International Journal of Medicine and Pharmaceutical Research
Home Page: https://pharmaresearchlibrary.org/journals/index.php/ijmpr
CODEN (USA): IJCPNH | ISSN: 2321-2624 | Publisher: Pharma Research Library
DOI: https://doi.org/10.30904/j.ijmpr.2025.4739
Int. J. Med. Pharm. Res., 2025, 13(1): 01-09

Formulation and Evaluation of Delayed Release Enteric Coated Tablets of Repaglinide

Dekonda Malavika[1], Dr. G.S. Valluri[2], Dr. Vijay Kumar Gampa*[3]
[1]Department of Pharmaceutics, KGR Institute of Technology and Management, Rampally, Keesara(m), Medchal-Malkajgiri District, Hyderabad -501302, Telangana, India.
[2]Professor and HOD, KGR Institute of Technology and Management, Rampally, Keesara(m), Medchal-Malkajgiri District, Hyderabad -501302, Telangana, India.
[3]Principal and Professor, KGR Institute of Technology and Management, Rampally, Keesara(m), Medchal-Malkajgiri District, Hyderabad -501302, Telangana, India

A B S T R A C T
This study focuses on the preparation& examination of SR tablets of Repaglinide. A CC graph of Repaglinide in KH2PO4 buffer 6.8 was established, showing compliance with in the conc. extent of 2 to 10 µg per ml, with a R^2 value of 0.999. Precompression investigation demonstrated good flow properties across all formulations, with bulk density, index of compressibility, & flow ability ratio of within acceptable limits. Post-compression evaluations showed that the tablets complied with USP standards, displaying consistent weight, thickness (3.93-4.15 mm), hardness (5.56-6.63 kg/cm²), and friability below 1%. Drug content was within the 98-102% range, ensuring uniformity. In vitro dissolution studies revealed significant sustained drug release, with formulations achieving 100% liberate within 12 hours. Kinetic modeling indicated a combination of 1st-order and Higuchi release mechanisms. The R^2 values extent from 0.812 to 0.979,&Peppas plots suggested diffusion and erosion-controlled release in most formulations, making these SR tablets suitable for therapeutic use.
Keywords: Repaglinide, Index of compressibility, Flowability ratio.

A R T I C L E I N F O

***Corresponding Author**
Dr. Vijay Kumar Gampa
Principal and Professor,
KGR Institute of Technology and Management,
Rampally, Keesara(M), Hyderabad -501302, Telangana, India

Article History:
Received : 10 Oct 2024
Revised : 27 Oct 2024
Accepted : 19 Nov 2024
Published : 10 Jan 2025

Citation: *Vijay Kumar Gampa, et al. Formulation and Evaluation of Delayed Release Enteric Coated Tablets of Repaglinide. Int. J. Med. Pharm. Res., 2025, 13(1):01-09.*

Contents

1. Introduction

The management of diabetes mellitus, particularly type 2 diabetes, necessitates effective pharmacological interventions to regulate blood glucose levels and mitigate associated complications. Repaglinide, a short-acting insulin secretagogue of the meglitinide class, plays a significant role in the management of postprandial glucose levels by stimulating pancreatic beta cells to release insulin. Despite its therapeutic efficacy, the conventional immediate-release formulations of Repaglinide pose challenges, including frequent dosing requirements and potential gastrointestinal side effects due to its rapid absorption and quick onset of action. The development of delayed-release enteric-coated tablets of Repaglinide offers a promising solution to these limitations by providing controlled and targeted drug release.

Significance and Rationale

Repaglinide's mechanism of action involves binding to and inhibiting the ATP-sensitive potassium channels on pancreatic beta cells, resulting in insulin release. This rapid action is beneficial for controlling postprandial

hyperglycemia; however, it necessitates administration multiple times a day, which can be inconvenient for patients and potentially lead to poor compliance. Moreover, immediate-release formulations can cause gastrointestinal irritation due to the exposure of the drug to the acidic environment of the stomach.

The rationale for developing delayed-release enteric-coated tablets lies in their ability to bypass the acidic stomach environment and release the drug in the more neutral pH of the intestine. This targeted release not only minimizes gastrointestinal side effects but also provides a more controlled and sustained drug release profile, reducing the frequency of dosing. Such formulations can improve patient adherence to therapy, enhance therapeutic efficacy, and offer better glycemic control throughout the day.

Design Considerations

The design of delayed-release enteric-coated tablets involves multiple critical considerations to achieve the desired drug release characteristics and therapeutic outcomes. The choice of enteric coating materials, core tablet formulation, and optimization of the coating process are pivotal factors influencing the performance of the final dosage form.

Enteric Coating Materials:

The selection of appropriate enteric polymers is crucial for ensuring that the tablet remains intact in the acidic environment of the stomach and only disintegrates in the more alkaline conditions of the intestine. Commonly used enteric polymers include methacrylic acid copolymers, cellulose acetate phthalate (CAP), and hydroxypropyl methylcellulose phthalate (HPMCP). These polymers provide a protective barrier that prevents premature drug release in the stomach while allowing controlled release in the intestine.

