An Elsevier Indexed Journal ISSN-2230-7346

Journal of Global Trends in Pharmaceutical Sciences

ENHANCEMENT OF SOLUBILITY, PREPARATION AND EVALUATION OF IMMEDIATE RELEASE TABLETS OF POORLY SOLUBLE DRUG REPAGLINIDE

Lakshmi Usha Ayalasomayajula*, Radha Rani Earle, V.Swapna, Ch. Satyavathi

Department of Pharmaceutical Technology, Maharajah's College of Pharmacy, Vizianagaram, A.P., India.

***Corresponding author E-mail:** alakshmiusha@gmail.com

ARTICLE INFO

Key Words

Oral disintegrating tablets, Repaglinide, Diabetes mellitus, Soluplus, Poloxamer.

ABSTRACT

Oral disintegrating tablets or immediate release tablets are those which will disintegrate rapidly within few seconds when placed upon the tongue. The main aim of the study is to enhance the dissolution solubility and to formulate and evaluate immediate release tablets of poorly soluble drug Repaglinide. Repaglinide is an oral anti hyperglycemic agent used for the treatment of non-insulin-dependent diabetes mellitus (NIDDM). The solubility of the drug was enhanced by preparation of solid dispersions using solublising agents such as soluplus and poloxamer. The formed solid dispersions were formulated into immediate release tablets by direct compression technique using various concentrations of crosspovidone as the super disintegrant. The prepared tablets were evaluated for their hardness, weight variation, content uniformity, tablet thickness, friability, disintegration time and *in vitro* dissolution studies. Stability studies were also performed. The ability of the tablet to release the drug faster depends on the concentration of the super disintegrant. In this study the immediate release tablets containing soluplus as the solublising agent and crosspovidone as the super disintegrant in the concentration of 5% showed better release of drug. About 99.4% of the drug was released in 25 mins from the tablets. Therefore, based on the physicochemical properties, *in vitro* drug release profile F 8 containing 5% of cross povidone is optimized as the best formulation.

INTRODUCTION:

Oral route of administration is preferred to be the best route of administration due to several advantages like ease of administration, accurate dosage, self-medication and most importantly patient compliance. Comparatively the tablet dosage form is the most popular dosage form, because of its ease of transportability and lower manufacturing cost [1]. Dysphasia or difficulty in swallowing is the most common disadvantage with conventional dosage forms like tablets and capsules among all age groups. Therefore such an advantage with conventional tablets and capsules led to the development of a novel approach which aims at formulating a convenient dosage form for administration and for better patient compliance to enhance safety and efficacy of the drug. One such approach is Oro-dispersible tablet or Immediate Release tablet. United States Food and Drug Administration (FDA) defined ODT as "A solid dosage form containing medical substances or active ingredient which disintegrates rapidly usually within a matter of seconds when placed upon the tongue".

The disintegration time for ODTs generally ranges from few seconds to a minute [2]. Repaglinide is an oral antihyperglycemic agent used for the treatment of non-insulin-dependent Diabetes Mellitus (NIDDM). It belongs to the Meglitinide class of Short-acting Insulin secretagogues. The objective of the present research is to enhance the solubility of the poorly soluble drug Repaglinide and to prepare and evaluate immediate release tablets [3]. Repaglinide is BCS class II drug. Solubility of Repaglinide is enhanced by preparation of solid dispersions using Soluplus, Poloxamer as solublising agents. The solid dispersions thus prepared are compressed into immediate release tablets using crospovidone as super disintegrant.

2. MATERIALS AND METHODS

2.1 Materials:

The active ingredient Repaglinide was received from Natco Pharma Ltd., Hyderabad. The other excipients such as Soluplus, Poloxamer, Microcrystalline cellulose, Lactose mono hydrate, Crospovidone XL, Magnesium stearate are received from Sd Fine Chem. Limited, Mumbai. Aerosil was received from H. D. Pharmachem, Ahemdabad. All the ingredients used in the formulation are of pharmaceutical analytical grade.

2.2 Methods:

2.2.1 Identification of drug:

The drug was identified by melting point determination and Ultra Violet spectroscopy (UV).

