

## Formulation and Evaluation of Liquisolid Compacts of Carvedilol

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**Abstract:** The purpose of this study is to develop a novel liquisolid technique to enhance the dissolution rate of poorly water soluble drug Carvedilol, a BCS class II drug, which is a  $\beta$ -blocker, by using different excipients. The main components of a liquisolid system are a non volatile solvent, carrier and coating materials and a disintegrant. Liquisolid system refers to the formulations that are formed by conversion of liquid drugs, drug suspensions or drug solution in non-volatile solvents into dry, non adherent, free flowing and compressible powder mixture by blending with suitable carrier and coating materials. Hence the dissolution step, a pre-requisite for drug absorption, is by passed and better bioavailability of poorly soluble drug is achieved. Liquisolid tablets of carvedilol are prepared by using PEG, PG, glycerine as non volatile liquid vehicles and Avicel PH 101 and 102, Aerosil as carrier and coating materials respectively. Optimized formulation containing 20% drug in PEG 400, with Avicel 101 as carrier and Aerosil as coating material has shown 98.4% drug release within 20 min which is better than marketed product (CARCA 12.5mg, Intas). The DSC and X-RD studies are performed to investigate the physicochemical properties of formulation and drug excipient interactions. The results are found to be satisfactory.

**Keywords :** drug release, DSC, liquisolid technique and X-RD studies.

### I. Introduction

It is well established that the active ingredient in a solid dosage form must undergo dissolution before it is available for absorption from the G. I.T (Gastro Intestinal Tract). The poor dissolution of water insoluble drugs is a substantial problem confronting the pharmaceutical industry. The absorption rate of a poorly water-soluble drug, formulated as an orally administered solid dosage form, is controlled by its dissolution rate in the fluid at the absorption site. The dissolution rate is often the rate-determining step in drug absorption.<sup>1</sup> Therefore, the solubility and dissolution behaviour of a drug are the key determinants of the oral bioavailability. These two aspects form the basis of the Biopharmaceutical classification system (BCS).

#### Biopharmaceutical Classification System (7, 8, 9, 10)

The BCS was developed primarily in the context of immediate release (IR) solid oral dosage forms. It is the scientific framework for classifying drug substances based on their aqueous solubility and intestinal permeability. It is the drug development tool that allows estimation of the contributions of three major factors, dissolution, solubility and intestinal permeability that affect oral drug absorption from immediate release solid oral dosage forms. It was first introduced into regulatory decision making process into guidance document of immediate release solid oral dosage forms: scale up and post approval changes.

Class	Dissolution in aqueous environment	Permeation over (intestinal) membrane
I	Fast	Fast
II	Slow	Fast
III	Fast	Slow
IV	Slow	Slow

#### Strategies to increase amount of drug at the absorption Site (2, 11, 12)

Different approaches have been attempted to increase aqueous solubility of poorly soluble drugs, such as conversion of crystalline molecule to its amorphous state, a particle size reduction via micronization, solubilization in surfactant systems, cosolvency, hydrotropic solubilization, cyclodextrin complexation.

Solid dispersions improve solubility, wettability, dissolution rate of the drug. However, only few solid dispersion products are commercially available. This is due to poor physical characteristics for dosage form formulation. Similarly use of large quantity of organic solvent in preparation of solid dispersions may pose

environmental and safety concerns. The surface solid dispersions were introduced to overcome these shortcomings. But still there are limitations of this technique which lie with the use of solvents for preparation of surface solid dispersions. Finding a suitable solvent to dissolve the drug and carrier is difficult. Complete removal of solvent is difficult and residual solvent toxicity should be considered. Solution, suspension, powdered filled capsule, compressed tablet, coated tablet. The main disadvantage of soft gelatin capsules is their high production cost.

Therefore, a more recent technique, entitled “**powdered solution technology**”, has been applied to prepare water-insoluble drugs into rapid-release solid dosage forms. Powdered solutions are designed to contain liquid medications in powdered form. The concept of powdered solutions enables one to convert a liquid drug or poorly water-soluble solid drug dissolved in a suitable non-volatile solvent into a dry, non-adherent, free-flowing and readily compressible powder by its simple admixture with selected carrier and coating materials. This method does not involve drying or evaporation. It is well established that better bioavailability of a relatively water-insoluble drug is achieved when the drug is in solution form.