Core Tablet Formulation:

The core tablet formulation must be designed to ensure compatibility with the enteric coating and achieve the desired drug release profile. This involves selecting suitable excipients, such as diluents, binders, disintegrants, and lubricants, which contribute to the tablet's mechanical strength and dissolution properties. The core tablet formulation should also consider factors such as drug solubility, stability, and the potential interaction between the drug and excipients.

Coating Process Optimization:

The optimization of the coating process involves controlling various parameters such as coating thickness, spray rate, and drying conditions to achieve uniform and consistent coating. The coating thickness must be sufficient to withstand the acidic environment of the stomach while allowing timely disintegration in the intestine. Additionally, the coating process should ensure that the enteric coat adheres well to the core tablet and does not compromise the tablet's mechanical integrity.

Optimization Techniques

The optimization of delayed-release enteric-coated tablets involves systematic experimentation and statistical analysis to identify the optimal formulation parameters. Techniques such as factorial design, response surface methodology (RSM), and in vitro dissolution testing play a crucial role in this optimization process.

Factorial Design:

A factorial design is used to evaluate the effects of multiple formulation variables on the performance of the enteric-coated tablets. This experimental design allows for the simultaneous investigation of factors such as polymer concentration, coating thickness, and core tablet composition, providing valuable insights into their interactions and influence on drug release.

Response Surface Methodology (RSM):

RSM is a powerful statistical tool used to optimize formulation parameters by generating response surface plots. This methodology helps identify the optimal combination of variables that result in the desired delayed-release profile. By analyzing the response surfaces, researchers can determine the most effective formulation parameters and predict the behavior of the enteric-coated tablets under various conditions.

In Vitro Dissolution Testing:

In vitro dissolution testing is conducted to assess the drug release profile of the enteric-coated tablets under simulated gastrointestinal conditions. These tests involve exposing the tablets to different pH environments that mimic the stomach and intestinal fluids. The dissolution data obtained from these studies provide critical information on the release kinetics and help refine the formulation to achieve consistent and predictable drug release.

Evaluation and Assessment

The evaluation of delayed-release enteric-coated tablets involves comprehensive in vitro and in vivo testing to ensure their efficacy, safety, and stability. The following parameters are typically assessed during the evaluation process:

Enteric Coating Integrity: The integrity of the enteric coating is evaluated by subjecting the tablets to various pH conditions that simulate the gastrointestinal environment. The tablets should remain intact in the acidic conditions of the stomach (pH 1.2) and only disintegrate in the more alkaline conditions of the intestine (pH 6.8). This ensures that the drug is released at the desired site of absorption without premature release.

Drug Release Profile: The drug release profile of the enteric-coated tablets is characterized using in vitro dissolution studies. These studies provide detailed information on the release kinetics and ensure that the tablets provide a controlled and sustained release of Repaglinide in the intestine. The dissolution data are analyzed using various kinetic models to understand the release mechanisms and optimize the formulation.

Physicochemical Properties: The physicochemical properties of the enteric-coated tablets, such as hardness, friability, and weight variation, are assessed to ensure the quality and consistency of the dosage form. These properties are critical for maintaining the stability and performance of the tablets during storage and administration.

In-Vivo Pharmacokinetic Studies: In-vivo pharmacokinetic studies in animal models or human subjects are conducted to validate the drug release profile

and therapeutic efficacy of the enteric-coated tablets. These studies provide valuable data on the bioavailability, absorption, and overall performance of the formulation in a physiological setting. Pharmacokinetic parameters such as peak plasma concentration (Cmax), time to reach peak concentration (Tmax), and area under the plasma concentration-time curve (AUC) are analyzed to assess the effectiveness of the delayed-release formulation.

Stability Studies:

Stability studies are conducted to evaluate the robustness of the enteric-coated tablets under different storage conditions. These studies assess the stability of the drug and the enteric coating over time, ensuring that the formulation remains effective and safe throughout its shelf life. Parameters such as drug content, dissolution behavior, and physical integrity are monitored to detect any changes that may occur during storage.

The formulation and evaluation of delayed-release enteric-coated tablets of Repaglinide represent a significant advancement in the management of type 2 diabetes mellitus. By leveraging enteric coating technology, it is possible to enhance the therapeutic efficacy of Repaglinide, providing controlled and sustained drug release with improved patient compliance. The meticulous selection of enteric coating materials, core tablet formulation, and optimization techniques, coupled with comprehensive evaluation studies, ensures the development of a robust and reliable dosage form.

2. Methodology

Table 2: Chemicals Used

The materials used in this study were sourced from various suppliers. Repaglinide was supplied by Mylan Labs. HP-β-Cyclodextrin, Crospovidone, Purified Talc, Magnesium Stearate, and Microcrystalline Cellulose were all procured from Qlaychrome Research Labs Pvt Ltd. These high-quality materials ensure the reliability and accuracy of the research outcomes.

Table 3: List of Instrument's utilized

The instruments utilized in this study include a UV-Vis spectrophotometer (M-700d), a balance (SYSTRONICS-335). The pH scale was sourced from Systronic Electronics, Mumbai, while the dissolution machine (Agilent 708-DS) and the oven from. Thermoscientific were also employed. Hardness measurements were conducted using a Monsanto Tester. Friability tests were performed with a Roche Friabilator from Electrolab, Mumbai. Finally, a punching machine from Cadmach, Ahmedabad, was used for the tablet formulation process.

