Pharmacophore 2014, Vol. 5 (4), 451-466 USA CODEN: PHARM7 ISSN 2229-5402

Pharmacophore

(An International Research Journal)

Available online at http://www.pharmacophorejournal.com/

Original Research Paper

FORMULATION DEVELOPMENT AND IN VITRO CHARACTERIZATION OF CARVEDILOL SUSTAIN RELEASE TABLET BY USING LIQUISOLID TECHNIQUE

Tushar N. Patel*, Zankhana P. Sheth, Bhagirath K. Patel and Pritesh Patel

Sat Kaival College of Pharmacy, Sarsa, India

ABSTRACT

The in-vitro dissolution property of poorly water soluble Carvedilol was improved by exploring the potential of Liquisolid system. Liquisolid technique as an approach was developed to sustain the drug release from matrix compacts. Different Liquisolid compacts were prepared using the required quantities of powder and liquid ingredients to produce acceptably flowable and compressible admixture. Eudragit (S, L, RL or RS), Aerosil 200 and PVP were employed as carrier, coating material and binder respectively for preparing Liquisolid compacts. The prepared Liquisolid compacts were evaluated for their flow properties and compressibility. The results suggested that the presence of non-volatile cosolvent is vital to produce slow release pattern for some of liquisolid compacts. The type of cosolvent had significant effect on drug release and it was revealed that by changing the type of cosolvent, the desirable release profile was achievable. PEG 400 was optimizing for this study. The sustained release action of different grade of Eudragit i.e., S 100, L 100, RS 100 & RL 100 was studied from which Eudragit RL 121.5 mg shown better dissolution profile till 12hr. Eudragit RL 100 resulted in fine network and matrix with lower porosity and higher tortuosity could formed and the particle are surrounded by the polymer network resulting in the lower diffusion of drug. This could reason for greater retardation properties. From this study it concludes that the Liquisolid technique is a promising alternative for improvement of dissolution property of water-insoluble drugs.

Keywords: Liquisolid compacts, Eudragit, Drug Release, Physico mechanical property, Dissolution parameters

INTRODUCTION

Carvedilol is beta-adrenergic receptor blocking agent and use as Anti-hypertensive drug. In order for a drug to be absorbed into the systemic circulation following oral administration, the drug must be dissolved in the gastric fluids. The most challenging task in development of a formulation is the solubility of drug, availability at the site of action and stability of drug. Aqueous solubility of any therapeutically active substance is a key property as it governs dissolution, absorption and thus the in vivo efficacy. Drug efficacy can be severely limited by poor aqueous solubility and some drugs also show side effects due to their poor solubility. Therefore, drug release profiles are exhibited by such formulations for poorly soluble drugs to improve the solubility of such poorly soluble drugs. Most of drugs which are weakly acidic and basic show poor aqueous solubility hence various methods like, salt formation, co-solvency, Micronization, addition of agent, solid dispersion, liquisolid compact, Complexation , etc., are some of the vital approaches routinely employed to enhance the solubility of poorly

soluble drugs.[1] Among various technique of solubility enhancement, Liquisolid Technique is one of the promising method to improve the solubility of poorly water soluble drug, The development of Liquisolid technique as a practically viable method to enhance bioavailability of poorly water soluble drugs overcome the limitation of previous approaches such as salt formation, solubilization by co-solvent, particle size reduction, etc. Liquisolid technique prepares a liquisolid compact by addition of carrier and coating material. These compacts are release fast and enhance dissolution and bioavaibility.[2,3]

MATERIALS AND METHODS

Materials

Carvedilol was obtained from Zydus Cadila, Ahmedabad. PEG 200, 400 and 600, Tween 20 & 80, Propylene Glycol, Aerosil 200, Talc and Magnesium Stearate were obtained from S.D Fines, Mumbai. Eudragit S100, L 100, RL 100, RS 100 were obtained from Loba Chemie, Mumbai.

Methods

Calibration Curve for Carvedilol

Calibration curve of Carvedilol was prepared in 0.1 N HCl and in pH 6.8 phosphate buffer using UV visible spectrophotometer (UV 1700, Shimadzu).

(A) In 0.1N HCl

The standard stock solution was prepared by dissolving Carvedilol in diluted with 0.1N HCl to make final concentration of 100 µg/ml. Different aliquots were taken from stock solution and diluted with 0.1N HCl separately to prepare series of concentrations from 5-35 µg/ml. The λmax was found by UV spectrum of Carvedilol in 0.1 N HCl, in the range of 200-400 nm and it was found to be 242 nm. Absorbance was measured at 242 nm 0.1 N HCl as blank. The calibration curve was prepared by plotting absorbance versus concentration of Carvedilol. [4]

(B) In pH 6.8 phosphate buffer

The standard stock solution was prepared by dissolving Carvedilol in 6.8 pH phosphate buffer to make final concentration of 100 µg/ml. Different aliquots were taken from stock solution and diluted with 6.8 pH phosphate buffer separately to prepare series of concentrations from 5-35 µg/ml. The λmax was found by UV spectrum of Carvedilol in 6.8 pH phosphate buffer, in the range of 200-400 nm and it was found to be 242 nm. Absorbance was measured at 242 nm against 6.8 pH phosphate buffer as blank. The calibration curve was prepared by plotting absorbance versus concentration of Carvedilol.[5,6]

Drug Excipient Compatibility Study by FTIR Spectrum Interpretation

The IR spectral analysis of a drug and other excipients were taken using press pellet technique (using KBr.) the IR spectra were determined by using 8400 S Shimadzu FTIR.

Solubility Study of Pure Drug

Solubility study of the drug was found in-

- Water
- 0.1N HCL
- PH 6.8 phosphate buffer

The solubility of drug was determined by adding an excess amount of drug to snap-cap Eppendorf tube containing 1 mL of solvent. The resulting mixture was thoroughly vortexes and then placed in a 37°C incubator for two days. Aliquots were centrifuged at 1000 rpm for 10 min. The supernatant layer was carefully removed and then diluted with a solution. The concentration of drug was then measured using UV/Visible spectrophotometer by comparison with a standard calibration curve.[7]

Dose Calculation as per Robinson Erikson Method[8]

Usual Dose: 12.5

Half-life: 6hr

Elimination Rate Constant:K=0.693/6

=0.1155mg/hr

Available rate (R) =KD

=0.1155×12.5

=1.4437mg/hr

Maintenance Dose (Dm) = R × h

=1.4437×12.5

=17.32mg

h is number of hr. for Which Sustain is Desired.

Total Dose= D + Dm

=12.5+17.32

=29.82

=30mg

Dose (corrected) = D-R (tp)

=12.5-1.44(1)

(tp) Time Required to Achieve Peak Plasma level.

