colour, odorless, convex in shape with smooth surface with zero defects. The prepared tablets were elegant and lot – to – lot tablet uniformity, free from any surface texture problems.

The average weight of the prepared tablet was found 123.11 to 126.68 mg. so it was predicted that all the formulation exhibited uniform weight with low standard deviation values within the acceptable variation as per IP. The thickness of the tablet was found 2.85 mm. The diameter of the tablets was found to be 7.8 mm. These all results shows the uniformity of playing and filling of die and punch of punching machine and no any processing problem like capping, lamination, picking and sticking were shown. The thickness of a tablet is determined by the diameter of the die, the amount of fill permitted to enter the die, and the force or pressure applied during compression. The uniform tablet thickness shows the uniform die filling and uniform pressure to prepare tablet. The degree of pressure not only affects the thickness of the tablet but also hardness of tablet. Hardness is perhaps the more important criterion since it can affect

disintegration and dissolution. Thus, for tablets of uniform thickness and hardness, it is doubly important to control pressure. A tablet requires certain amount of hardness to withstand the mechanical shocks in handling, packaging and at the time of application. The hardness of the prepared tablet varied from 2.1 to 3.3 Kg/cm$^2$. Which have satisfactory strength to withstand the mechanical shocks?

Tablet hardness is not an absolute indicator of strength since some formulations, when compressed into hard tablets, tend to "cap" on attrition, losing their crown portion. Therefore, another measure of a tablet's strength is its friability. Tablet tend to powder, chip, fragment when handled lack elegance and consumer acceptance. They can also add to a tablet weight variation or content uniformity problem. The friability of all the formulation was found to be less than 1.0 %. The results shows resistance to loss of weight indicates the tablet's ability to withstand abrasion in handling, packaging and shipment.

A disintegrates was added in most of the formulations to facilitate a breakup or disintegration of the tablet when it contacts water in the mouth. Disintegrants may function by drawing water into the tablet, swelling and causing the tablet to burst apart. Such tablet fragmentation may be critical to the subsequent dissolution of the drug and to attain the satisfactory drug bioavailability. In the formulation of fast dissolving tablet the two super disintegrates were used in different concentrations. The tablets with Ac-Di-Sol may disintegrate faster than the tablets with the crosspovidone. The tablets prepared with effervescent technology and by performing technology the tablets were disintegrate much faster then only the addition of the only super disintegrates. The tablets may disintegrate in less than one minute. The in vitro swelling time of all the formulations were varied between 09 to 16 seconds. The comparative study of disintegration time with the effect of using various super disintegrates in different ratios and various technologies by fast dissolving tablets were formed were shown in Figure 4 and 5.