Analytical Method Development

Phosphate bufffer Making

6.8 grams of potassium dihydrogen OPA was placed in a 1LVF, solubulize in distilled H2O, &topped up to 1 liter with distilled H2O. The pH was then adjusted to 6.8 using NaOH solution.

λ_{max} of Repaglinide in 6.8phosphatebufffer

Operational standard: 100mg of Repaglinide was solubulizes in 10ml MeOH, then diluted to volume with phosphate buffer 6.8 to yield a 1000µg per ml solution.

1st Dilution: Take out 10ml solution from the above solution &makeup to 100ml using phosphate buffer 6.8, it will give 100µg per ml conc. solution.

2nd Dilution: Take out 10ml solution from the above solution &makeup to 100ml using phosphate buffer 6.8, it will give 10µg/ml conc. solution.

The solution was measured between 200-400nanometers, & the wavelength with the maximum absorbance, noted as lambda max, was recorded.

Making of CC graph of Repaglinide in 6.8 phosphate buffer

Process:

Operational standard:

100mg of Repaglinide was solubulizes in 10ml MeOH, then diluted to volume using phosphate buffer 6.8 to yield a 1000µg per ml solution.

1st Dilution:

Take out 10ml solution from the above solution &makeup to 100ml using phosphate buffer 6.8, it will give 100µg per ml conc. solution.

2nd Dilution:

From above solution, 0.2, 0.4, 0.6, 0.8, & 1ml were makeup to the margin with 6.8 phosphate buffer in 10ml VF to prepare 2, 4, 6, 8, & 10µg per ml solutions, with maximum abs noted at 238nm.

Making of the solid dispersions

- For the physical mixture method, the drug and polymers in molar ratios of 1:1 and 1:2 were triturated in a mortar for one hour, sieved through #. 80.
- In the kneading technique, drugs and polymers in 1:1 and 1:2 molar ratios are mixed with cyclodextrin, 50% C2H5OHl is added to form a slurry, drugs are incorporated, then the mixture is air dried at 25°C for 24 hours, pulverized, sieved (#. 80).
- In the coprecipitate technique, the drug was solubulizes in C2H5OH, and the polymer in distilled water, mixed in 1:1 and 1:2 molar ratios, stirred for 1 hr, then evaporated with the help water bath; the crystalline complex inclusion was pulverized, sieved (#. 80).

Evaluation Studies on solid Dispersions

***In-vitro* disso studies for solid distributions**

Solubulization profile was conducted using type II instrument with 900 ml of phosphate buffer 6.8 at 50 rpm & 37°C, sampling 5 ml at time points (5-60 min), filtered, diluted, assayed for Repaglinide at 238nm, and replaced with fresh buffer, performed in triplicate.

Making of sustained Release Pills of Repaglinide

In the direct compression method for Repaglinide SR tablets, all ingredients (Drug+HP-Betacyclodextrin complexes + polymer + DCP) were accurately weighed, sifted through #22, combined in a bag of poly for 5 min, sliding with #40 Talc & Mg stearate, and with 8mm to 12mm dies, achieving an avgestrenth of 6.0kg/cm².

Examination of Sustained Liberatepills of Repaglinide

The formulated tablets underwent pre- and post-compression quality control assessments, as well as solubulizes studies.

A) Pre Compression investigation:

1. Repose Angle:

The angle of repose, defined as the steepest angle among the pile surface of powder & the plane horizontal, was determined using the funnel techniques, which involved measuring the powder cone's diameter and calculating the angle to assess flow properties related to inter-particulate friction.

Examination of Sustained Liberate pills of Repaglinide

The formulated tablets underwent pre- and post-compression quality control assessments, as well as solubulizes studies.

A) Pre Compression investigation:

1. Repose Angle:

The angle of repose, defined as the steepest angle among the pile surface of powder & the plane horizontal, was determined using the funnel techniques, which involved measuring the powder cone's diameter and calculating the angle to assess flow properties related to inter-particulate friction.

2. Density:

a. BD: The apparent bulk density, calculated as the ratio of over alll powder wt to its BV, is determined by precisely weighing 25 g of sieved granules, transferring them to a 10 ml measuring cylinder, leveling the API without compacting, & reading the apparentvolume.

b. TD: The tapped density, defined as the ratio of total powder mass to its tapped volume, is determined by weighing 25 g of sieved granules, transferring them to a 100 ml vessel, & operating a tap density tester until the powder bed volume stabilizes.

3. Index Compressibility: Index of compressibility was used to determine the compressibility index of the API blend, which is a straightforward test to assess BD&TD, as well as the packing rate.

Post compression investigation:

The prepared tablets are evaluated for physical appearance (shape, colour, texture, odour), & weight difference where 20 tablets were weighed collectively and individually, ensuring no more than two deviated from the average by 7.5percent for 300 mg pills, with none exceeding double that%. The pills' thickness was measured using Verniercalipers; hardness was assessed with a Monsanto hardness tester by noting the force required to fracture the tablets; and friability was evaluated by weighing 20 tablets, subjecting them to abrasion in a Friabilator at 25rpm for 4 minutes, and calculating the weight loss percentage, which should ideally be between 0.5 and 1.0%.