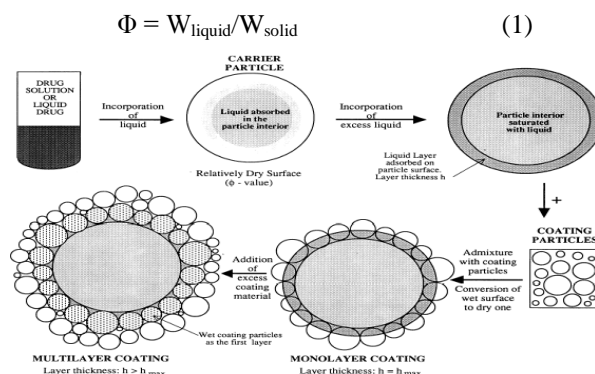
Liquid lipophilic drugs (e.g. chlorpheniramine and clofibrate) or solid drugs (e.g., prednisone, prednisolone, hydrocortisone, theophylline, polythiazide and spiranolactone) dissolved in nonvolatile, high-boiling point solvent systems (e.g., polyethylene & polypropylene glycols, glycerin, N,N-dimethylacetamide, various oils) have been formulated in powdered solutions by admixture with various carriers (e.g., cellulose) and coating materials (e.g. silica).

**Liquisolid Technology (13-39)**

Theoretical considerations in powdered solution formulations.

Absorption of a liquid by a powder material occurs when the absorbate molecules diffuse inside the absorbent and are eventually captured and held by the powder particles within their bulk. In some cases, the liquid is not truly absorbed, and instead of being dispersed throughout the interior of the solid, the liquid molecules only cling to its available surface i.e., internal and external. This process is known as adsorption.

The flowable liquid-retention potential ( $\Phi$  value) of a powder material describes its ability to retain a specific amount of liquid while maintaining good flow properties. The  $\Phi$  value is defined as the maximum weight of liquid,  $W_{\text{liquid}}$  that can be retained per unit weight of the sorbent,  $W_{\text{solid}}$ , yielding a mixture with acceptable flowability.



**Figure 1:** Theoretical model of powdered solutions. When the weight of incorporated liquid per unit weight of carrier material exceeds the  $\Phi$  value of the carrier material, a liquid layer is formed around the carrier particle which must be effectively covered by coating particles. Depending on the amount of coating material, the coating may be monolayered or multilayered.

**Principal hypothesis for the mechanism of powdered solutions (5, 40, 41)**

Depending on the holding capacity of the material, a part of the liquid, say,  $V_{\Phi}$ , is absorbed and retained in the interior of the carrier particles. This volume is dependent on the flowable liquid retention potential ( $\Phi$ ) of the carrier material. The remaining liquid,  $V_L$ , is uniformly distributed and adsorbed onto the internal and external surfaces of the particles, forming a layer of certain thickness,  $h$ , (Fig 1). Thus, mathematically, the volume distribution can be expressed as

$$V = V_{\Phi} + V_L \quad (2)$$

When a coating material, having a very small particle size, large specific surface, and high flowable liquid retention potential, e.g., silica, is added to such a mixture, its fine particles will cover the wet carrier material retaining the excess liquid, thereby maintaining acceptable flow properties.

If only a specific volume ( $V_{\Phi}$ ) of liquid is incorporated into the carrier material, the liquid would be absorbed in the interior of the particles without significantly wetting their surface, and consequently, the powder would be

dry and free flowing. This portion of the liquid is represented by  $V_{\phi}$ , since it depends on the flowable liquid retention potential,  $\Phi$ , and the quantity,  $Q$ , of the carrier material used. Since  $W_{solid} = Q$  and  $W_{liquid} = V_{\phi}\rho$ , where  $\rho$  is the density of the liquid incorporated into the carrier material, Eq (1) can be expressed as

$$\Phi = V_{\phi}\rho / Q \quad (3)$$

Which can be rearranged to give

$$V_{\phi} = Q\Phi / \rho \quad (4)$$

## II. Aim and Objective

The main aim of present study was to increase the dissolution rate of Carvedilol, a BCS class-II (low soluble and high permeable drug) by developing the liquisolid tablets by using different carrier and coating materials with different liquid loading factors and excipient ratios and with different non-volatile liquid vehicles.