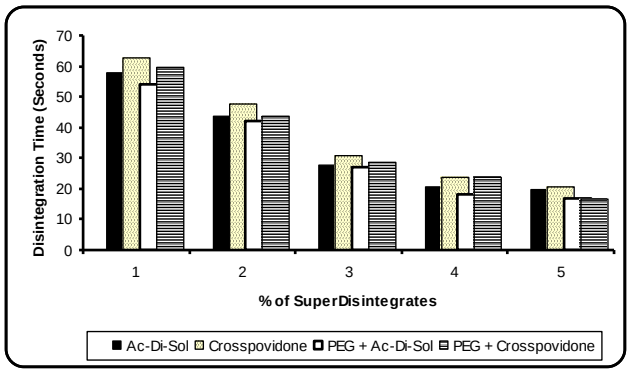


**Figure 4:** Effect of concentration of super disintegrate on disintegration time

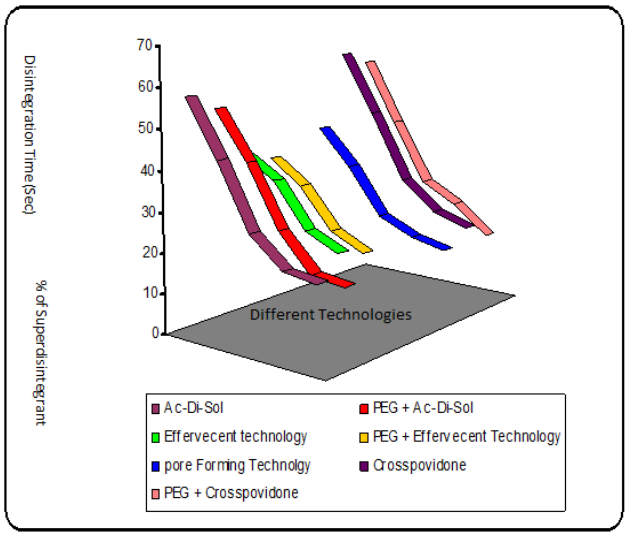


**Figure 5:** Effect of various technology and concentration on disintegration time

**Characterization of Fast dissolving tablets of Carvedilol**

On the characterization of the drug free tablet the best formulations were selected and the drug Carvedilol was incorporated in these formulation. The characterization of mixed blend done for the flow property of powder that are bulk density, tapped density, angle of repose, Compressibility index, Hausner's ratio were shown in Table 6.

The prepared drug tablets were evaluated as similar as the drug free tablets. After compression of powder the tablet were evaluated for physical organoleptic characteristics like colour, odour, taste, diameter, Thickness, Hardness, Friability, dispersion time, Disintegration time, wetting time. All the formulations were exhibit in white colour, odorless, convex in shape with smooth surface with zero defects. The average weight of the prepared tablet was found 123.11 to 126.68 mg. The thickness of the tablet was found 2.85 mm. The diameter of the tablets was found to be 7.8 mm. These results were shown in Table 7. The hardness of the prepared tablet varied from 2.1 to 3.3 Kg/cm$^2$. Which have satisfactory strength to withstand the mechanical shocks. The friability of all the formulation was found to be less than 1.0 %. The results shows resistance to loss of weight indicates the tablet's ability to withstand abrasion in handling, packaging and shipment. The disintegration time of the tablets was varied from 19 to 60 seconds. The in vitro swelling time of all the formulations were varied between 09 to 20seconds. The results were shown in Table 7.

**Table 6:** Characterization of blend of Carvedilol tablet

| Parameters | Bulk Density | Tapped Density | Hausners Ratio | Compressibilty Index | Angle of Repose |
|---|---|---|---|---|---|
| Formulation | (mg/ml) | (mg/ml) | | (%) | 0 |
| $FDT_1$ | 0.428 | 0.459 | 1.072 | 7.242 | 25.34 |
| $FDT_2$ | 0.461 | 0.491 | 1.065 | 6.507 | 24.42 |
| $FDT_3$ | 0.418 | 0.431 | 1.031 | 3.11 | 26.34 |
| $FDT_4$ | 0.447 | 0.473 | 1.058 | 5.816 | 28.24 |
| $FDT_5$ | 0.392 | 0.419 | 1.068 | 6.887 | 27.66 |
| $FDT_6$ | 0.397 | 0.421 | 1.06 | 6.045 | 29.47 |
| $FDT_7$ | 0.379 | 0.419 | 1.105 | 10.554 | 29.98 |
| $FDT_8$ | 0.382 | 0.417 | 1.091 | 9.162 | 28.64 |
| $FDT_9$ | 0.411 | 0.439 | 1.068 | 6.812 | 26.22 |
| $FDT_{10}$ | 0.417 | 0.441 | 1.057 | 5.755 | 28.39 |
| $FDT_{11}$ | 0.419 | 0.437 | 1.042 | 4.295 | 29.88 |
| $FDT_{12}$ | 0.423 | 0.455 | 1.075 | 7.565 | 28.36 |
| $FDT_{13}$ | 0.386 | 0.421 | 1.09 | 9.067 | 26.66 |
| $FDT_{14}$ | 0.387 | 0.425 | 1.098 | 9.819 | 28.71 |
| $FDT_{15}$ | 0.401 | 0.478 | 1.192 | 9.202 | 27.28 |
| $FDT_{16}$ | 0.403 | 0.436 | 1.081 | 8.188 | 29.61 |