- 10 tablets were api, & an amount equal to 100 mg of Repaglinide was solubulizes in methanol, adjusted to 100 ml with water, filtered, diluted, and the Repaglinide content was findout by measuring abs at 238nm, using the standard calibration curve, with Avg% drug content findout from three determinations.
- In-vitro liberate kinetics investigation analyzed the drug liberate mechanism from matrix s, using zero or first order kinetics, and studied the ER mechanism with Higuchi and Peppa's- equations.
- 0 Order Release Kinetics describes a parallel relationship among drug release fraction and time, where $Q=k_0t$, with Q as the drug fraction liberated at time t, & k_0 as the zero-order liberate rate constant, showing a linear plot if release follows zero-order kinetics.

Wagner suggested that, due to the exponential decrease of a tablet's exposed surface area during dissolution, slow release tablets follow first-order kinetics, where the equation describes it, and a plot of log cumulative percentage of drug remaining versus time yields a straight line if it follows 1st-order release kinetics.

Korsemeyer-Peppa's- equation

To better model the formulation, dissolution data was further analyzed using Peppa's-Korsemeyer equation (Power Law).

3. Results and Discussion

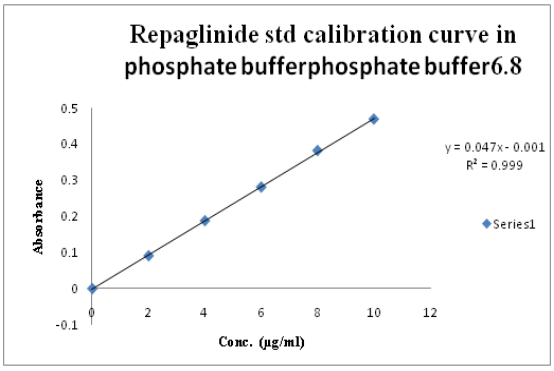

Figure 1: Standard CC graph of Repaglinide

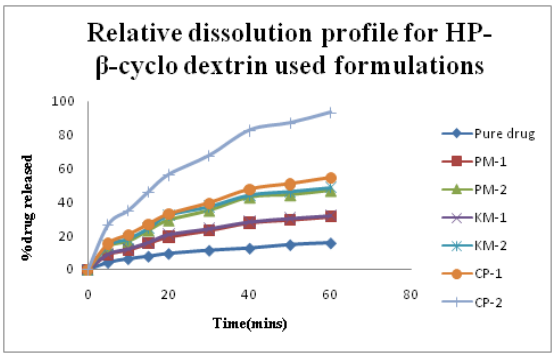

Figure 2: Relative Dissolution profiles for pure drug and formulations using HP-β-cyclodextrin were evaluated.

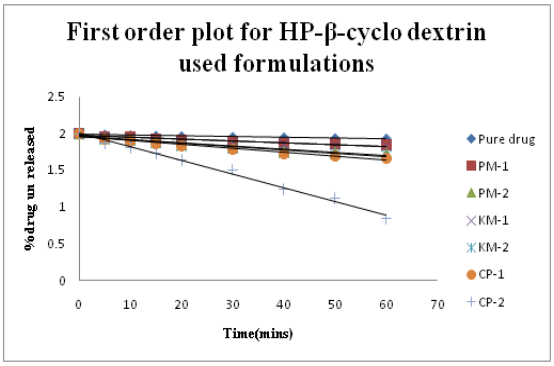

Figure 3: 1st order Graph of pure drug formulations and those using HP-β-cyclodextrin.