Commercially available conventional tablets show 81% release after 20min. Thus the pharmacokinetic profile and solubility in non-volatile liquids provide strong rationale for the drug to formulate as liquisolid tablets. The objective of the study was

- a) To study the effect of different carrier and coating materials on dissolution rates. Avicel PH 101, Avicel PH 200, Aerosil PH 200 are used as carrier and coating materials respectively with different ratios and with different liquid loading factors. Some may decrease the release by incorporating the drug hence it was carefully monitored.
- b) To improve the dissolution rates by improving the physical parameters.
- c) To study the solubility of drug in liquid vehicles and effect of different concentrations of drug in different liquid vehicles on dissolution rates.

Poly ethylene glycol 400, Poly ethylene glycol 200, Propylene glycol and glycerine are used as non-volatile liquid vehicles with different concentrations of drug. The release of drug is dependent on the solubility in different vehicles. Higher the solubility of drug in vehicle higher will be the release, hence the solubility of drug in different liquid vehicles was studied and the vehicle in which it was more soluble was preferred.

- d) To know the effect of different ratios carrier and coating materials on physical properties and drug release.

The carrier and coating materials cause flowability and compressibility to the preparation, hence the ratio should be optimum.

## III. Materials And Methods

**Table1.** List of Materials Used

No	S. MATERIALS	SUPPLIER
1.	Carvedilol	Shandong Xinhua Pharmaceutical Co., Ltd, China
2.	Avicel PH 101	Colorcon
3.	Avicel PH 102	Colorcon
4.	Aerosil	Aqualon
5.	Crospovidone	Colorcon
6.	Sodiumstarch glycolate	Colorcon
7.	Lactose	DMV- Fonterra excipients
8.	Dicalcium Phosphate	Merck laboratories
9.	AcDiSol	Merck laboratories
10.	Polyethyleneglycol	Synero
11.	Propyleneglycol	Colorcon
12.	Glycerine	Synero

### **Methodology (13-39)**

#### **Preformulation studies**

Pre formulation involves the application of biopharmaceutical principles to the physicochemical parameters of drug substance are characterized with the goal of designing optimum drug delivery system.

#### **Drug-Excipients compatibility studies**

Drug Excipients compatibility studies were carried out by mixing the drug with various excipients in different proportions (in 1:1 ratio were prepared to have maximum likelihood interaction between them) was placed in a vial, and closed with rubber stopper and sealed properly. Studies were carried out in glass vials at Accelerated conditions,  $40^{\circ}C \pm 2^{\circ}C / 75\% RH \pm 5\% RH$  and A storage period of 12 weeks.

**Table 2:** Drug-Excipients compatibility studies

S.No	Ingredients	Ratio	Qty.	Code
1.	Pure drug(Carvedilol)		1gm	A
2.	Carvedilol + Avicel PH 200	1:1	5 + 5gm	B
3.	Carvedilol + AerosilPH200	1:1	5 + 5gm	C
4.	Carvedilol+Dicalcium phosphate	1:1	5 + 5gm	D
5.	Carvedilol + Lactose	1:1	5 + 5gm	E
6.	Carvedilol + SSG	1:0.1	5 + 0.5gm	F
7.	Carvedilol+crospovidone	1:0.1	5 + 0.5gm	G

To investigate the possible physical and chemical interactions between the drug and excipient Differential scanning calorimetry studies were performed. 2-3 mg of pure carvedilol, Avicel PH 200, Aerosil PH 200 and liquisolid system physical mixture were weighed and were sealed in a 40- $\mu$ l aluminium pans. The scanning rate of sample was 5<sup>o</sup> C/ min under nitrogen atmosphere at a heating range from 5<sup>o</sup> C to 150<sup>o</sup> C.

#### IV. Preformulation Studies

##### Solubility studies

For the selection of best non volatile solvents solubility studies are used, in this procedure, pure drug was dissolved in five different non volatile solvents. Excess amount of pure drug was adding to the non volatile solvents. From this obtained saturation solution were shaking on the rotary shaker for 48 hours at 25<sup>o</sup> C under constant vibration. After 48 hours period the saturated solution were filtered through a filter paper, and analyzed by UV spectrophotometer. The liquisolid tablets contain a solution of the drug in suitable solvent , the drug surface available for dissolution is tremendously increased.