Total Dose (Corrected) =17.32+11.06

=28.38

=28 mg

Calculation of Liquid Load Factor (Lf)

Different concentrations of non-volatile solvents are taken and the drug is dissolved. Such liquid medication is added to the carrier-coating material admixture and blended. Using equation, drug loading factors are determined and used for calculating the amounts of carrier and coating materials in each formulation.[9,10,11]

Lf=w/q

Optimization of Carrier and Determination of Liquid-Retention Potential

In constant weight of carrier/ coating material increasing amount of solvent was incorporated and on each addition angle of repose was determined. The flowable liquid-retention potential (Ø -value) of each liquid/powder admixture was calculated using the following equation,

Ø -value = weight of liquid/weight of solid

The Ø -values were plotted against the corresponding angle of repose (for optimal flow properties).

Corresponding to 33° of a liquid/powder admixture represented the flowable liquid-retention potential.[12, 13, 14]

Tablet Weight Variation

By following USP monographs it was calculated. In this 20 tablets from the each formulation randomly taken and their total average weight was calculated and then the individual tablet weight was calculated by comparing with the average weight.[15]

Tablet Hardness

The test will be done as per the standard methods. The hardness of three randomly selected tablets from each formulation (F1 to F4) will be determined by placing each tablet diagonally between the two plungers of tablet hardness tester (with the nozzle) and applying pressure until the tablet will break down into two parts completely and the reading on the scale will be noted down in Kg/cm^2. [15]

Tablet Friability[36]

The friability of tablets using 10 tablets as a sample will be measure using a Roche Friabilator. Tablets will be rotate at 25 rpm for 4 minutes or up to 100 revolutions. The tablets will take de-dust and reweight. The percentage friability will be calculated from the loss in weight as given in equation below.

$$\%Friability = \frac{\text{Initial Weight-Final Weight} * 100}{\text{Initial weight}}$$

Friability less than 1% are considered acceptable.

In-Vitro Drug Release Study

The test was performed on the prepared Carvedilol liquisolid tablets using the USP dissolution apparatus basket type. Six individual tablets from each formula were tested. Test was performed in 900 ml of two different dissolution medium (0.1 N HCL & 6.8 pH phosphate buffer). In all studies, the temperature of the dissolution medium was maintained at 37± 0.5 °C. The aliquots of 5 ml were withdrawn at regular time intervals 1,2,3,4,5,6,7,8,9,10,11 and 12 hr, filtered, and analyzed spectrophotometrically at 242 nm. For assessment and comparison, drug dissolution rates (DR) of drug were used. For this, amount

of drug (in µg) dissolved per hr that presented by each tablet formulation during the first 1 hr were calculated as follows:

DR= (M ×D) / 1000 where M is the total amount of valsartan in each tablet (in this study, it is 40000 µg) and D denotes percentage of drug dissolved in first 1hr.[16]

Kinetic Modeling

In order to understand the kinetics and mechanism of drug release, the results of *in vitro* drug release were fitted into various kinetic equations like zero order (cumulative% release *vs.* time), first order (log% drug remaining *vs.* time), Higuchi's model (cumulative% drug release *vs.* square root of time), Korsmeyer peppas plot (log of cumulative % drug release *vs.* Log time). *R*2 (coefficient of correlation) and *n* (Diffusion exponent) values were calculated for the linear curve obtained by regression analysis of the in vitro drug permeation plots.[17]

RESULTS AND DISCUSSION

Flow Property of Carvedilol

Flow Property like Angle of repose of Carvedilol was found to be 27.38 (Std 20-30), which shows good flow of drug. Bulk Density & Tapped Density of Carvedilol were found to be 0.31& 0.37 respectively, and Carr's index was 14.64 (Std 12-16), Hausnar Ratio 1.18 (Std <1.25), These all Value indicated that the Carvedilol had good compressibility and passable with std value. So it can be used for direct compression technique.

Solubility of Carvedilol in Different Solvent

Carvedilol Shows Maximum Solubility in Poly Ethylene Glycol 400.

Precompression Parameters of Powder Blend

Flow Property Like Bulk Density & Tapped Density of all Batch were found to be in the range of 0.362 & 0.430, Angle of repose of all batch 25.82 (Std 20-30), Carr's index of F15 Batch 14.64(std 12-16), Hausnar Ratio 1.14 (Std <1.25) , These all Value indicated that the F15 Batch has good flow property compared with other batch and passable with std value.

Post Compression Parameters of Prepared Tablet

The hardness values of tablets were within the range of 4-6 kg/cm^2. Friability values of all formulations were less than 1%. Drug Content Value of all formulation were in between 97.17 to 102.78%. In determinations of tablet weights, all Formulations were found to be within limits as per weight variation test. It show all batches pass within Range as per Pharmacopoeial standard.

In-Vitro Drug Release Study

The release rate of Liquisolid tablets were increased by preparing a Liquisolid Compact. All batches would not Release More than 5 % the drug in 0.1N HCl and release whole amount of drug in pH6.8 phosphate buffer; hence they were acceptable as per predetermined criteria. Here F1-F4 batches were prepared by using carrier to coating material ratio of (100:5, 100:10, 100:15, 100:20, 100:20 percentages). From these batches initial drug releases in 0.1N HCl at 2 hr were 6.47±0.99, 7.14±1.41, 5.91±0.91 & 6.11±2.22 respectively & almost all drug was released at about 8 hrs for all batches. This shows poor dissolution profile than required, so again trials were taken by using different Eudragit types with different amount to get better dissolution profile. F5-F8 batches were prepared by using carrier to coating material ratio of (100:5, 100:10, 100:15, 100:20, 100:20 percentages). From these batches initial drug release in 0.1N HCL at 2 hr (7.14±1.45, 6.80±2.11, 5.66±2.34, 7.24±1.40) respectively & almost all drug was released at about 10 hrs for all batches. This Shows poor dissolution profile than is required, so again trial were taken by using other Eudragit types with different amount of carrier to get good dissolution profile. F9-F12 batches were prepared by using carrier to coating material ratio of (100:5, 100:10, 100:15, 100:20, 100:20 percentage). From these batches initial drug release in 0.1N HCL at 2 hrs (7.26±0.99, 6.63±5.02, 5.02±1.67, 76.88±1.56) respectively & almost all drug was released at about 11 hrs for all batches. This Shows poor dissolution profile than is required, so again trial were taken by using other Eudragit types with different amt to get good dissolution profile. F13-F16 batches were prepared by using carrier to coating material

ratio of (100:5, 100:10, 100:15, 100:20,100:20 percentage). From these batches initial drug release in 0.1N HCL at 2 hr (6.21±1.78, 5.99±1.11, 5.13±1.13, 6.90±1.21) respectively & almost all drug was released at 12 hrs for F15 batches. This shows good dissolution profile than other all batches. This may be because Eudragit RL 100 Resulted in Fine Network and Matrix with Lower Porosity and Higher Tortuosity Could Formed and the particle are surrounded by the Polymer Network Resulting in the lower Diffusion of Drug. This could Reason for the Result greater Retardation Properties as Compared to Eudragit S, Eudragit L, Eudragit RS.