**Table 7:** Characterization of Carvedilol fast dissolving tablet

| Parameters | Diameter | Thickness | | Hardness | Friability | Disintegration Time | |
|---|---|---|---|---|---|---|---|
| Formulation | (mm) | (mm) | Weight (mg) | ($Kg/cm^2$) | (%) | (Sec) | Swelling Time (Sec) |
| $FDT_1$ | 7.8 | 2.85 | 124.61±0.39 | 2.3±0.1 | 0.55±0.23 | 28±2 | 15±6 |
| $FDT_2$ | 7.8 | 2.85 | 125.10±0.12 | 2.2±0.3 | 0.62±0.51 | 21±4 | 12±3 |
| $FDT_3$ | 7.8 | 2.85 | 125.48±0.19 | 2.5±0.1 | 0.41±0.37 | 31±2 | 17±2 |
| $FDT_4$ | 7.8 | 2.85 | 124.89±0.41 | 2.5±0.4 | 0.55±0.24 | 24±5 | 14±4 |
| $FDT_5$ | 7.8 | 2.85 | 125.38±0.87 | 3.1±0.1 | 0.77±0.13 | 54±4 | 16±2 |
| $FDT_6$ | 7.8 | 2.85 | 125.54±0.28 | 3.2±0.2 | 0.48±0.29 | 42±6 | 14±1 |
| $FDT_7$ | 7.8 | 2.85 | 125.21±0.18 | 3.1±0.3 | 0.43±0.11 | 60±3 | 20±3 |
| $FDT_8$ | 7.8 | 2.85 | 126.25±0.83 | 3.1±0.2 | 0.77±0.27 | 44±5 | 17±1 |
| $FDT_9$ | 7.8 | 2.85 | 124.99±0.57 | 2.5±0.1 | 0.48±0.19 | 25±1 | 13±3 |
| $FDT_{10}$ | 7.8 | 2.85 | 125.02±0.09 | 2.1±0.1 | 0.75±0.24 | 21±3 | 11±4 |
| $FDT_{11}$ | 7.8 | 2.85 | 125.09±0.22 | 2.3±0.2 | 0.81±0.32 | 23±3 | 11±3 |
| $FDT_{12}$ | 7.8 | 2.85 | 124.87±0.27 | 2.5±0.1 | 0.57±0.25 | 19±5 | 9±2 |
| $FDT_{13}$ | 7.8 | 2.85 | 123.48±0.85 | 2.2±0.2 | 0.54±0.52 | 38±4 | 15±4 |
| $FDT_{14}$ | 7.8 | 2.85 | 123.11±0.57 | 2.1±0.2 | 0.84±0.61 | 26±3 | 11±2 |
| $FDT_{15}$ | 7.8 | 2.85 | 123.86±0.23 | 2.5±0.1 | 0.29±0.18 | 35±4 | 17±4 |
| $FDT_{16}$ | 7.8 | 2.85 | 124.03±0.59 | 2.5±0.3 | 0.45±0.26 | 23±5 | 13±3 |

The drug content of all the formulations was determined spectrophotometrically at 285 nm. It varied from 12.293 to 12.600 mg per tablet. The correlation of variation was found to be less than 0.054 %, indicating uniformity of the drug content in the prepared tablets.

**In vitro Drug release profile**

In vitro drug relase experiments were performed at 37± 1°C in six basket dissolution rate apparatus (USP 24 paddle). The data obtained in *in- vitro* Drug release study are tabulated and represented graphically as:

(a) Cumulative percentage drug release v/s time
(Zero order release kinetic)
(b) Log cumulative percentage drug retained v/s time
(First order release kinetics)
(c) Cumulative percentage drug release v/s square root of time
(Higuchi model)
(d) Log dose fraction v/s Log time
(Kosmeyer data curve).
(e) Cube root of Weight Fraction v/s Time
(Hixon – Crowell's Cube Root Law)

The drug release from the various producs and marketed preparation is shown in figure 6 and table 8. The in-vitro release data were fitted and data is listed in table 9 & 10.

The results showed that all the formulation releases the drug within 6 to 7 minutes. The maximum drug release was found in formulation $FDT_{14}$ (98.275%). The order of drug release was found to be:

**$FDT_{14}$ > $FDT_{13}$ > $FDT_{16}$ > $FDT_6$ > $FDT_2$ > $FDT_5$ > $FDT_{12}$ > $FDT_8$ > $FDT_{15}$ > $FDT_1$ > $FDT_7$ > $FDT_{10}$ > $FDT_{11}$ > $FDT_4$ > $FDT_9$ > $FDT_3$**

Formulations $FDT_1$, $FDT_2$, $FDT_3$, $FDT_4$ which contain 3 and 4 % disintegrant, Ac-Di-Sol and Crosspovidone respectively. The release found to be at the end of five minutes 90.671, 96.063, 77.789 and 85.323 respectively. The formulations with Ac – Di- Sol shows more release than the tablets with Crosspovidone.