##### Calculation of loading factor ( $L_f$ )

Loading factors were calculated for different carriers, using various solvents. By using  $L_f = W/Q$  formula (W: Amount of liquid medication and Q: Amount of carrier material). The drug loading factors were obtained and used for calculating the amount of carrier and coating materials in each formulation. The results showed that if the viscosity of the solvent is higher, lower amounts of carrier and coating materials are needed to produce flowable powder.

#### V. Formulation Development

##### Preparation of liquisolid tablets

##### a)Preparation of drug solution:

For the preparation of liquisolid compacts of carvedilol, a non-volatile solvent is chosen for dissolving the drug. From the results of solubility studies and evaluation of flow properties, liquisolid powders containing PEG 400 as the liquid medicament, Avicel PH 101 as carrier and Aerosil PH 200 as the coating material is selected for the preparation of liquisolid compacts. Various ratios of carrier to coating materials are selected. According to solubility of carvedilol, desired quantities of drug and PEG 400 were accurately weighed in a beaker and then stirred with constantly, until a homogenous drug solution was obtained. Selected amounts (W) of the resultant liquid medication were incorporated into calculated quantities of carrier contained in a mortar.

##### b) Mixing

The mixing procedure was conducted in three stages. During the first stage, the system was blended at an approximate mixing rate of one rotation/sec for approximately one minute in order to evenly distribute the liquid medication into the powder.

In the second mixing stage, calculated quantities of coating material was added to the system and blended for 2 min. the liquid/powder admixture was evenly spread as a uniform layer on the surfaces of the mortar and left standing for approximately 5min to allow the drug solution to be absorbed in interior of the powder particles.

In the third stage, the powder was scraped off the mortar surfaces by means of aluminium spatula and then blended with a calculated quantity of disintegrant (5%) for another 30se, and punched with 6.4 mm round, flat and plain punches on a single station tablet machine (Cadmach India). The thickness of the tablet was 3.6 mm.

**Strategy 1:** Using 10%, 20%, 30%, 40% concentration of drug in PEG400, Aviel PH 200, Avicel PH 101 as carrier .

**Table 3.** Composition of liquisolid tablets

Formulation	Carvedilol conc.in PEG 400	R	L <sub>f</sub>	Avicel PH 200 (mg)	Avicel <sup>®</sup> PH 101(mg)	Aerosil PH 200(mg)	Total tablet weight (mg)
F1	10%	5	0.312	400	-	80.0	635.0
F2		10	0.312	400	-	40.0	592.5
F3		15	0.312	400	-	26.5	579.0
F4		20	0.312	400	-	20.0	572.5
F5	20%	5	0.312	200	-	40.0	317.5
F6		10	0.312	200	-	20.0	295.5
F7		15	0.312	200	-	13.2	288.2
F8		20	0.312	200	-	10.0	285.0
F9	30%	5	0.208	200	-	40.0	294.1
F10		10	0.208	200	-	20.0	274.1
F11		15	0.208	200	-	13.2	267.3
F12		20	0.208	200	-	10.0	264.1

Note : All formulations contain 5% crospovidone as a super disintegrant.

L<sub>f</sub> = Load factor; R= carrier and coating material ratio; PEG 400 =Poly ethylene glycol 400.

### VI. Evaluation of Liquisolid Tablets.

#### *Pre Compression Parameters:*

Angle of repose, Bulk density, Tapped density, Compressibility Index, Hausner's ratio.

#### *Post Compression Parameters:*

Thickness, Weight variation, Friability, Assay, Disintegration test, Dissolution test, Differential scanning calorimetry (DSC) studies, X-Ray Powder diffraction (XRD) studies, Stability studies.

### VII. Results And Discussion

#### *Preformulation Studies*

Drug-Excipient compatibility study at 40°C/75% RH.

After 4 Weeks of study physical appearance of these compositions were made and compared with the initial observations.

**Table 4.** Visual observation for Drug-Excipient Ratios for Compatibility Study.

Composition Code	Initial	I week 40°C/75% RH	II weeks 40°C/75% RH	IIIweeks 40°C/75% RH	IVweeks 40°C/75% RH
A	-	-	-	-	-
B	-	-	-	-	-
C	-	-	-	-	-
D	-	-	-	-	-
E	-	-	-	-	-
F	-	-	-	-	-
G	-	-	-	-	-

Negative sign indicates that there was no characteristic change after the storage, the samples were observed physically for liquefaction, caking, and discoloration.