2.2.1.1. Melting point determination:

Melting point of Repaglinide was determined by capillary tube method. Fine powder of the drug was filled into a glass capillary tube which was sealed at one end. The capillary tube was tied to a thermometer and subjected to increasing temperatures, and the temperature at which Repaglinide melts was recorded.

2.2.1.2 Ultraviolet spectroscopy:

The samples were subjected to UV spectrophotometric analysis and were scanned for absorption maxima (λ_{max}) in the range of 200-400nm using UV-Visible spectrophotometer in an appropriate medium. The obtained data was compared with that of reference values in literature [4].

3. PRE COMPRESSION PARAMETERS:

3.1 Bulk density:

Weighed quantity of powder was transferred into a 50 ml measuring cylinder without tapping. After transferring, the volume occupied by the powder was measured. It is expressed in gm/ml.

Bulk density was calculated by using the formula.

$$\mathbf{P = m/V_o}$$

Where,

P = Bulk density, V o = Untapped volume, m = mass of the blend.

3.2 Tapped density:

Weighed quantity of powder was taken into graduated cylinder. The cylinder was subjected to 100 tappings and the volume was noted which is known as "Tapped Volume".

Tapped density was calculated by using the formula.

$$\mathbf{P_t = m/V_i}$$

Where,

P_t = Tapped density, V_i = Tapped volume, m = Mass of the blend.

3.3 Angle of repose:

The powder blend was assessed for its flow property by determining the angle of repose. The angle of repose was measured by allowing the powder to fall over a graph sheet placed on horizontal surface through a funnel kept at a certain height. The height of the heap was measured and then circumference of the base of heap was drawn on graph sheet with the help of a pencil. The radius of the circle obtained was measured. The angle of repose is given as,

$$\mathbf{\tan \theta = h/r \text{ or } \theta = \tan^{-1} (h/r)}$$

Where,

θ = angle of repose, h = height of the heap, r = radius of the base of the heap

3.4 Carr's compressibility Index:

Using bulk density and tapped density, the percentage compressibility of the powder was determined, which is given as Carr's compressibility index.

Carr's compressibility index (%) =
Tapped density-bulk density * 100
Tapped density

3.5 Hausner's Ratio:

It was determined by the ratio of tapped density and bulk density [5, 6, 7]

Hausner's ratio = V_o/V_i

Where

V_o = Bulk density, V_i = Tapped density

4. DRUG-EXCIPIENT COMPATIBILITY STUDIES:

Drug is in intimate contact with one or more excipients in all the dosage forms which will affect the stability of the drug. Knowledge of drug-excipient interaction is useful in selecting an appropriate excipient. Drug and excipients are stored at 55^0C for 14 days, 40^0C at RH 75% for one month. After one month they are subjected for analysis of description, assay, LOD, purity. After the pre-formulation studies were performed the powder is converted into tablets using direct compression method.

5. PREPARATION OF TABLETS:

Solid dispersions of Repaglinide were prepared using various concentrations of soluplus or poloxamer as the solublising agents and sifted through 40 # mesh. Then the remaining ingredients such as lactose monohydrate, microcrystalline cellulose, PH102, crospovidone, aerosil were weighed and sifted individually through 40 # mesh. The solid dispersions and excipients were transferred into a poly bag and mixed for 3 minutes. Then the above blend was passed through 40 # mesh. Magnesium stearate was weighed, passed through 40 # mesh and added to the above mixture and blended for few minutes. Lastly the mixture was compressed into tablets using a tablet compression machine [8, 9].

6. EVALUATION OF IMMEDIATE RELEASE TABLETS: [10,11,12]

6.1 General Appearance:

The general appearance of a tablet, its identity and general elegance is essential for consumer acceptance, for control of lot-to-lot uniformity and tablet-to-tablet uniformity. The control of general appearance involves the measurement of size, shape, colour, presence or absence of odour, taste etc.

6.2 Tablet Hardness:

The hardness of the tablet indicates its tensile strength and is measured in terms of load or pressure required to crush it when placed on its edge. Hardness has influence on disintegration and dissolution times and may affect bioavailability. This can be tested by using one of the following hardness testers i.e. Monsanto hardness tester, Strong Cobb tester, Pfizer tester, Erweka and Varian tester.

6.3 Thickness and diameter:

The thickness and diameter of 10 tablets were recorded during the process of compression using Vernier callipers.