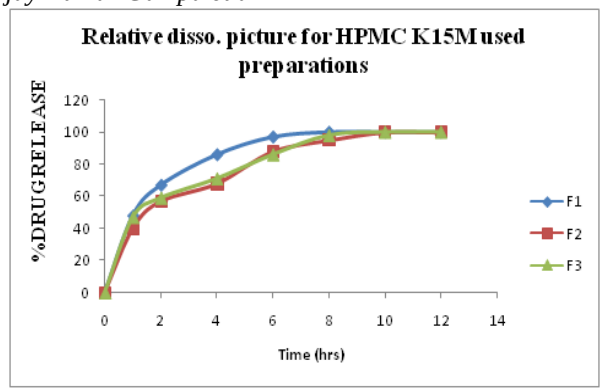

Figure 4: Disso. profiles of Repaglinide SR tablets for F-1, F-2 & F-3

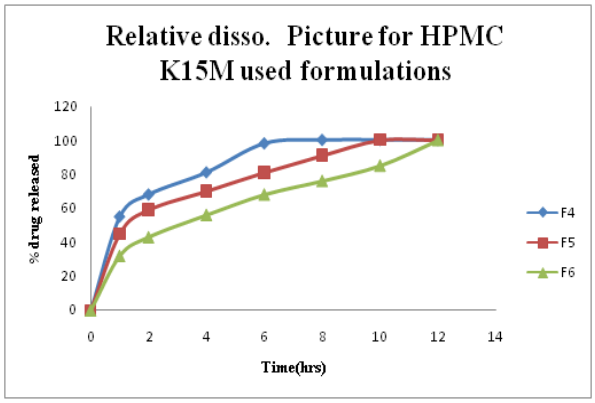

Figure 5: Disso. profiles of Repaglinide SR pills for F-4, F-5& F-6

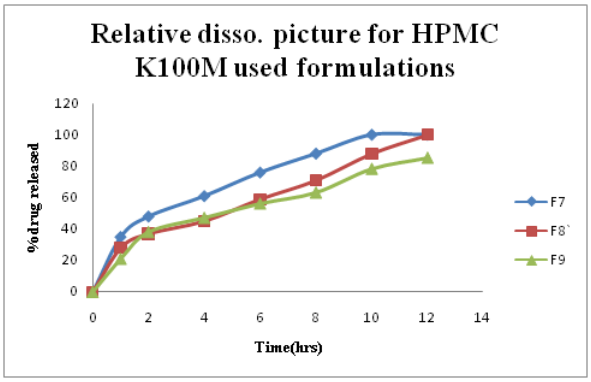

Figure 6: Disso. profiles of Repaglinide SR Pills for F-7, F-8 & F-9

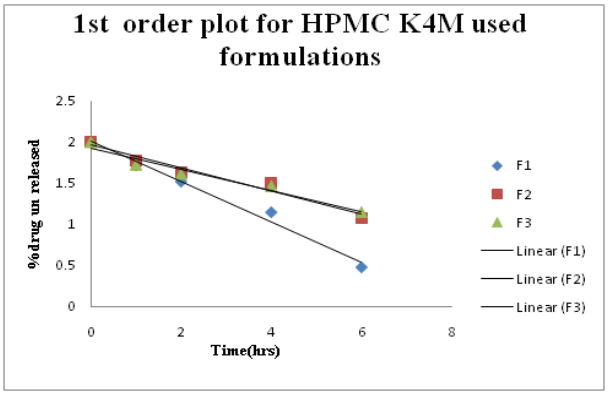

Figure 7: 1st order plot for F-1, F-2 & F-3

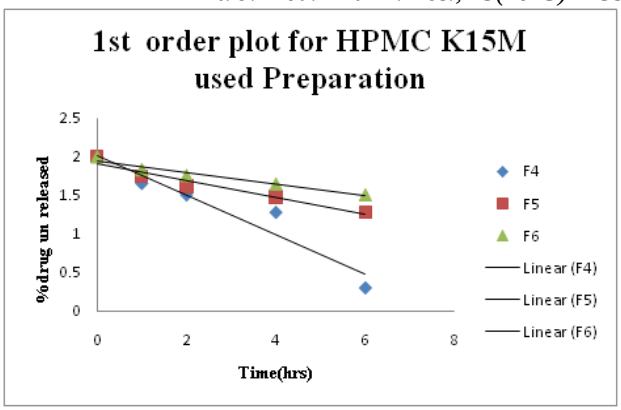

Figure 8: 1st order plot forF-4, F-5 & F-6

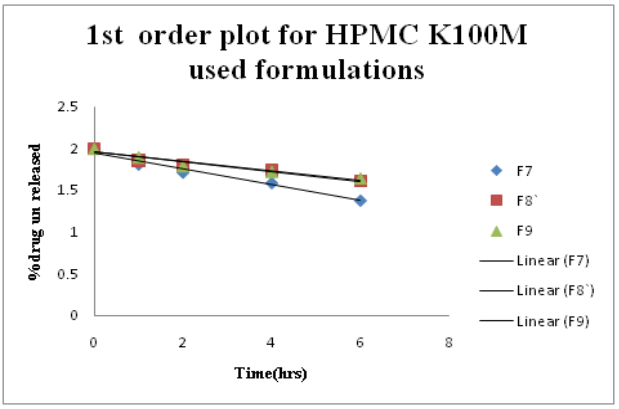

Figure 9: 1storderplot for F-7, F-8 & F-9.