#### *Solubility studies:*

**Table 5 :** Solubility studies of Carvedilol in non volatile solvents.

S.No	Solvent	Solubility (mg/ml)
1.	PEG 400	125±9
2.	PEG 200	110±5
3.	Glycerin	90±5
4.	Propylene Glycol	40±6
5.	Tween 80	25±6

### VIII. Formulation Studies

**Table 6.** Evaluation of tablets containing PEG 400 20% drug solution by using Avicel PH 200 as carrier.

Evaluation Parameters	F5	F6	F7	F8
Angle of repose	25±0.2	34.7±0.3	36.2±0.4	36.4±0.4
Bulk density(gm/cc <sup>3</sup> )	206.5±1.6	206.6±1.9	209.1±1.6	206.8±1.2
Tapped density(gm/cc <sup>3</sup> )	235.7±0.2	238.4±0.9	252.6±0.5	250.0±0.8
Carr's index (%)	12.5±0.6	13.3±0.9	17.2±0.4	17.28±0.3
Hausner's ratio	1.14±0.02	1.15±0.01	1.2±0.01	1.2±0.01

data represents mean ± S. D (n=3).

Powder flow is a complicated matter and is influenced by so many interrelated factors; the factors' list is long and includes physical, mechanical as well as environmental factors. Therefore, in our study, because of the subjective nature of the individual types of measurements as indicators of powder flow, three flow measurement types were employed; the angle of repose, Carr's index (compressibility index), and Hausner's ratio.

Powders showing Carr's index (%) up to 21 are considered of acceptable flow properties. In addition to Carr's index, Hausner's ratio found that the ratios of approximately 1.25 indicating good flow.

### IX. Characterization Of Post Compression Parameters

**Table 7.** Evaluation of tablets containing PEG 400 10% drug solution by using Avicel PH 200 as carrier.

Evaluation Parameters	F1	F2	F3	F4
Hardness (kg/cm <sup>2</sup> )	4.5±0.3	4.4±0.2	4.4±0.4	4.5±0.3
Disintegration time (sec)	190±4	220±5	160±5	170±4
Thickness (mm)	4.6±0.02	4.5±0.02	4.5±0.02	4.4±0.01
Weight variation(mg)	636.5±1.3	595.3±1.7	580.0 ±1.3	575.8±1.5
Friability (%)	0.76	0.45	0.43	0.45
Content of uniformity(%)	98±0.2	98.8±0.8	97.5±0.6	99.2±0.5
% Cumulative drug release (10 min)	72.8±2.4	71.9 ±1.0	64.1±2.8	64.6±2.2
% Cumulative drug release (20 min)	98.4±0.2	94.6±1.3	93.4±1.2	92.4±2.3

data represents mean ± S. D (n=3).

**Table 8.** Evaluation of tablets containing PEG 400 20% drug solution by using Avicel PH 200 as carrier.

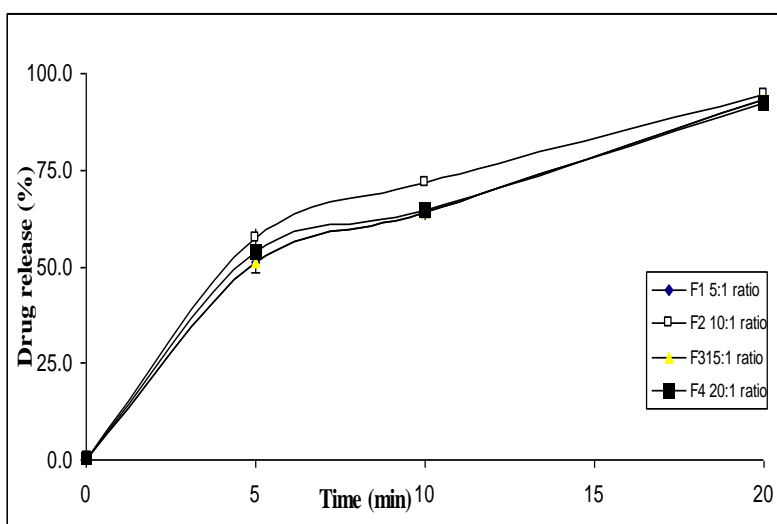
Evaluation Parameters	F5	F6	F7	F8
Hardness (kg/cm <sup>2</sup> )	5.9±0.4	5.8±0.2	5.8±0.2	5.7±0.3
Disintegration time (sec)	115±5	100±4	90±5	90±4
Thickness (mm)	3.0±0.01	3.1±0.01	3.0±0.01	3.1±0.02
Weight variation(mg)	318.2±1.7	300.0±1.6	290.5±1.5	288.1±1.9
Friability (%)	0.33	0.35	0.30	0.25
Content of uniformity(%)	99.6±0.6	96.8±0.3	99.6±0.4	96.6±1.2
% Cumulative drug release (10 min)	76.0±3.5	72.5±3.9	68.7±0.5	71.4±2.2
% Cumulative drug release (20 min)	98.4±1.4	95.4±2.1	93.3±0.9	90.1±3.3