6.4 Wetting time:

The wetting time of the tablets was measured by a simple procedure. A circular tissue paper of 10 cm diameter was placed in a petri dish containing 10 ml of water containing Eosin blue. A tablet was carefully placed on the surface of tissue paper. The time required for developing blue color on the upper surface of the tablet was noted as the wetting time.

6.5 Weight variation test:

The weight of the tablet is measured to ensure that the tablet contains the required amount of drug. 20 tablets were selected randomly from each formulation and were weighed individually using an electronic balance. Average weight of the tablets was calculated. The individual weight o the tablets was compared with average weight. The tablets meet the USP specifications if not more than 2 tablets are outside the percentage limit and if no tablet differs by more than 2 times
the percentage limit.

Percentage Deviation=

(W avg) - (W initial) × 100
(W avg)

6.6 Friability:

This test evaluates ability of tablet to withstand abrasion and edge damage during packing, handling and shipping. Friability occurs due to poor cohesion of tablet ingredients. Friability was measured with the help of Roche Friabilator. 10 tablets were weighed and placed in plastic chamber which revolves at 25 rpm for 4 minutes. Tablets were weighed again after removal of fines (de-dusted). The friability was calculated by the formula

%Friability =

$$\frac{\text{Initial weight} - \text{Final Weight}}{\text{Initial weight}} X100$$

6.7 Disintegration time:

The disintegration time of the tablet is the time taken for the tablet to break into small particles and was determined using USP disintegration test apparatus. Six tablets were placed individually in each tube of disintegration test apparatus in which bath temperature was maintained at 37±0.5 ˚C and disc was placed on each tablet. The disintegration time of each tablet was noted.

6.8 Content Uniformity:

The content uniformity test is used to ensure that every tablet contains the amount of drug substance intended with little variation among tablets within a batch. 30 tablets were selected randomly from each formulation. 10 tablets from each formulation were assayed individually. The tablets pass the test if 9 of the 10 tablets contain not less than 85% and not more than 115% of the labelled drug content and the 10th tablet may not contain less than 75% and more than 125% of the labelled content. If these conditions are not met, remaining 20 tablets are assayed individually and none may fall outside of the 85 to 115% range.

6.9 *In vitro* dissolution studies:

In vitro dissolution studies of the tablets were carried out in USP dissolution apparatus (Type II) by using a paddle at 100 rpm. 900 ml of 0.1 N HCl maintained at 37 ± 0.5 ℃ was used as a dissolution medium. One tablet from each formulation was used in the test. Aliquots of 10 ml each were withdrawn at specified time intervals and replaced with equal volume of fresh dissolution medium. The withdrawn aliquots were analyzed for drug content spectrophotometrically at λ_{max} 242 nm. The dissolution studies were carried out in triplicate. Cumulative percentage drug released was calculated and plotted against time.

6.10 Stability Studies:

Accelerated stability studies were performed on Repaglinide formulation (F8), by storing 15 tablets in amber colored rubber stopper vials at elevated temperature of 40 ±2°C and 75±5% RH for a period of 30 days (1 months). At intervals of 15days, the tablets were visually examined for any physical changes, changes in drug content and *in vitro* disintegration time.

7. RESULTS AND DISCUSSION:

Pre-formulation testing encompasses all studies enacted on a new drug compound in order to produce useful information for subsequent formulation of a stable and bio-pharmaceutically suitable drug dosage form. Before starting prototype formulation of immediate release tablets of Repaglinide pre-formulation studies for the pure drug were performed.

7.1 Drug excipient compatibility study (Physical observation):

The pure drug along with excipients was subjected to compatibility studies, the results of the physical observation were shown in the table. The FTIR spectra of pure Repaglinide showed characteristics peaks at 1687.36 cm^{-1} which indicates C=O stretching vibration. 2935.03 cm^{-1} indicates that C–H group is present, 3308.38 cm^{-1} indicates N-H bond is present, 1217.12 cm^{-1} indicates --CH3 group is present. The FTIR of Repaglinide with soluplus shows a peak at 1686.20cm^{-1}, 2934.48cm^{-1}, 1218.35cm^{-1}. The FTIR of Repaglanide with crosspovidone shows peaks at 1684.85cm^{-1}, 2934.49cm-^{1}, 1217.37cm^{-1}. From these results it is clear that there is no interaction between drug and excipients.