Kinetic Modeling

The release study data of Carvedilol in Sustain Release Formulation (F15 Batch) and Marketed formulation (MF) was analyzed using rate constant equations such as zero order, first order, Higuchi and Korsmeyer peppas equations showed that F 15 Batch formulation had the tendency to follow zero order Dissolution of drug Release, whereas MF had first order Dissolution of drug Release. So F15 batch were good release mechanism.

DISCUSSION

The present investigation used Carvedilol belonging to BCS class-II drugs and also has a half-life of 5-6 hr. The BCS class-II drugs having low solubility and high permeability, so, these drugs have a high absorption number but a low dissolution number. *In-vivo* drug dissolution is the rate limiting step for absorption except at a very high dose number. So, the prime objective of present work was accomplished by liquisolid technique which enhance the solubility of these BCS class-II drugs. The IR spectra indicate that the chemical structure of the drug is not changed before and after liquisolid technique. We conclude that The liquisolid tablet technique can prove to be an effective and efficient way for dissolution rate improvement of water insoluble drugs such as Carvedilol as it shows Enhance the drug Dissolution than that of pure drug. Poly ethylene glycol was used as a liquid vehicle. Enhanced dissolution rates obtained in the present study can be attributed to increased wetting and surface area available for dissolution. This novel approach to the formulation may be helpful to improve oral bioavailability. Use of Sustain Release carrier such as Eudragit RL 100 resulted in fine network and matrix with lower porosity and higher tortuosity could be formed and the drug particles are surrounded by the polymer network resulting in the lower diffusion of the drug. This could be a reason for the resulted greater retardation properties of the liquisolid tablets compared to the conventional tablet. The results suggested that zero-order release can be achieved with liquisolid formulations.

CONCLUSION

Carvedilol liquisolid compact were prepared by this method showed significant improvement in the saturation solubility of the pure drug. By formulating carvedilol liquisolid compact, the saturation solubility can be increased about 25% more than the pure drug. The drug content study of the liquisolid product showed about 25% more increase in the concentration of the drug. The optimized batches of the liquisolid product were converted to the tablet form to compare the liquisolid sustain release tablet with the marketed product. The comparison of the liquisolid tablets with market product and pure drug tablets showed increase in the dissolution characteristics which may significantly improve its oral bioavailability.

ACKNOWLEDGEMENT

The authors express their gratitude to Sat Kaival College of pharmacy for providing necessary facilities to carry out our research work.