data represents mean ± S. D (n=3).

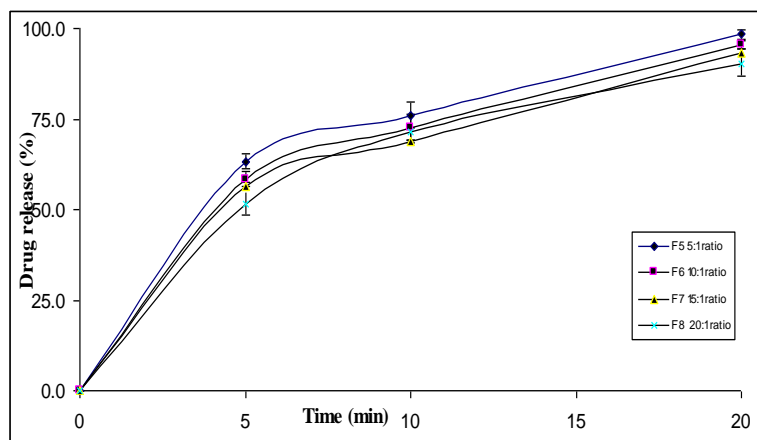
**Table 9.** Evaluation of tablets containing PEG 400 30% drug solution by using Avicel PH 200 as carrier

Evaluation Parameters	F9	F10	F11	F12
Hardness (kg/cm <sup>2</sup> )	6.1±0.4	5.5±0.3	5.9±0.2	5.8±0.2
Disintegration time (sec)	120±2	130±5	150±5	140±5
Thickness (mm)	2.9±0.02	3.0±0.01	2.9±0.02	2.8±0.02
Weight variation(mg)	295.1±3.2	280.1±3.0	271.5±2.8	266.7±3.3
Friability (%)	0.34	0.25	0.34	0.26
Content of uniformity(%)	96.8±0.9	97.2±0.5	99.2±0.5	97.6±0.2
% Cumulative drug release (10 min)	64.1±3.8	59.2±1.9	54.3±3.9	60.1±1.3
% Cumulative drug release (20 min)	92.3±1.3	89.4±1.9	87.4±2.1	85.1±1.7

data represents mean ± S. D (n=3)



**Figure 2.** Dissolution profiles of PEG 400 10% drug solution of carvedilol liquisolid tablets.



**Figure 3.** Dissolution profiles of PEG 400 20% drug solution of carvedilol liquisolid tablets.  
data represents mean ± S. D (n=3).

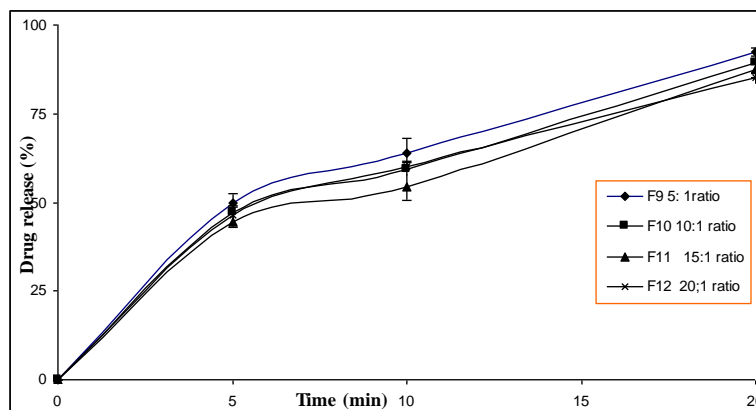


Figure 4. Dissolution profiles of PEG 400 30% drug solution of carvedilol liquisolid tablets.