7.2 Bulk Density:

The bulk densities of the powder blends of all the formulations ranged in between 0.325 to 0.45 gm/cc.

7.3 Tapped Density:

The Tapped densities of the powder blends of all the formulations ranged from 0.46 to 0.55gm/cc.

7.4 Compressibility index or Carr's index:

The Carr's index of the powder blends of all the formulations ranged in between 16 to 28.70%. The formulation F5, F7 and F8 were having good compressibility index where as formulations F1, F2, F3, F4 and F6 were having fair Compressibility index.

7.5 Hausner's Ratio:

The Hausner's ratio values ranged from 1.18 to 1.40. The formulations F8 showed good Hausner's ratio and the formulations F1, F2, F3, F4, F5, F6 and F7 were having fair Hausner's ratio.

7.6 Angle of Repose:

The angle of repose of the powder blends of all the formulations was determined and the values ranged from 24 ± 0.02^0 to 32 ± 0.02^0. The formulations F2, F3, F5, F6 and F8 were having excellent flow property and the formulations F1, F4 and F7 were having good flow property.

8. EVALUATION PARAMETERS FOR IMMEDIATE RELEASE TABLETS OF REPAGLINIDE:

The formulated immediate release tablets of Repaglinide were evaluated for the following post compression parameters.

8.1 Weight variation: The weight variation test was performed and the weights of the tablets were between 50 ± 0.04 to 50 ± 0.28 mg. The pharmacopoeial specification for weight variation limit is ±10%, for uncoated tablets weighing less than 80mg as the weight of the tablet is 50 mg. Hence all the formulations passed the weight variation test and the % weight variation was within the pharmacopoeial specifications.

8.2 Thickness:

Tablets thickness was measured by using Vernier Callipers. The thickness of all the formulations was between 2.97 ± 0.2 to 3.04 ± 0.02mm. Tablet mean thickness was almost uniform in all the formulations and was within the pharmacopoeial specifications.

8.3 Hardness:

The hardness of all the formulations ranged from 4 to 5.01 kg/cm^2. The pharmacopoeial limit for hardness is 4-8 kg/cm^2. Therefore, all the formulations passed the test for hardness.

8.4 Friability:

The friability of all the formulations was determined, and the values were in the range from 0.32 to 0.54%. Friability values below 1% were an indication of good mechanical resistance of the tablets. Hence all the formulations were within the pharmacopoeial limits

8.5 Content uniformity:

The percentage drug content of all the tablets was found to be in the range of 98.8 to 100.02% of Repaglinide, and was within the acceptable limits. The preparation complies with the test if each individual content is 85 to 115% of the average content; and the preparation fails to comply with the test if one of the tablet's content is outside the limits of 75 to 125% of the average content. Hence all the formulations passed the test and the values are within the pharmacopoeial limits.

8.6 Wetting time:

All the formulations were evaluated for wetting time and the values ranged from 10 to 14 seconds which were observed to be according to the specifications of the pharmacopoeia.

8.7 Disintegration Time:

All the formulations were evaluated for disintegration time and the values ranged from 12 to 15 seconds which were observed to be according to the specifications of the pharmacopoeia.

Table 1: Formulation of Repaglinide tablets

S.No	INGREDIENTS	F1	F2	F3	F4	F5	F6	F7	F8
1	Repaglinide + poloxamer (1:1)	4	4	4	4	-	-	-	-
2	Repaglinide + Soluplus(1:1)	-	-	-	-	4	4	4	4
3	Microcrystalline cellulose	23.8	23.3	22.8	22.3	23.8	23.3	22.8	22.3
4	Lactose mono hydrate	20	20	20	20	20	20	20	20
5	Crospovidone XL	1	1.5	2	2.5	1	1.5	2	2.5
6	Magnesium stearate	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6
7	Aerosil	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6
	Total	50	50	50	50	50	50	50	50