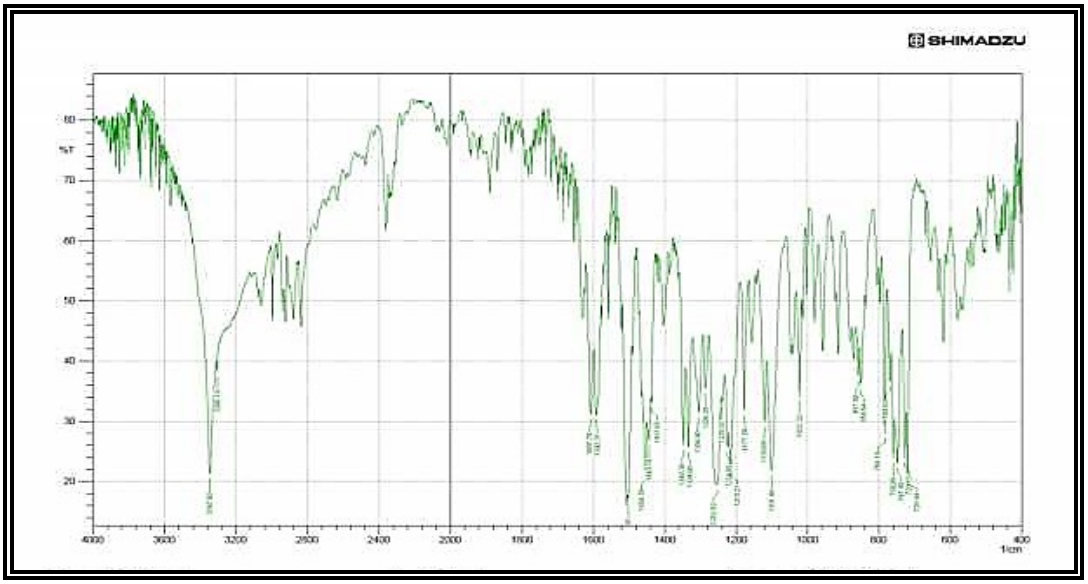

Figure1: FTIR of Carvedilol

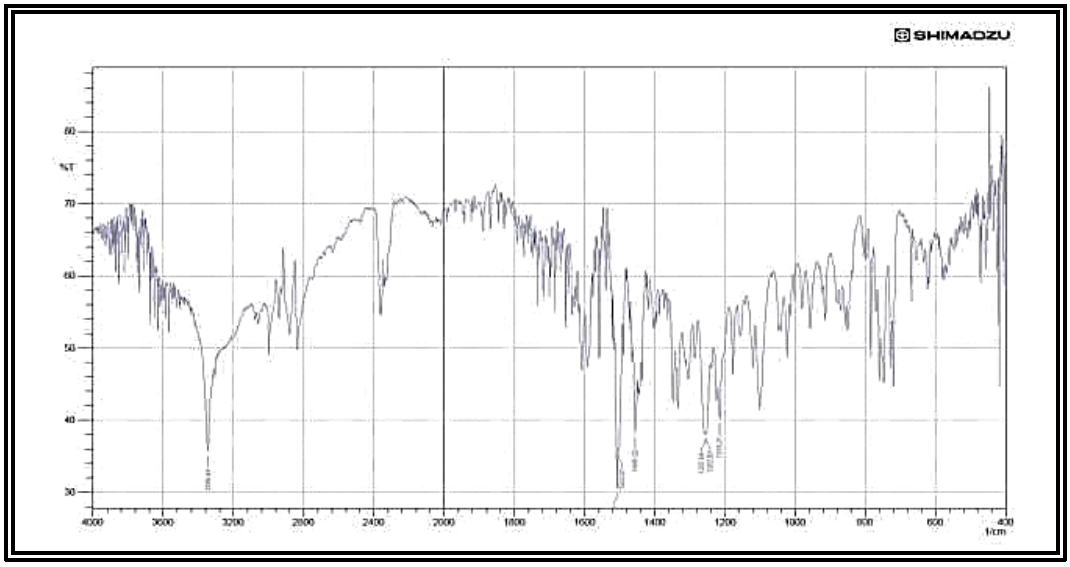

Figure 2: FTIR of Eudragit RL100

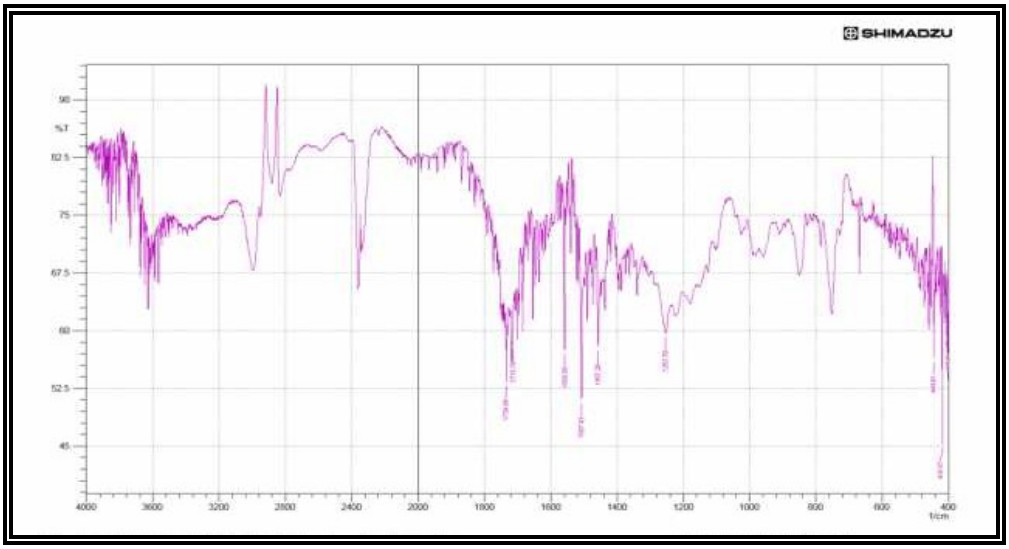

Figure 3: Carvedilol + Eudragit RL100+ PEG 400

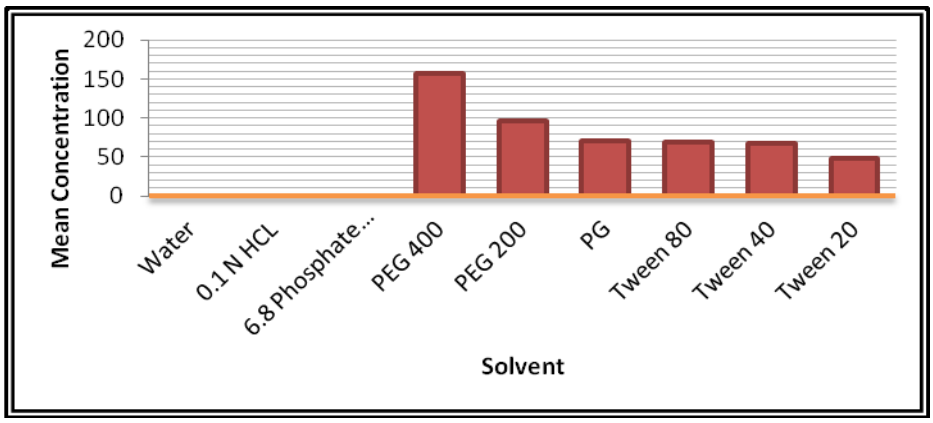

Figure 4: Solubility in Different Solvent

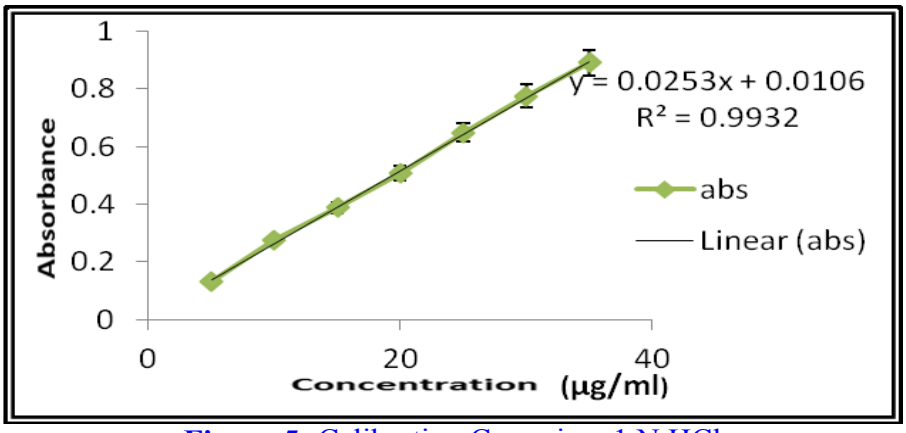

Figure 5: Calibration Curve in o.1 N HCl

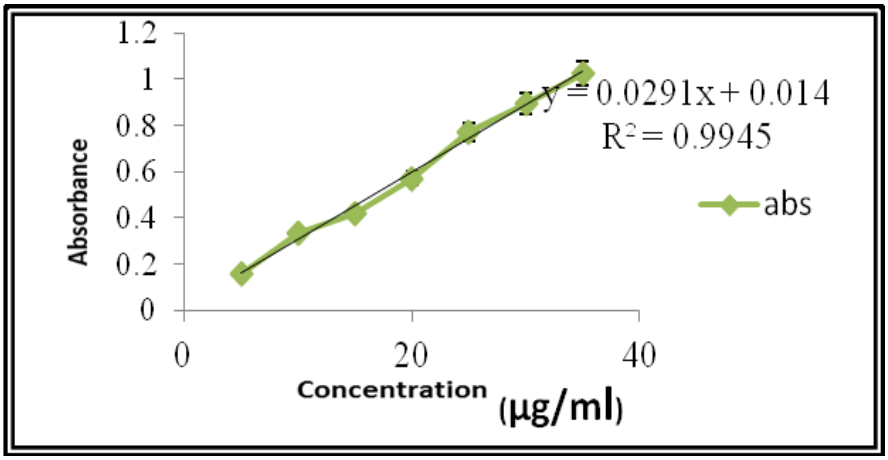

Figure 6: Calibration Curve in 6.8 Phosphate Buffer