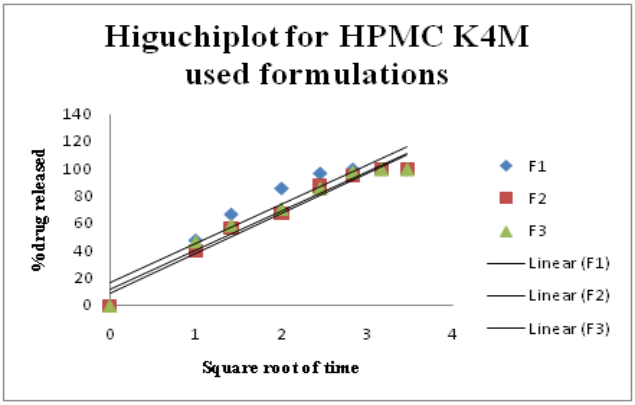

Figure 10: Higuchi plot for F-1, F-2 & F-3

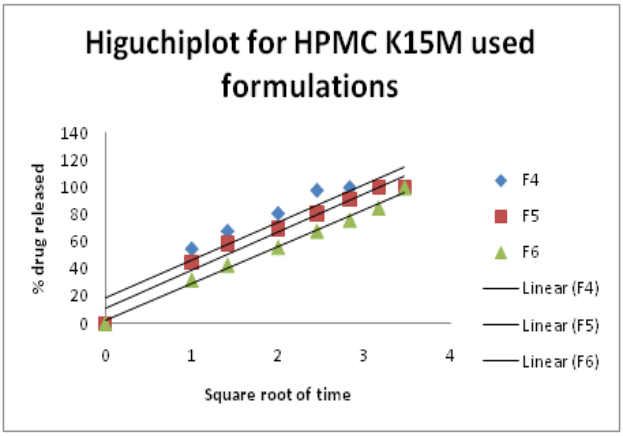

Figure 11: Higuchi plot for F-4, F-5 & F-6

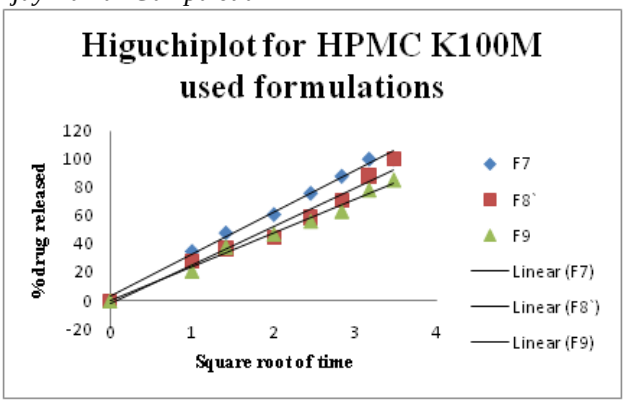

Figure 12: Higuchi plot for F-7, F-8 & F-9.

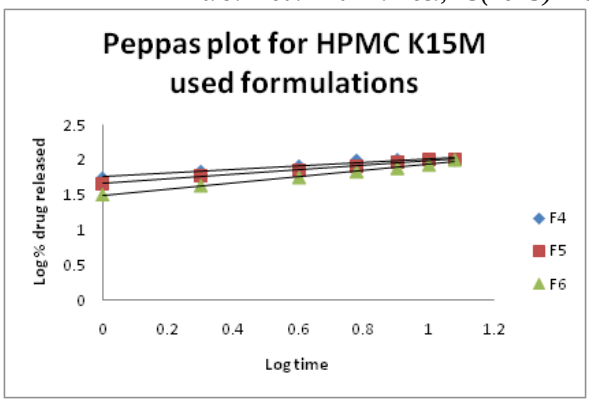

Figure 14: Peppas plot for F-4, F-5 & F-6

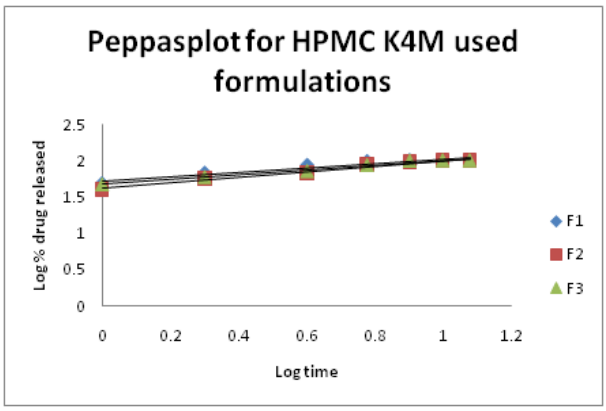

Figure 13: Peppas plot for F-1, F-2 & F-3

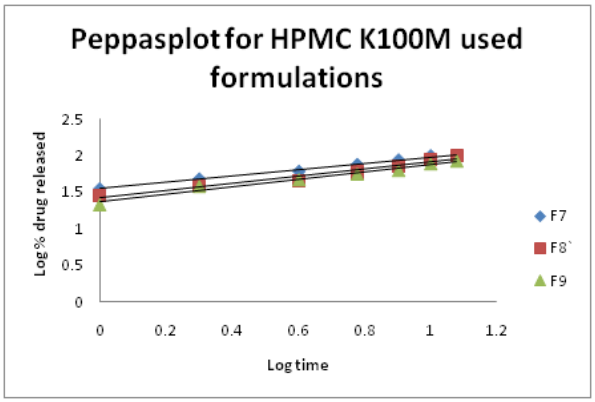

Figure 15: Peppas plot for F-7, F-8 & F-9

Table 1: Preparation codes for the solid distributions prepared by various techniques

S.no.	Mixture consists	Method of Preparation of solid distributions		
		Physical Composition	Kneading technique	Coprecipitate technique
1	API (Repaglinide)			
2	API: HP-β –CD (1.0:1.0)	PM-1	KM-1	CP-1
3	API: HP- β –CD (1.0:2.0)	PM-2	KM-2	CP-2