Table 2: Pharmacopeial specifications of Pre-formulation Studies

S.No	Type of Flow	Angle of Repose	Carr's Index	Hausner's Ratio
1.	Excellent	<25	<10	1.00-1.11
2.	Good	25-30	11-15	1.12-1.18
3.	Fair	31-35	16-20	1.19-1.25
4.	Passable	36-40	21-25	1.26-1.34
5.	Poor	>40	26-31	1.35-1.45
6.	Very poor		32-37	1.46-1.59
7.	Very very poor		>38	>1.60

Table 3: Pharmacopeial specifications for tablet weight variation

Average weight of tablets (IP)	Average weight of tablets (USP)	Maximum % difference allowed
Less than 80 mg	Less than 130 mg	10
80 mg-250 mg	130 mg-324 mg	7.5
More than 250 mg	More than 324 mg	5

Table 4: Results of organoleptic characteristics of drugs

S.No	Parameter	Character
1	Colour	White
2	Odour	Odourless

Table 5: Results of Drug Excipient Compatibility studies

S.No	Excipient (with drug)	Ratio	1st week	4rd week
1	Soluplus	1:2	No colour change	No colour change
2	Microcrystalline Cellulose	1:15	No colour change	No colour change
3	Lactose	1:10	No colour change	No colour change
4	Crosspovidone	1:1	No colour change	No colour change
5	Magnesium Stearate	1:1	No colour change	No colour change
6	Aerosil	1:1	No colour change	No colour change

Inference: The compatibility studies of the drug with different excipients showed no characteristic changes in the color.

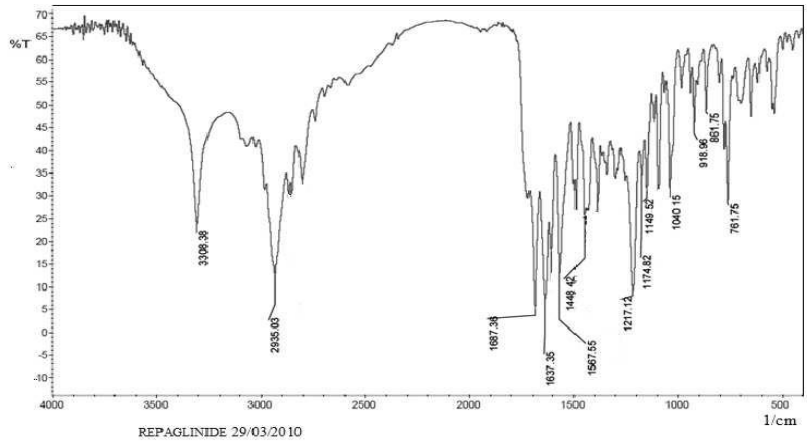

Figure 1: FTIR spectral studies of Repaglinide pure drug.