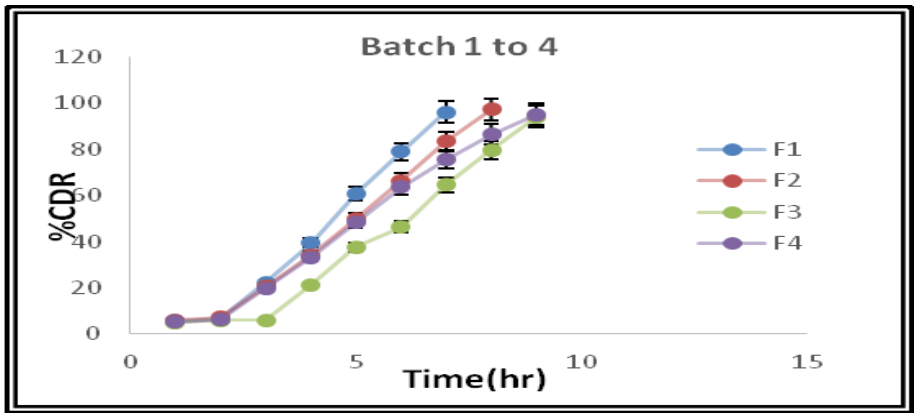

Figure 7: *In-Vitro* Drug Release in F1 to F4 Batch

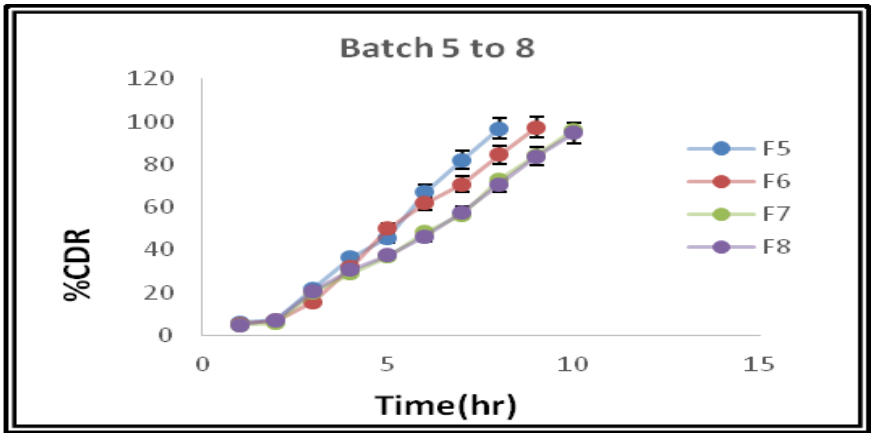

Figure 8: *In- Vitro* Drug Release of F5 to F8 Batch

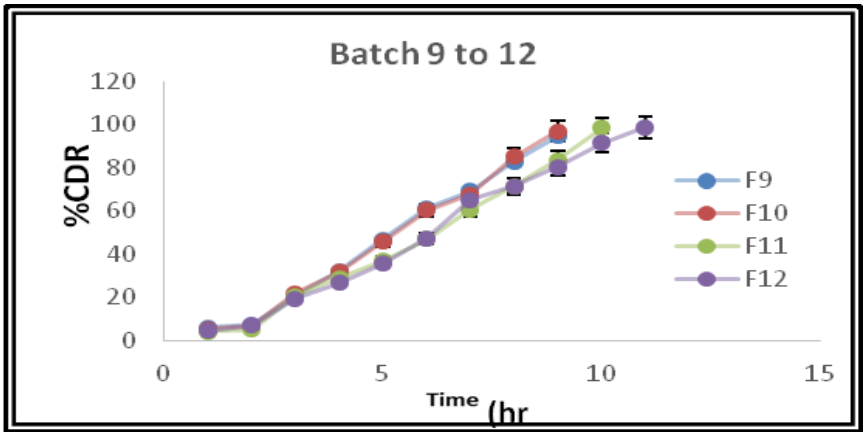

Figure 9: *In- Vitro* Drug Release of F9 to F12 Batch

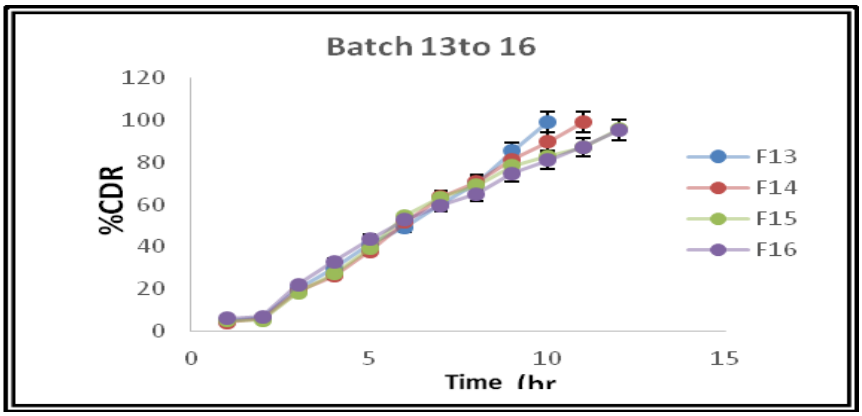

Figure 10: *In- Vitro* Drug Release of F9 to F12 Batch

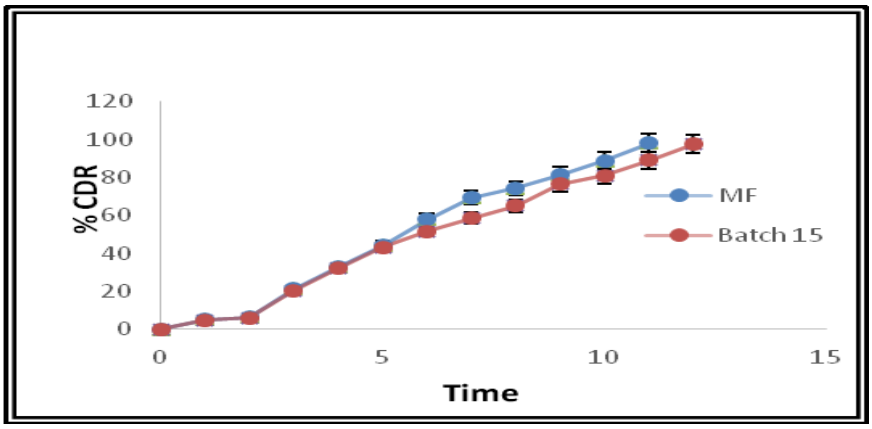

Figure 11: *In-Vitro* Drug Release Study of Marketed Formulation&F15 Optimize Batch