Table 2: Formulae of Repaglinide SR Tablets

Chermicals	Batch code's								
	F-1	F-2	F-3	F-4	F-5	F-6	F-7	F-8	F-9
HP-β-CD (1:2)	12	12	12	12	12	12	12	12	12
hydroxypropyl methylcellulose K4M.	8	16	24	-	-	-	-	-	-
hydroxypropyl methylcellulose K15M.	-	-	-	8	12	24	-	-	-
hydroxypropyl methylcellulose K100M.	-	-	-	-	-	-	8	12	24
dicalcium phosphate, calcium hydrogen phosphate.	136	128	120	136	128	120	136	128	120
magnesium silicate, talcum powder.	2	2	2	2	2	2	2	2	2
Mg stearate.	2	2	2	2	2	2	2	2	2
Over all weight (mg), total mass (mg).	160	160	160	160	160	160	160	160	160

Table 3: Repose Angle

Flowability	Repose Angle (degrees)
V. Good	24–31
Good	30–36
Fair	35–41
Pasable	40–46
bad	45–56
V. poor	55–66
VV. poor	>67

Table 4: Index of Compressibility

Index Compressibility (%)	Flow	Ratio Hausner's
≤ 11	V.good	1.01-1.12
10-16	Good	1.11-1.19
15-21	Fair	1.18-1.26
20-26	Pasable	1.25-1.35
25-32	Bad	1.34-1.46
32-38	V.poor	1.45-1.58
> 39	VV. poor	> 1.61

Table 5: Wt difference Tolerance for Tablets

Avg wt of tablet(mg)	% difference limit
130 or <	± 11
131-323	± 7.4
> 324	± 6

Table 6: Dissolution Parameters

Parameter	Details
Disso apparatus	paddle
Buffer	Phosphate buffer and 6.8
Volume taken	900 ml
Rate	50rpm
Temp	37± 0.5 ºC
withdrawn volume	5mL
Intervels	1, 2, 4, 6, 8, 10, 12hours
Analytical technique	UV Spectroscopy
λ_{max}	238nm

Table 7: Drug liberate kinetics mechanism

exponent of Diffusion (n)	process
0.46	Normal expantion
0.46 < n <0.88	Irregular diffusion
0.88	Relaxation-controlled transport
n > 0.88	Accelerated relaxation-controlled transport

Table 8: Dissolution data for API and HP-β-cyclodextrin utilized in synthesis

Time (min)	Cumulative % drug release						
	Pure drug	PM-1	PM-2	KM-1	KM-2	CP-1	CP-2
0	0	0	0	0	0	0	0
5	4.22	8.91	13.6	9.28	14.35	15.43	26.65
10	6.32	11.55	16.77	12.26	18.21	20.68	35.05
15	7.8	15.56	23.32	16.15	24.51	26.97	46.15
20	9.4	19.34	29.27	20.86	32.32	32.87	56.35
30	11.3	23.19	35.07	24.31	37.32	39.45	67.60
40	12.57	27.75	42.92	28.40	44.24	47.58	82.60
50	14.62	29.47	44.32	30.46	46.31	50.76	86.90
60	15.65	31.26	46.87	32.09	48.54	54.38	93.12

Table 9: Pre-compression studies of Repaglinide Sustained release tablets

Formulations	BD (Kg/cm^3)	TD (Kg/cm^3)	Compre. index	Flowability ratio	repose Angle
F-1	0.38	0.42	9.76	1.2	21.62
F-2	0.44	0.53	17.4	1.42	22.63
F-3	0.41	0.45	13.1	1.51	22.28
F-4	0.45	0.52	13.6	1.26	20.28
F-5	0.3 8	0.48	17.1	1.57	28.22
F-6	0.43	0.53	19.3	1.46	23.25
F-7	0.42	0.51	18.1	1.51	27.5
F-8	0.42	0.52	19.5	1.52	22.27
F-9	0.45	0.53	15.4	1.41	23.63

Table 10: Post compression investigation of Repaglinide sustained release pills

Batch Code's	% wt difference	Thickness	% frigility	%Drug	Stiffness (Kg/cm^2)
F-1	Passed	4.04	0.15	98.8	6.1
F-2	Passed	3.94	0.12	100.1	5.6
F-3	Passed	4.05	0.15	101.2	5.57
F-4	Passed	4.05	0.16	101.4	6.04
F-5	Passed	4.04	0.63	100.2	6.16
F-6	Passed	4.2	0.16	100.6	6.62
F-7	Passed	3.98	0.24	99.2	6.36
F-8	Passed	4.16	0.18	100.3	6.24
F-9	Passed	4.1	0.16	99.8	5.97

Table 11: Disso. data of various sustained release pills of Repaglinide

T(hrs)	Drug liberate in %								
	F-1	F-2	F-3	F-4	F-5	F-6	F-7	F-8`	F-9
0	0	0	0	0	0	0	0	0	0
1	48	40	47	55	45	32	35	28	21
2	67	57	59	68	59	43	48	37	38
4	86	68	71	81	70	56	61	45	47
6	97	88	86	98	81	68	76	59	56
8	100	95	98	100	91	76	88	71	63
10	100	100	100	100	100	85	100	88	78
12	100	100	100	100	100	100	100	100	85