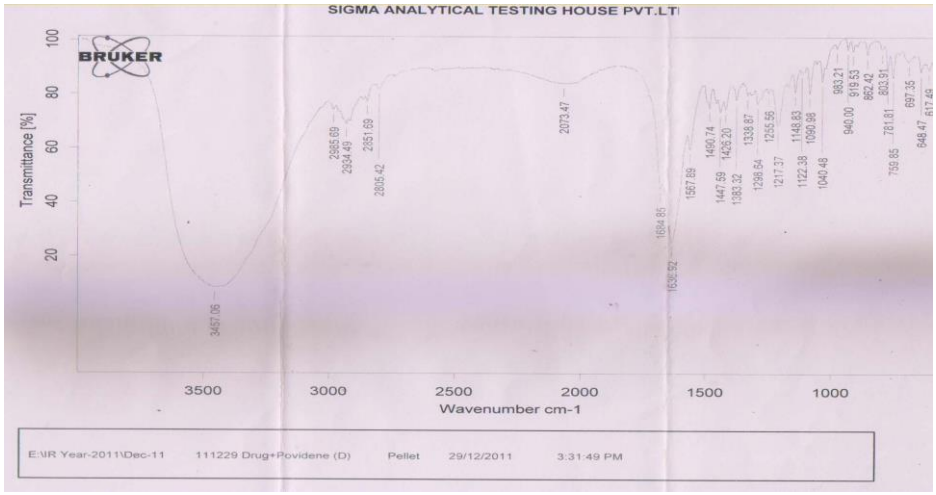

Figure 2: FTIR of Repaglanide with Soluplus

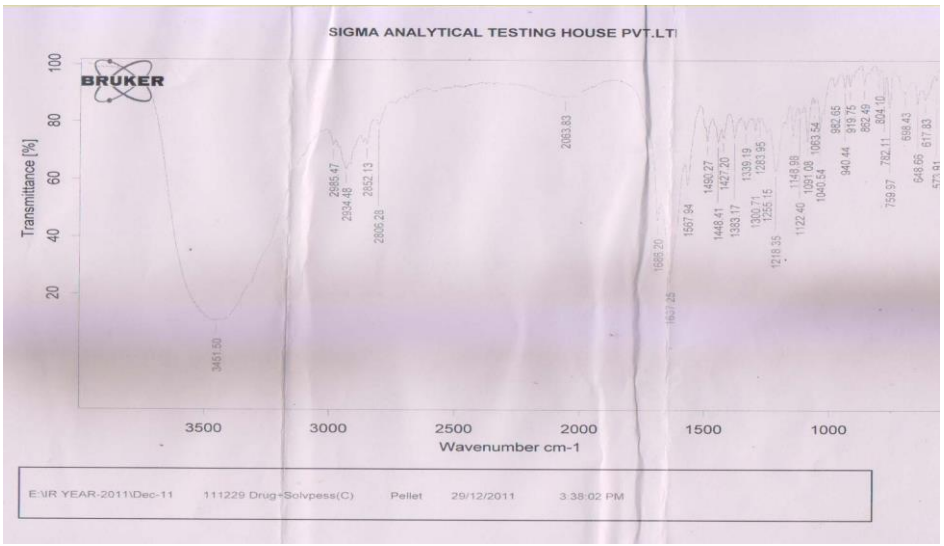

Figure 3: FTIR of Repaglanide with crosspovidone

Table 6: Pre-Compression Characteristics of the Powder Blend

Formulation code	Bulk Density (gm/cc) (Mean±SD)	Tapped Density (Mean±SD)	Compressibility index (%)	Hausners's ratio	Angle of repose (n=3) (Mean±SD)
F1	0.375 ±.0011	0.526 ±0.005	28.70±1.517	1.4 ±0.0321	32 ± 0.02
F2	0.414 ±0.002	0.550±0.001	24.10±0.577	1.31 ±0.005	26 ± 0.04
F3	0.416 ±0.001	0.542 ±0.005	23.10±0.2516	1.30 ±0.064	28 ± 0.01
F4	0.338 ±0.001	0.499±0.001	20.79±0.3214	1.26±0.01	31 ± 0.02
F5	0.445 ±0.001	0.5 ±0.005	17.19±0.5715	1.20±0.01	27 ± 0.03
F6	0.425 ±0.005	0.53±0.001	20.56±0.1524	1.25±0.264	25 ± 0.01
F7	0.41 ±0.0005	0.5±0.0005	17.56±0.5773	1.21±0.01	32 ± 0.04
F8	0.3 ±0.00058	0.4±0.0005	16.02±0.573	1.18 ±0.005	24 ± 0.02

Table no 7: Post Compression Evaluation Parameters of IR tablets of Repiglinide

Formulation code	Weight variation (Mean±SD)	Thickness (mm) (Mean±SD)	Hardness (Kg/cm^2) (Mean±SD)	Friability (%)	Content uniformity (%) (Mean±SD)
F1	50 ± 0.13	2.97 ± 0.2	4 ± 0.03	0.32	100 ± 0.1
F2	50 ± 0.51	3.0 ±1 0.3	4.5 ± 0.04	0.44	99.8 ± 0.3
F3	50 ± 0.15	2.99 ± 0.04	4.2 ± 0.3	0.37	98.5± .01
F4	50 ± 0.04	3.04 ± 0.02	4.8 ± 0.04	0.49	99.6 ± 0.02
F5	50 ± 0.28	3.01 ± 0.03	4.5 ± 0.02	0.51	100.01 ± 0.9
F6	50 ± 0.25	2.99 ± 0.03	4.5 ± 0.02	0.53	99.98 ± 0.01
F7	50 ± 0.14	3.03 ± 0.04	4.6 ± 0.04	0.54	99.95 ± 0.01
F8	50 ± 0.18	3.00 ± 0.02	5 ± 0.01	0.32	100 ± 0.09