Liquisolid formulations (F9,F10, F11, F12) containing 30% drug solution in the Figure 5 showed lowest drug release profiles (92.3%, 89.4%, 87.3%,85.1%) when compared to 10% drug solution and 20% drug solution , because of low amount of PEG 400.

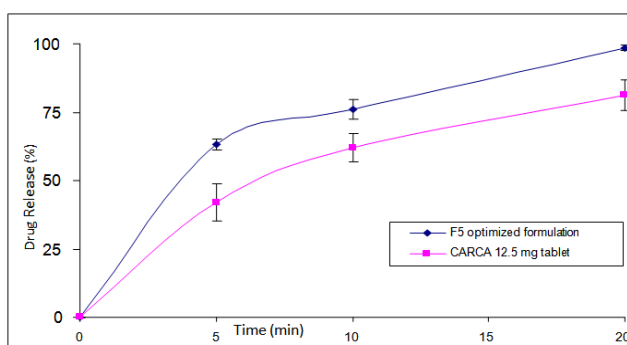


Figure 5. Dissolution profiles optimized formulation (F5) comparison with marketed product CARCA<sup>®</sup> 12.5mg.

In above Figure , optimized formulation F5 was showing highest dissolution rate (98.4%) when compared with marketed product (CARCA<sup>®</sup> 12.5 mg tablets), it was showing less dissolution rate (81.0%) within twenty minutes. Data represents mean  $\pm$  S. D (n=3).

#### X. Effect of ageing on Carvedilol liquisolid formulations(Stability studies)

Effect of ageing on hardness and dissolution rate of carvedilol liquisolid compact was also investigated. To this end, six tablets from F5 optimized formulation were kept at  $40^{\circ}\text{C} \pm 2^{\circ}\text{C} / 75 \pm 5\%$  RH (relative humidity) for 3 months. Then results showed that was no significant difference between the hardness, disintegration time, thickness, average weight, friability, of fresh and aged liquisolid tablets. Figure 6 shows similar dissolution profiles fresh and aged liquisolid tablets.

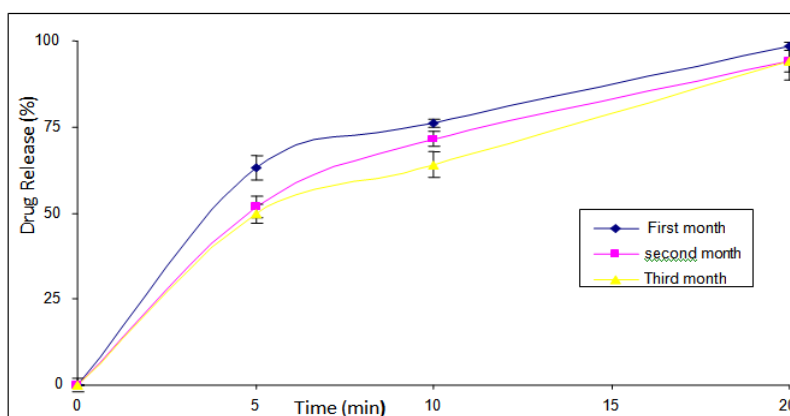


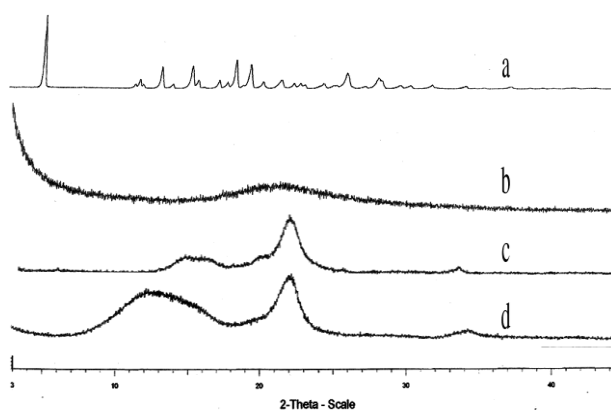
Figure 6: Effect of ageing on dissolution profiles of Carvedilol liquisolid tablets