An increase in the drug release was observed when the drug used as solid dispersion with PEG 4000 in ratio of 1:4. The formulations contain solid dispersion $FDT_5$, $FDT_6$, $FDT_7$, $FDT_8$ with low concentration of disintegrant (1 and 2%) Ac-Di- Sol, Crosspovidone respectively. The drug release at end of five minutes was found to 96.042, 99.266, 90.633and 94.948 respectively.

The drug release was found to be 84.272, 88.587, 88.531, and 94.967 respectively for the formulation for the formulations $FDT_9$, $FDT_{10}$, $FDT_{11}$, $FDT_{12}$ which were formed by the Effervescent Technology and by effervescent in combination of solid dispersion without addition of any super disintegrants.

**Table 8:** In-Vitro drug release of marketed formulation

| Time (min) | Sqrt. Time | Log Time | Cum. % Drug Release | Log % Drug Retained | Log (Mt/M*) X 1000 | $Wo^{1/3} - Wt^{1/3}$ |
|---|---|---|---|---|---|---|
| 0 | 0 | #NUM! | 0 | 2 | #NUM! | 4.641589 |
| 0.5 | 0.707107 | -0.30103 | 1.212 | 1.994704 | 1.083503 | 3.5754 |
| 1 | 1 | 0 | 3.389 | 1.985027 | 1.530072 | 3.139518 |
| 2 | 1.414214 | 0.30103 | 5.527 | 1.975308 | 1.742489 | 2.873531 |
| 3 | 1.732051 | 0.477121 | 7.001 | 1.968478 | 1.84516 | 2.728567 |
| 4 | 2 | 0.60206 | 9.029 | 1.958903 | 1.95564 | 2.559273 |
| 5 | 2.236068 | 0.69897 | 11.627 | 1.94632 | 2.065468 | 2.376131 |
| 10 | 3.162278 | 1 | 22.113 | 1.891465 | 2.344648 | 1.83476 |
| 15 | 3.872983 | 1.176091 | 41.542 | 1.766844 | 2.618487 | 1.178243 |
| 20 | 4.472136 | 1.30103 | 64.248 | 1.5533 | 2.80786 | 0.636429 |
| 25 | 5 | 1.39794 | 78.547 | 1.331488 | 2.89513 | 0.358966 |
| 30 | 5.477226 | 1.477121 | 82.235 | 1.249565 | 2.915057 | 0.292961 |
| 45 | 6.708204 | 1.653213 | 96.025 | 0.599337 | 2.982384 | 0.062334 |

The rapid drug dissolution might due to easy breakdown of particles and rapid absorption of drug into the dissolution

medium. The fast dissolving tablets formulated by sublimation technology by vacuum drying the formulations $FDT_{13}$, $FDT_{14}$, $FDT_{15}$, $FDT_{16}$ the drug release was found at the end of five minute 97.451, 98.257, 94.253, 96.325 respectively. This signifies that super disintegrates Ac- Di – Sol in concentration of 4% and within combination of solid dispersion the concentration of 2 % Ac – Di- Sol is sufficient for the formulation of fast dissolving tablets of Carvedilol. The tablets formulated by sublimation technology and effervescent technology were also signified for rapid release if the drug Carvedilol.

Next the release data obtained were subjected for the kinetic treatment to know the type and order of drug release. From the in-vitro drug release profile it is evident that the kinetics of drug release is first order for all the prepared fast dissolving tablets as the plot between log percent drug retained versus time showed good linearity. The coefficient of determination of $R^2$ values much closer to 1 for the higuchi plots, thus indicating the drug release from the tablets followed a diffusion controlled mechanism. The value of n obtained from Kosemeyer curves was in the range of near to one which is a further indication of the diffusion-controlled release. The good relationship was evidenced in the Hixon – Crowell's Cube Root Law which signifies the drug is assumed to dissolve out from matrix or from surface of the device. As the drug is released the distance for diffusion becomes increasing greater. The permeation kinetics data are shown in Table 9 &10.