Table 8: Post-compression characteristics of the IR tablets of Repaglinide

Formulation code	Wetting time (sec)	Disintegration time (sec)	Uniformity of dispersion
F1	10 ± 2	13 ± 2	Passed
F2	11 ± 2	14 ± 1	Passed
F3	10 ± 1	12 ± 1	Passed
F4	9 ± 1	11 ± 2	Passed
F5	11 ± 3	12 ± 2	Passed
F6	10 ± 3	11 ± 3	Passed
F7	9 ± 1	12 ± 1	Passed
F8	9 ±2	10 ± 2	Passed

Table no 9: *In vitro* Dissolution studies of formulated immediate release tablets of Repaglinide

Time (min)	Cumulative % drug release								
	F1	F2	F3	F4	F5	F6	F7	F8	INNOVATOR
0	0	0	0	0	0	0	0	0	0
5	35.1	44.5	47.2	55.6	39.4	46.21	51.9	57.5	50.1
10	58.3	68.5	67.2	65.6	60.4	60.21	59.9	61.9	59.2
15	63.7	71.2	69.1	76.9	75.4	78.2	79.7	81.7	71.1
20	72.4	75.6	71.6	88.4	85.4	86.5	85.1	93.1	85.4
25	76.4	78.6	76.6	93.5	91.4	96.3	96.4	99.4	95.6

Table no 10. Stability data of F3 formulation at 40 ± 2^{0}C / 75 ±5% RH

Description	Initial (n=3) Avg ± SD	After one month (n=3)Avg± SD
	White to half white round tablets side.	No change
Thickness (mm)	2.99 ± 0.24	2.99 ± 0.04
Hardness	2.5 ± 0.26	2.4 ± 0.09
% Friability	0.39 ± 0.09	0.40 ± 0.95
Wetting time(sec)	9 ± 0.05	10 ± 0.86
Disintegration time (sec)	11 ± 0.23	11 ±0.58
Cumulative % drug release	99.4±0.5	99.1±0.17

Table no 11: Drug content data for stability of F8 formulation

S. No.	Time in days	Physical changes	% Drug content
1.	1st day (initial)	--	99.94±0.20
2.	30th day	No changes	99.12±0.13

Table no 12: Drug content data for stability studies

S. No.	Trial	1st day (A)	30th day (B)	A – B
1.	1	99.8	98.3	1.5
2.	2	99.14	98.07	1.07
3.	3	100.74	99.61	1.13
4.	Mean percent drug content	99.89	98.66	1.23

Discussion: Tablets were prepared with Crosspovidone. All the formulations from F1-F8 showed quick disintegration. The quick disintegration may be attributed due to the wicking type of disintegrants (crosspovidone) formed thus facilitating the disintegrants to bring about faster disintegration.

All the formulations were evaluated for uniformity of dispersion and all formulation passed the uniformity test.

Formulations F1 to F4 were formulated using Poloxamer as solubility enhancer and Crosspovidine as superdisintegrant in increasing concentrations of 2%, 3%, 4% and 5% respectively. F4 formulation with highest concentration of crospovidone showed better drug which was showed in the graph. Formulations F5 to F8 were formulated using Soluplus as solubility enhancer and Crosspovidine as superdisintegrant in increasing concentration

of 2%, 3%, 4% and 5% respectively. F8 formulation with highest concentration of Crospovidone showed better results which was showed in the graph. The results indicate that the drug release depends on concentration of super disintegrant. Hence it is clear that formulations containing Soluplus as solublising agent has better dissolution profile when compared with formulations containing Poloxamer. Among the Soluplus containing formulations (F5-F8) F8 containing Crosspovodine in the concentration of 5% showed better results. So F8 formulation containing Soluplus and Crosspovidine in 5% concentration is the best formulation. After comparison of F8 formulation with the innovator product it is clear that F8 formulation showed a better release profile than the innovator product.

Short-term stability studies on the above promising formulation at 40^0C/ 75% RH for 1 month have shown no significant changes in physical appearance, thickness, hardness, friability, wetting time, disintegration time and drug content as shown in the above table.