Table 12: R^2& N outcomes table for Repaglinide SR pills

Batch code	R^2 value				N value
	0 order	1st order	Higuchi	Peppas	
F-1	0.818	0.994	0.945	0.963	0.298
F-2	0.898	0.982	0.982	0.988	0.378
F-3	0.882	0.978	0.975	0.991	0.325
F-4	0.813	0.962	0.942	0.976	0.255
F-5	0.893	0.967	0.982	0.997	0.328
F-6	0.955	0.977	0.997	0.995	0.438
F-7	0.942	0.986	0.997	0.998	0.436
F-8	0.978	0.967	0.988	0.982	0.502
F-9	0.963	0.968	0.995	0.988	0.521

4. Conclusion

By the three methods employed, order of enhanced solubility is Physical mixture < Kneading method < Co-precipitate technique. In all the three techniques the drug: solid dispersion ratios, the 1:1< 1:2. In the solid dispersions used HP-β-cyclodextrin. The formulation/drug: solid dispersions of CP-2 & by Co-precipitate method) is having the better solubility enhancement. The dissolution & solubility rate of Repaglinide were markedly increased by complexation with HP-β-cyclodextrin. Repaglinide – HP-β-cyclodextrin tablets exhibited significantly higher dissolution rate and efficiency than plain Repaglinide tablets as well as Repaglinide – HP-β-cyclodextrin tablets.

From the above solid dispersions Repaglinide SR formulations are made by HPMC K4M, K15M and K100M. This study demonstrated that Repaglinide can be formulated for sustained release, extending its therapeutic action without reaching toxic levels, thus reducing dosing frequency compared to conventional forms.

5. Bibliography

[1] D.M. Brahmankar, Sunil B. Jaiswal, Biopharmaceutics and Pharmakokinetics, A Treatise, 1sted, Vallabh Prakasan, Delhi, 2005; 27, 5-6.

[2] James Swarbrick., James C Boylan., Encyclopedia of Pharmaceutical Technology, 2nd edition, Vol-1:8.

[3] Christian Leuner., Jennifer Dressmann., Improving drug solubility for oral delivery using solid dispersions. European Journal of Pharmaceutics and Biopharmaceutics, 2000, 50, 47-48.

[4] Leon Shargel., Andrew B.C, Applied Biopharmaceutics and Pharmacokinetics, Appleton-Century-Crofts, 4th Ed, 1985. 134.

[5] H.A. GareKani., F. Sadeghi., A. Badiee., S.A. Mostafa and A.R. Rajabisiahboomi., Crystal habit modifications of Ibuprofen and their Physicochemical Characteristics. Drug Development and Industrial Pharmacy, 2001, 27 (8), 803-809.

[6] Leon Shargel., Andrew B.C, Applied Biopharmaceutics and Pharmacokinetics, Appleton-Century-Crofts, 4th Ed, 1985. 135.

[7] D.M.Brahmankar, Sunil B. Jaiswal,Biopharmaceutics and Pharmakokinetics, A Treatise, 1sted, VallabhPrakasan, Delhi, 2005; 27,29-30.

[8] Nandita G. Das and Sudip K. Das., Formulation of Poorly Soluble Drugs. Drug Delivery Report Spring/Summer, 2006, 52-55.

[9] Chiou WL and Riegelman SJ. JPharm Sci 1971; 60: 1283-1297.

[10] James Swarbrick., James C. Boylan., Encyclopedia of Pharmaceutical Technology, 2nded, Vol: 1:641-647.

[11] Christian Leuner., Jennifer Dressman., Improving Drug solubility for oral delivery using solid dispersions. European Journal of Pharmaceutics and Biopharmaceutics, 2000, 50, 48-51.

[12] Modi A., Tayade P., Enhancement of dissolution profile of solid dispersion (Kneading) technique. AAPS Pharm Sci Tech., 2006, 7 (3), 1-13.

[13] Devarajan, Padma V, Gore SP. Melt-in-mouth tablets- innovative oral drug delivery systems. Express Pharma Pulse. 2000; 7(1): 16-18.

[14] Reddy L.H., Ghosh B, Rajneesh. Fast dissolving drug delivery systems: A Review of Literature. Indian J Pharm Sci. 2002; 64(4): 331-36.

[15] Kuchekar B S, Bhise S B, Armugam V. Design of fast dissolving tablets. Ind. J. Pharm. Edu. 2001; 35(4): 150-152.

[16] Tetsuya O et al. Design of rapidly disintegrating oral tablets using acid-treated yeast cell wall: A Technical Note. AAPS PharmSciTech 2003; 4(4).

[17] Beatrice P. Formulation design of carbamazepine fast-release tablets prepared by melt granulation technique. Int. J. Pharma 256 (2003) 53–63.

[18] Abdelbary G et al. The preparation of orally disintegrating tablets using a hydrophilic waxy binder. Int. J. Pharma 278 (2004) 423–433.

[19] Okuda Y et al. A new formulation for orally disintegrating tablets using a suspension spray-coating method. Int. J. of Pharma 382 (2009) 80–87.

[20] Sastry SV, Nyshadham JR, Joseph AF. Recent technological advances in oral drug delivery – a review, PSTT 2000; 3(4).