Figure 12: Zero order Kinetic Release Of Optimize batch and Marketed Formulation

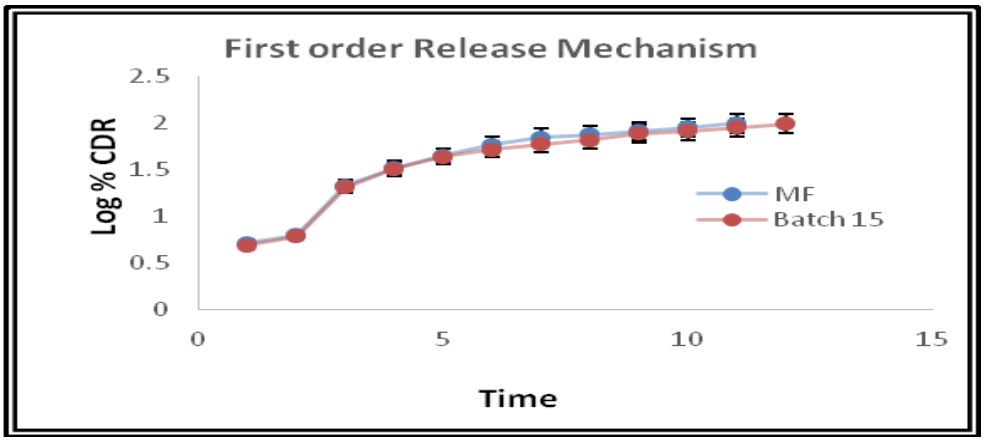

Figure 13: First order Kinetic Release Of Optimize batch and Marketed Formulation

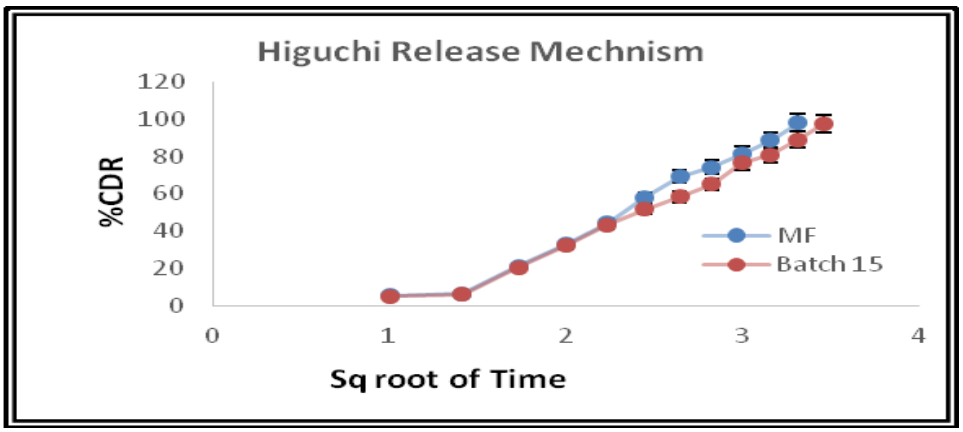

Figure 14: Higuchi Kinetic Release of Optimize batch and Marketed Formulation

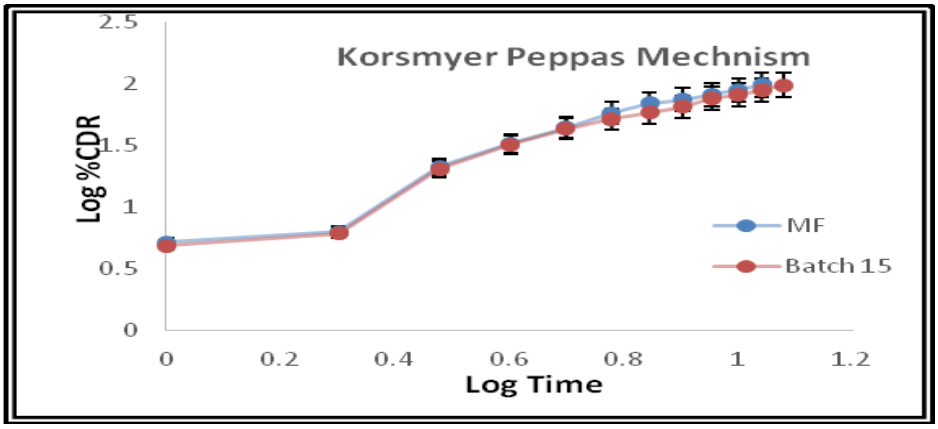

Figure 15: Korsmyer Peppas order Kinetic Release of Optimize batch and Marketed Formulation

Table 1: Flow property of Carvedilol

Drug	Angle of Repose (Θ)	Bulk density (gm/ml)	Tapped density (gm/ml)	Hansnour ratio	Carr's index
Carvedilol	27.38	0.31	0.37	1.18	14.64

Table 2: Solubility in Different Solvent

Solvent	Mean Concentration(mg/ml) AM±SD
Water	0.058 ±0.004
0.1 N HCL	0.0792 ±0.003
6.8 pH buffer	0.092 ±0.01
Poly ethylene glycol 400	157.41±1.9
Ploy ethylene glycol 200	96.34±2.1
Propylene Glycol	70.49±1.4
Tween 80	69.48±1.3
Tween 40	67.25±1.7
Tween 20	48.28±1.5

Table 3: Evaluation of Powdered Blend

Formulation code	Bulk density (gm/cc) AM±SD	Tapped density (gm/cc) AM±SD	Compressibility index (%) AM±SD	Hausner's Ratio AM±SD	Angle of repose (θ)
F1	0.367 ± 0.0046	0.421 ± 0.0032	12.82 ± 1.02	1.14 ± 0.026	32.84
F2	0.362 ± 0.0070	0.435 ± 0.0056	16.78 ± 1.32	1.20 ± 0.012	37.52
F3	0.345± 0.0030	0.452 ± 0.0048	23.67 ±1.67	1.31 ± 0.035	29.56
F4	0.358± 0.0012	0.434 ± 0.0017	17.51 ±1.45	1.21 ± 0.018	31.22
F5	0.352± 0.0076	0.446 ± 0.0053	21.07 ±1.27	1.26 ± 0.023	28.56
F6	0.363± 0.0032	0.457 ± 0.0064	20.56 ±1.83	1.25 ±0.014	29.06
F7	0.372± 0.0021	0.438 ± 0.0046	15.06 ±1.18	1.17 ± 0.041	31.26