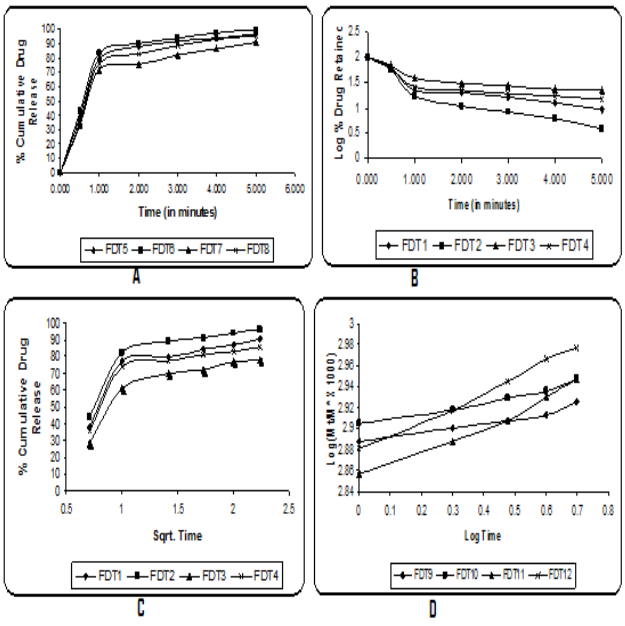


**Figure 6:** In-Vitro drug release of model of various formulations; A: Zero Order Release model, B: First Order Release model, C: Higuchi Model, D: Korsemeyer Model

**Table 9:** Fit of Various Kinetic Models for Fast Dissolving Tablet of Carvedilol.

| Code | Zero order | | | First order | | |
|---|---|---|---|---|---|---|
| | Intercept | $R^2$ | K(mg.min$^{-1}$) | Intercept | $R^2$ | K min$^{-1}$) |
| $FDT_2$ | 0.8356 | 0.7932 | 0.1179 | 2.4388 | 0.9463 | 2.4388 |
| $FDT_6$ | 0.8027 | 0.8652 | 0.1326 | 8.2123 | 0.9579 | 3.6023 |
| $FDT_{12}$ | 0.8073 | 0.8756 | 0.1090 | 5.7384 | 09888 | 2.8142 |
| $FDT_{14}$ | 0.9110 | 0.8568 | 0.1220 | 0.1352 | 0.9950 | 3.1204 |

**Table 10:** Fit of Various Kinetic Models for Fast Dissolving Tablet of Carvedilol.

| Code | Hixon Crowell Cube Root Law | | | Higuchi Model | | | Korsemeyer Data Curves | | |
|---|---|---|---|---|---|---|---|---|---|
| | Intercept | $R^2$ | K (mg.min$^{-1}$) | Intercept | $R^2$ | K (mg min$^{-1/2}$) | Intercept | $R^2$ | n |
| $FDT_2$ | 2.0594 | 0.9951 | 2.3065 | 12.531 | 0.9602 | 13.434 | 1.3487 | 0.9759 | 1.0562 |
| $FDT_6$ | 0.851 | 0.9987 | 2.9789 | 20.871 | 0.9362 | 18.958 | 1.4179 | 0.9962 | 1.0943 |
| $FDT_{12}$ | 3.954 | 0.9952 | 2.5501 | 17.881 | 0.9165 | 15.724 | 1.4067 | 0.9957 | 1.0222 |
| $FDT_{14}$ | 0.1306 | 0.9985 | 2.5797 | 20.905 | 0.8859 | 16.752 | 1.3413 | 0.9835 | 1.0757 |

**STABILITY STUDIES [52-57]:**

Stability studies were conducted for the formulations $FDT_2$, $FDT_6$, $FDT_{12}$, $FDT_{14}$. The reasons for selection are, these four formulations have shown best results in-vitro disintegration, hardness, friability, in-vitro drug release studies. Stability studies of the prepared fast dissolving tablets were performed at different temperatures/humidity and under U.V. radiation ($\lambda_{max}$ – 254nm). The tablets were analyzed for weight of tablet, hardness, friability, in-vitro disintegration time, in-vitro swelling time (dispersion), and for drug content in each formulation at a time interval of fifteen days till a period of two months or sixty days.

All the formulations showed no significant variation in all the parameters under the test period at different conditions excepts the tablets were stored in humidity showed softness at the end of the one month due to hyroscopicity imparted by the super disintegrates, PEG 4000, and reaction between sodium bi carbonate and citric acid in the presence of humidity, which may results the low hardness, more friability, low in-vitro disintegration time and low in-vitro dispersion time. The tablets were found to be stable under U.V. radiations.