CONCLUSION:

The present study has been focused on the development of immediate release tablet of Repaglinide. The formulations F1-F8 were formulated using microcrystalline cellulose, lactose monohydrate, crosspovidone, and magnesium stearate. All Formulations were prepared by the direct compression technique. Formulations F1 t0 F4 were prepared using Poloxamer as solublising agent and formulations F5 to F8 were prepared using Soluplus. The above formulations were evaluated for their hardness, weight variation, content uniformity, tablet thickness, friability, disintegration time and in vitro dissolution studies. Stability studies were also performed. The ability of the tablet to release the drug depends on the concentration super disintegrant. In this study the immediate release tablets containing Soluplus as the solublising agent and Crosspovidone as the super disintegrant in the concentration of 5% showed better release of drug. About 99.4% of the drug was released in 25 mins from the tablets. Therefore, based on the physicochemical properties, in vitro drug release profile F 8 containing 5% of Cross povidone is optimized as the best formulation. The formulation F8 was best in economic factor when compared to innovator product.

REFERENCES:

1. Lachmann L, Lieberman H, Kanig J, the Theory and Practice of Industrial Pharmacy, 3rd ed. Pg. No. 293-345, 346-373.
2. Aulton M, Pharmaceutics: The Science of Dosage from Design, International Student Edition. Pg. No. 304-321, 347-668.
3. Dhirendra K, Lewis S, Udupa N, Atin K. Solid Dispersions, A Review. Pak J Pharm Sci.2009, 22(2), pp234-246.
4. Reynolds JEF, Martindale: The Extra Pharmacopoeia, 30th ed. The Pharmaceutical Press, London, 1993.
5. The Merck Index**,** In: An Encyclopedia of Chemicals, Drugs and Biologicals, Published by- Merck Research Laborateries Division of Year NJ-2001 Merck & Co.,Inc:Article no-8297,
6. Kathleen P., Martindale. The Complete drug reference. Thirty-third edition, Pharmaceutical press, 2002.
7. Culy C, Jarvis B. Repaglinide, a review of its therapeutic use in Type 2 diabetes mellitus. Drugs, 2001, vol61, pp1625-1660.
8. Malaisse W. Repaglinide, a new oral antidiabetic agent: a review of recent preclinical studies, Eur J Clin Invest. 1999, vol29, pp21-29.
9. Wang FEI. Focus on Repaglinide: an oral hypoglycemic agent with a more rapid onset and shorter duration of action than the sulfonylureas. Formulary, 1998, vol33, pp25-30.
10.Amidon GL. A theoretical basis for a biopharmaceutical drug classification: the correlation of *in vitro* drug product dissolution and *in vivo* bioavailability. Pharm Res. 1995, vol12, pp413-420.
11. Raymond CR, Paul JS, Sion CO. In: Hand book of pharmaceutical excipients, 5th Edition, Pharmaceutical press,Great Britain, 2006.

12.Najmuddin, Tousif, Mohsin, Shelar S, Patel V. Enhancement of dissolution rate of Ketoconazole by Solid Dispersion Technique, Int J Pharmacy Pharm Sci. 2010,vol2(3),pp132-136.
13. Gupta, Srivastav, Vajpai. Comparative study of solubility enhancement of poorly soluble drug by Solid Dispersion and Inclusion Complex. J. Pharm Res. 2010,vol3(4),pp692-696.
14. Higuchi, Connors, Phase solubility techniques, Adv. Anal. Chem. Instrum. 1965, vol4, pp117-123.
15. Venkatesh, Arunkumar, Verma PRP, Rani C. Preparation and in-vitro characterization of Valsartan
16. Solid Dispersion using Skimmed Milk Powder as Carrier. Ind J Pharm Tech Res. 2009,vol1(3),pp431-437.
17. Heo MY, Piao Z, Kim TW, Cao QR, Kim A, Lee BJ. Effect of Solubilizing and Microemulsifying Excipients in Polyethylene Glycol 6000 Solid Dispersion on Enhanced Dissolution and Bioavailability of Ketoconazole, Arch Pharm Res, 2005,vol28,pp604-611.
18.Sapkal NP, Kilor VA, Bhusari KP, Daud AS, Evaluation of some Methods for Preparing Gliclazide- ß- Cyclodextrin Inclusion Complexes, Tropical J. Pharm. Res., 2007,vol 6, pp833-840.