F8	0.357± 0.0043	0.439 ± 0.0088	18.67 ±1.53	1.22 ± 0.012	27.86
F9	0.399± 0.0036	0.455 ± 0.0060	19.65 ± 1.26	1.21 ± 0.054	32.99
F10	0.370± 0.0060	0.422 ± 0.0036	15.67 ± 1.09	1.24 ± 0.034	29.82
F11	0.355± 0.0045	0.469 ± 0.0056	21.89 ±1.54	1.20 ± 0.022	31.42
F12	0.415± 0.0032	0.454 ± 0.0057	18.16 ±1.72	1.19 ± 0.034	33.59
F13	0.373± 0.0056	0.470 ± 0.0022	20.50 ±1.45	1.22 ± 0.044	28.05
F14	0.387± 0.0038	0.454 ± 0.0023	18.66 ±1.69	1.27 ±0.019	23.62
F15	0.362± 0.0021	0.420 ± 0.0049	15.71 ±1.80	1.14 ± 0.023	25.82
F16	0.355± 0.0033	0.439 ± 0.0058	17.65 ±1.57	1.21 ± 0.019	22.34

Table 4: Post Compression Parameter

Formulation Code	Hardness (kg/cm2) AM±SD	Thickness (mm) AM±SD	Diameter (mm) AM±SD	Friability (%)	Weight variation (mg) AM±SD	%Drug Content
F1	4±1.2	3.3±0.14	4.99±0.075	0.32	91.64±1.04	97.17
F2	4.2±0.6	3.7±0.2	5.38±0.004	0.45	135.46±1.32	98.23
F3	3.9±1.41	4.1±0.04	6.04±0.037	0.51	179.47±1.02	101.12
F4	4.0±0.9	4.4±0.14	6.31±0.07	0.50	223.09±0.94	98.12
F5	4.3±0.5	3.2±0.09	4.92±0.075	0.37	91.04±1.32	100.05
F6	4.1±1.04	3.6±0.08	5.30±0.004	0.49	134.34±1.22	99.13

F7	4.2±1.06	4.0.±0.28	6.00±0.037	0.41	177.65±1.08	102.78
F8	4±0.5	4.3±0.21	6.26±0.07	0.51	220.95±1.11	96.05
F9	4.1±0.6	3.3±0.04	4.99±0.075	0.32	91.65±1.14	101.1
F10	4.0±1.12	3.8±0.21	5.39±0.004	0.45	135.9±1.0	99.15
F11	4±0.9	4.1±0.27	6.04±0.037	0.41	181.69±0.96	97.13
F12	4±0.5	4.4±0.05	6.38±0.07	0.39	224.99±1.39	98.14
F13	3.9±1.06	3.3±0.23	4.90±0.075	0.32	90.15±1.12	100.45
F14	4±0.7	3.6±0.16	5.30±0.004	0.44	132.73±1.06	103.23
F15	4.2±1.02	4.0±0.09	5.96±0.037	0.41	175.26±1.04	99.18
F16	4±0.5	4.4±0.12	6.20±0.07	0.39	217.28±0.99	98.12

Table 5: In- Vitro Drug Release of F1 to F4 Batch

Time (hr.)		F1 AM±SD	F2 AM±SD	F3 AM±SD	F4 AM±SD
0	In 0.1 N HCL	0	0	0	0
1		5.63±1.36	6.08±2.20	4.97±1.33	5.19±1.1
2		6.47±0.99	7.14±1.49	5.91±0.91	6.11±2.22
3	In 6.8 Phosphate Buffer	22.23±1.13	20.47±1.54	21.22±1.91	19.79±1.96
4		39.38±2.11	34.28±0.98	37.58±1.40	33.18±1.37
5		60.69±1.09	49.90±2.13	46.39±0.90	48.43±2.13
6		78.93±1.28	66.38±1.04	64.78±2.1	63.37±2.32
7		96.15±1.17	83.47±0.91	79.75±1.05	75.67±1.21
8		-	97.31±1.21	94.21±1.23	86.54±1.04
9		-	-	-	-
10		-	-	-	-
11		-	-	-	-
12		-	-	-	-

Table 6: In- Vitro Drug Release of F5 to F8 Batch

Time (hr)		F5 AM±SD	F6 AM±SD	F7 AM±SD	F8 AM±SD
0	IN 0.1 N HCL	0	0	0	0
1		5.96±0.98	5.52±1.18	4.79±1.20	5.00±1.26
2		7.14±1.45	6.80±2.11	5.66±2.34	7.24±1.40
3	IN 6.8 Phosphate Buffer	21.79±2.11	15.80±1.30	20.11±1.89	20.68±0.99
4		36.28±1.22	31.93±0.98	28.95±0.95	30.74±2.11
5		45.74±1.04	49.96±1.47	37.00±2.01	37.48±1.19
6		67.05±2.23	61.86±2.06	48.27±1.49	46.17±2.22
7		82.04±1.32	70.72±1.07	56.43±1.22	57.62±2.10
8		96.73±1.29	84.64±1.62	73.06±1.13	70.67±0.93
9		-	97.27±1.22	84.40±1.08	83.65±1.21
10		-	-	96.33±1.16	94.83±1.46
11		-	-	-	-
12		-	-	-	-

Table7: In- Vitro Drug Release of F9 to F12 Batch

Time (hr)		F9 AM±SD	F10 AM±SD	F11 AM±SD	F12 AM±SD
0	In 0.1 N HCL	0	0	0	0
1		5.95±1.38	5.30±2.11	4.20±1.30	4.52±1.27
2		7.26±0.99	6.63±1.23	5.02±1.67	6.88±1.56
3	In 6.8 Phosphate Buffer	20.58±1.41	21.78±2.10	20.68±1.10	19.46±0.91
4		32.07±0.99	31.85±1.27	28.75±1.29	26.63±1.11
5		46.56±1.66	45.57±2.06	35.90±0.99	35.43±1.06
6		61.41±1.05	60.31±1.45	46.94±2.11	47.28±1.19
7		69.28±0.92	67.50±2.10	60.61±1.22	65.03±1.89
8		82.96±1.11	85.15±1.39	71.33±0.92	71.38±1.23
9		94.59±0.90	95.89±1.10	83.49±1.05	80.22±0.99
10		-	-	98.42±0.98	91.59±1.02
11		-	-	-	98.75±1.3
12		-	-	-	-