The drug degradation was found to follow first order kinetics the data obtained from accelerated stability studies, when fitted to the Arrhenius studies, the $K_{25}$ value was found to between 0.0003 to 0.0014 weeks$^{-1}$. The shelf life of prepared tablet was found to be 520 to 832 days.

**Conclusion:**

Today we are thinking of developing unique delivery system for immediate release of drugs only due to recent advances in technology. In the present study fast dissolving tablet of Carvedilol was formulated, prepared and evaluated. The formulated tablets, which can disintegrate or dissolve rapidly once placed into the oral cavity. The tablet is the most widely used dosage form

because of its convenience in terms of self administration, compactness and ease in manufacturing. However, geriatric and paediatric patients experience difficulty in swallowing conventional tablets, which leads to poor patient compliance. To overcome this weakness, we have developed innovative drug delivery system known as “melt in mouth” or “mouth dissolving tablet”. These are novel type of tablets that dissolves in saliva. There characteristics advantages such as administration without water, anywhere, anytime lead to their suitability to geriatric and paediatric patients. They are also suitable for the mentally ill, the bedridden and patient who do not have easy access to water. The benefit in terms of patient compliance, rapid onset of action, increased bio-availability and good stability make these tablets popular as a dosage form for the treatment of hypertension.

In last few decades novel drug delivery systems have been developed to deliver antihypertensive drugs into the body in order to maintain rapid and constant drug level in the blood, to reduce the frequency of administration and to avoid excess drug loading in the body. Carvedilol is both an alpha and a beta adreno receptor-blocking agent used in the treatment of various cardiovascular disorders such as angina pectoris, cardiac arrhythmia and hypertension. Its biological half-life (6 hours) is very short and therefore is an ideal drug candidate for rapid release drug delivery system. It is 90% absorbed from GIT, but its bioavailability is only 10-20% indicating extensive first pass metabolism in liver. In view of substantial first pass effect and its shorter plasma half-life, Carvedilol was selected for incorporating in fast dissolving tablets.

The objective was to fabricate the fast dissolving tablet for rapid release of drug, their characterization, and in-vitro drug release studies. The Carvedilol drug was analyzed by IR, DSC, solubility, partition coefficient, maxima wavelength were determined. The drug sample was found to comply with all the specifications.

In this work different tablets were prepared using different super disintegrants, polymers for solid dispersion, effervescence and sublimation in different ratio by the various technologies. The blends of drug free tablet were evaluated for mass volume relationship, flow properties and for compressibility properties. The drug free tablets were prepared by the direct compression method by using single punch tablet machine. These tablets were evaluated for the color, odor, thickness, diameter, visual inspection for any defects, weight variation, hardness, friability, in-vitro disintegration time, in-vitro swelling time.

The tablets with drug were also evaluated for uniformity of drug content, in-vitro drug release and stability studies. The drug content in the fast dissolving tablets was found to be uniform and with low correlation of variation. The tablets prepared with solid dispersion in combination with super disintegrate showed better release profile as compared to only incorporation of super disintegrates. The tablets prepared by effervescent and pore forming technology provides satisfactory drug release. The release of drug followed first order kinetics and mechanism of drug release was found to be diffusion controlled.

The stability data at different temperature and humidity showed no significant degradation of Carvedilol and shelf life found to be more than 520 days.

Fast dissolving tablets prepared by the Ac – Di – Sol in 4% concentration are promising for rapid release of Carvedilol. Incorporation of solid dispersion (PEG 4000 : CARVEDILOL) (4:1) into Ac – Di – Sol in 2 % concentration enhanced the release rate of Carvedilol and thus therapeutic levels of the drug could be achieved through fast dissolving tablets. Tablets prepared by effervescent and pore forming technologies are also very promising for stable and rapid release of Carvedilol. Prepared tablets exhibited first order kinetics and the drug release profile was matrix diffusion type. From this study it is possible to design suitable fast dissolving tablets containing Carvedilol for the treatment of hypertension with more effectiveness and better patient compliance. Further in-vivo investigations are required to correlate in-vitro drug release studies for the development of suitable rapid release system for Carvedilol.

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