**Table 10.** Characteristics of the tablets during stability studies.

Evaluation Parameters	Storage condition 40 <sup>o</sup> C±2 <sup>o</sup> C / 75±5 % RH			
	Initial	1 <sup>st</sup> month	2 <sup>nd</sup> month	3 <sup>rd</sup> month
Hardness (kg/cm <sup>2</sup> )	5.9±0.4	5.8±0.4	5.8±0.4	5.8±0.4
Disintegration time (sec)	115±5	115±5	115±5	115±5
Thickness (mm)	3.0±0.01	2.8±0.01	2.9±0.01	2.9±0.01
Weight variation(mg)	318.2±1.7	317±1.7	317±1.7	317±1.7
Friability (%)	0.33	0.3	0.3	0.3
Content uniformity(%)	99.6±0.6	99±0.6	98±0.6	99±0.6
% Cumulative drug release (10 min)	76.0±3.5	75±3.5	76.0±3.5	76.0±3.5
% Cumulative drug release (20 min)	98.4±1.4	98.4±1.4	98±1.4	98±1.4

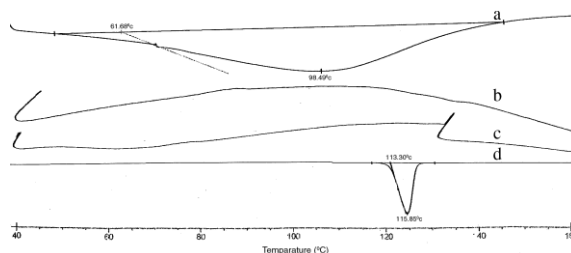
**X-Ray Diffraction (XRD) studies**



**Figure 7.** X-ray diffractions of (a) carvedilol (b) Liquisolid powder system (c) Carvedilol : Avicel PH 200 (d) carvedilol : Aerosil PH 200.

X Ray Diffraction (XRD) is a technique of choice to identify different polymorphic forms of a compound and also used to identify the solvated and un solvated forms of a compound. X-ray diffraction studies of carvedilol in Figure 7 (a) showed a sharp, distinct peaks notably at diffraction angles of 5.7<sup>o</sup>, 12.9<sup>o</sup>, 14.8<sup>o</sup>, 17.4<sup>o</sup>, 18.4<sup>o</sup> and 24.2<sup>o</sup> confirms that it is in the crystalline state. The mixture X-ray diffraction liquisolid powder shown in Figure 7 (b) indicates the absence of carvedilol constructive peaks and points out that carvedilol has almost entirely converted from crystalline to amorphous state due to carvedilol solubilization in the liquid vehicle that was absorbed into the carrier such as Avicel PH 200 and adsorbed on to the coating material such as Aerosil PH 200.

**Differential Scanning Calorimetry**



**Figure 8 .** Differential scanning calorimetry thermograms of (a) liquisolid system (b) Aerosil<sup>®</sup> PH 200 (c) Avicel<sup>®</sup> PH 200 (d) Pure carvedilol.

DSC thermograms of pure Carvedilol and involving excipients indicates a qualitative information about the physical mixture. Pure carvedilol shown in Figure 8 (a) sharp characteristic endothermic peak at 115.85 °C is an

agreement to its melting temperature ( $T_m$ ), denotes that carvedilol is in crystalline state. Thermo grams of Avicel PH 200 in Figure shows two broad endothermic peaks at  $43.2^{\circ}\text{C}$  and  $118^{\circ}\text{C}$  that might agree to the volatilization of absorbed water followed by melting decomposition.

## XI. Conclusion

Of the all lquisolid formulations prepared, F5 was found to be optimized formulation as it showing desired release along with acceptable physical properties. Our main aim was to improve the dissolution behaviour by improving the physical properties. F5 was showing 98.4 % release where as marketed formulation was showing 80% release in 20 min. So optimized formulation is showing better release which is due to enhanced dissolution behaviour which is useful for CHF patients for immediate action. DSC and XRD studies showed that there are no significant interactions between drug and excipients. Stability studies showed that there is no significant difference in physical properties and release in 3 months. From the above discussions it can be concluded that F5 formulation having 20% drug concentration in PEG, with R value 5 and Lf value 0.312 was showing 98.4% release.

## References

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