Table 8: In- Vitro Drug Release of F13 to F16 Batch

Time(hr)		F13 AM±SD	F14 AM±SD	F15 AM±SD	F16 AM±SD
0	0.1N HCL	0	0	0	0
1		4.55±1.34	3.97±1.07	4.86±0.99	5.96±1.76
2		6.21±1.78	5.99±1.11	5.13±1.11	6.90±1.21
3	In 6.8 Phosphate buffer	20.0±0.99	19.00±0.99	18.34±1.41	22.01±1.23
4		29.61±1.89	26.17±1.06	27.16±1.30	32.86±1.32
5		41.20±1.34	37.83±1.29	39.23±2.04	43.60±1.07
6		49.15±1.23	51.58±1.04	54.58±0.91	52.69±1.19
7		60.19±1.06	63.54±1.38	63.46±1.24	59.57±1.01
8		70.13±1.23	70.64±1.13	69.08±1.46	65.08±1.26
9		85.37±1.45	81.24±1.29	78.47±1.08	74.85±1.39
10		98.22±1.34	89.85±1.01	82.98±0.98	81.07±1.16
11		-	99.08±1.22	87.02±1.19	90.35±1.28
12		-	-	95.66±1.02	95.33±1.12

Table 9: Comparison of Post Compression Parameter of Optimize batch and Marketed Formulation

Formulation Code	Hardness (kg/cm2)	Thickness (mm)	Diameter (mm)	Friability (%)
MF	4.1±1.3	3.5±0.06	5.96±0.028	0.59
F15	4.1±1.02	3.6±0.09	6.00±0.029	0.41

Table 10: Comparison of in-vitro dissolution profile of Marketed Formulation with Optimized Batch

Time	MF AM±SD	Batch 15 AM±SD
0	0	0
1	5.18±1.23	4.86±1.32
2	6.32±1.05	6.13±1.23
3	21.28±2.10	20.34±1.54
4	32.78±1.56	32.16±1.20
5	44.24±1.42	43.23±1.10
6	57.97±1.23	51.58±2.01
7	69.31±1.67	58.46±1.22
8	74.34±1.32	65.05±1.54
9	81.39±1.69	76.47±1.33
10	88.66±2.16	80.98±1.16
11	98.23±1.02	89.02±1.36
12	-	97.66±1.27

Table 11: Kinetic fitting results of F15 Batch and MF

Formulation code	Correlation coefficient (r^2)			Peppas model	
	Zero order	First order	Higuchi	n^b	Correlation coefficient (r^2)
F 15	0.991	0.865	0.982	0.58	0.958
MF	0.953	0.979	0.880	0.79	0.936

REFERENCE

1. Yadav, VB and Yadav, AV (2010), "Enhancement of Solubility And Dissolution Rate Of BCS Class II Pharmaceuticals By Nonaquious Granulation Technique", ***International Journal Of Pharma Research And Development***, 1(12), 1-12.
2. Rakesh, Tiwle and Ajazuddin *et al.* (2012), "An Exhaustive Review on Solubility Enhancement for Hydrophobic Compounds by Possible Applications of Novel Techniques", ***Trends in Applied Sciences Research***, 7 (8), 596-619.
3. Sushmita, K and Satish, CS (2011), "Formulation and in vitro evaluation of sustained release matrix tablets of an anti-diabetic drug", ***Rajiv Gandhi University of Health Sciences***, Bangalore.
4. Izhar, Ahmed Syed and E, Pavani (2012), "The Liquisolid Technique: Based Drug Delivery System", ***International Journal of Pharmaceutics***, 4 (2), 88-96.
5. Nokhodchi, SA; Javadzadeh, Y and Siahi, MR (2007), "Liquisolid technique as a tool for enhancement of poorly water-soluble drugs and evaluation of their physicochemical properties", ***Acta Pharm***, 57, 99-109
6. Narender, Thakur; Sukhbir Lal, Khokra; Dharmesh, Sharma; Naseeb Singh, Thakur; Rahul, Purohit and Vikrant, Arya (2011), "Review of pharmaceutical application of liquisolid technique", ***American Journal of Pharmatech Research***,1 (3),1-18.
7. Gubbi, SR and Jarag, R (2010), "Formulation and characterization of atorvastatin calcium liquisolid compacts", ***Asian Journal of Pharmaceutical Sciences***, 5 (2), 50-60.
8. Stepnksky, D; Friedman, M; Scrourw, Raz I and Hoffman, A (2001), "pre clinical evaluation of pharmaco kinetic-pharmacodynemic rationale for oral controlled release Metformin formulation", ***Journal Of Control Release***, 71, 107-125.
9. Saadia, A Tayel; Iman, I Soliman and Dina, Louis (2008), "Improvement of dissolution properties of Carbamazepine through application of the liquisolid tablet technique", ***European Journal of Pharmaceutics and Biopharmaceutics***, 342–347.
10. RK, Goyal; Anita,A Mehta; R, Balaraman and Mahesh, D Burande (2008), "***Handbook of Derasari and Gandhi in Drug Pharmacology***", 7th Ed., 201-205.
11. Yadav, VB and Yadav, AV(2010), "Enhancement Of Solubility And Dissolution Rate Of BCS Class II Pharmaceuticals By Nonaquious Granulation Technique", ***International Journal of Pharma Research and Development***, 1(12), 1-12.
12. K, Rajesh; R, Rajalakshmi; J, Umamaheswari; CK and Ashok, Kumar (2011), "Liquisolid Technique a novel Approaches' to enhance solubility and Bioavaibility", ***International Journal of Biopharmaceutic***, 2(1), 8-13.
13. Izhar, Ahmed Syed and E, Pavani (2012), "The Liquisolid Technique: Based Drug Delivery System", ***International Journal of Pharmaceutics***, 4(2), 88-96.
14. MA, Hassan; MS, Suleiman and NM, Najib (1990), "Improvement of the invitro dissolution characteristics of famotidine by inclusion in bcyclodextrin", ***International Journal of Pharmaceutics*** , 3(2) , 19–24.

15. Wade and Waller, PJ (1994), "***Hand Book of Pharmaceutical Excipients***", 2nd Ed., Pharmaceutical Press, London.
16. Yadav, VB and Yadav, AV (2010), "Enhancement Of Solubility And Dissolution Rate Of BCS Class II Pharmaceuticals By Nonaquious Granulation Technique", ***International Journal of Pharma Research and Development***, 1(12), 1-12.
17. S, Spireas; S, Sadu and R, Grover (1998), "In-vitro release evaluation of hydrocortisone liquisolid tablets", ***European Journal of Pharmaceutics and Biopharmaceutics***, 3(7), 867–872.

Correspondence Author:
Tushar N. Patel
Sat Kaival College of Pharmacy, Sarsa, India

Cite This Article: Tushar, N Patel; Zankhana, P Sheth; Bhagirath, K Patel and Pritesh, Patel (2014), "Formulation development & *in vitro* characterization of carvedilol sustain release tablet by using liquisolid technique", ***Pharmacophore***, Vol. 5 (4), 451-466.