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FORMULATION DEVELOPMENT AND IN-VITRO EVALUATION OF SUSTAINED RELEASE MATRI TABLETS OF GLIBENCLAMIDE

[1]*M. Shiroja, [2]N. Rajitha and [3]Pola Kranthi Kumar

[1]Dept. of Pharmaceutics, Bhaskar Pharmacy College, Bhaskar Nagar, Moinbad(M), RR Dist. Telangana.

[2]Dept. of Pharmacy Practice, Bhaskar Pharmacy College, Bhaskar Nagar, Moinbad(M), RR Dist. Telangana.

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***Corresponding Author**
M. Shiroja
Dept. of Pharmaceutics,
Bhaskar Pharmacy College,
Bhaskar Nagar,
Moinbad(M), RR Dist.
Telangana.

ABSTRACT

The aim of the present study was to fabricate and evaluate controlled release tablets glibenclamide, using different polymers like Guar gum, Xanthun gum HPMC K 100 and CMC which is suitable for delivering the drug for sufficient long time and reduce frequency of dose. Modified release drug delivery systems are designed by different techniques like enteric coating, osmotic pump, pro-drugs, transdermal patches and matrix tablets. Among the various techniques used, recently the attention of pharmaceutical researchers has been attracted by the matrix tablets because of their ease of manufacturing. Different types of polymers are used to control the release of drugs from the dosage forms for absorption by the human body. Though a variety of polymeric substances are available to serve as release retarding matrix Materials there is a continued need to develop new, safe and effective release retarding materials for matrix tablets.

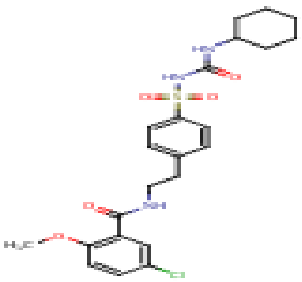
KEYWORDS: Glibenclamide, Guar gum, Xanthun gum HPMC K 100 and CMC.

1. INTRODUCTION

Glibenclamide is an oral antihyperglycemic agent used for the treatment of non-insulin-dependent diabetes mellitus (NIDDM). It belongs to the sulfonylurea class of insulin secretagogues, which act by stimulating β cells of the pancreas to release insulin. Sulfonylureas increase both basal insulin secretion and meal-stimulated insulin release.

IUPAC Name:5-chloro-N-[2-(4-{[(cyclohexylcarbamoyl)amino]sulfonyl}phenyl)ethyl]-2-methoxybenzamide.

Structure



2. METHODOLOGY

For the formulation of glibenclamide using different polymers like Guar gum, Xanthun gum HPMC K 100, Micro crystalline cellulose, magnesium sterate and CMC which is suitable for delivering the drug for sufficient long time and reduce frequency of dose.

3. Developmentof Calibrationcurve For Glibenclamide

3.1 Preparation of Standard Curve for Glibenclamide

Preparation of 6.8pH Phosphate buffer

Determination of Standard Curve: Stock solution of 1000µg/ml of Glibenclamide was prepared by dissolving 25mg of drug in small quantity of methanol and diluted with methanol to 25ml. From this take10ml and make upto100ml using buffer to get a stock solution of 100 µg/ml. From the above solution take 0.2, 0.4, 0.6 0.8,1.0 1.2,1.4 1.6,ml and dilute to10 ml with buffer to get a concentrations of 2,4, 6,8,10,12,14 and 16µg/ml. The absorbance of the different diluted solutions was measured in UVspectrophotometerat228nm. A calibration curve was plotted by taking concentration of the solution in µg/ml on X-axis and absorbance on Y-axis and correlation co-efficient "r^2" was calculated.

3.2 Preparation of Standard Curve for Glibenclamide

Preparation of 0.1N HCL

Determination of Standard Curve: Stock solution of 1000µg/ml of Glibenclamide was prepared by dissolving 25mgofdruginsmall quantity of methanol and diluted with methanol to 25ml. From this take10ml and make upto 100ml using 0.1N Hcl to get a stock solution of 100 µg/ml. From theabovesolutiontake0.2, 0.4, 0.6 0.8,1.0 1.2,1.4 1.6,ml and dilute to10 ml with buffer to get a concentrations of 2,4, 6,8,10,12,14 and 16µg/ml. The absorbance of the

different diluted solutions was measured in a UVspectrophotometerat228nm. A calibration curve was plotted by taking concentration of the solution in µg/ml on X-axis and absorbance on Y-axis and correlation co-efficient "r^2" was calculated.

3.3 Preparation of Glibenclamide Matrix Tablets: All the matrix tablets, each containing 8 mg of Glibenclamide, were prepared by wet granulation method and some of the formulations were prepared by direct compression method also to study the effect of method of manufacture on the drug release.

Direct compression: Accurately weighed amounts of drug, polymer, and diluent were mixed geometrically in a mortar. This mixture was passed through No.40 sieve and thoroughly mixed in a polythene bag for 15 minutes. The powder blend was then lubricated with magnesium stearate and for 2 minutes and compressed into tablets on a 8-station rotary tableting machine using8mmround, flat-faced punches. The drug polymer ratio was developed to adjust drug release as per theoretical release profile and to keep total weight of tablet constant for all the fabricated batches under experimental conditions of preparations. The total weight of the matrix tablets was 400mg with different drug polymer ratios. The various polymers used were HPMC, Guargum, CMC, EUDRAGIT and xanthum. fillers like MCC (water soluble),lubricants like magnesium stearate were used for the preparation of matrix tablets.

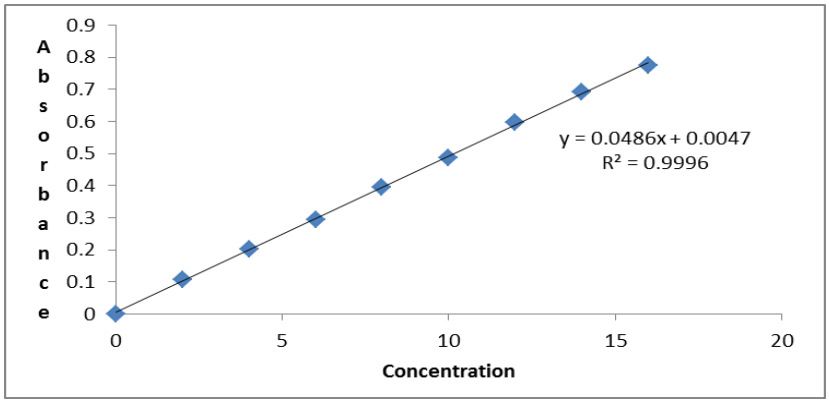
4. Formulations: In the formulations prepared, the release retardants included were MCC were used as filler. Magnesium stearate1% were used as lubricants. Compositions of different formulations were given in the following Tables (Table 6 to Table 14).

Table.1 Composition of Matrix Tablets containing glimeperide controlled release tablets.

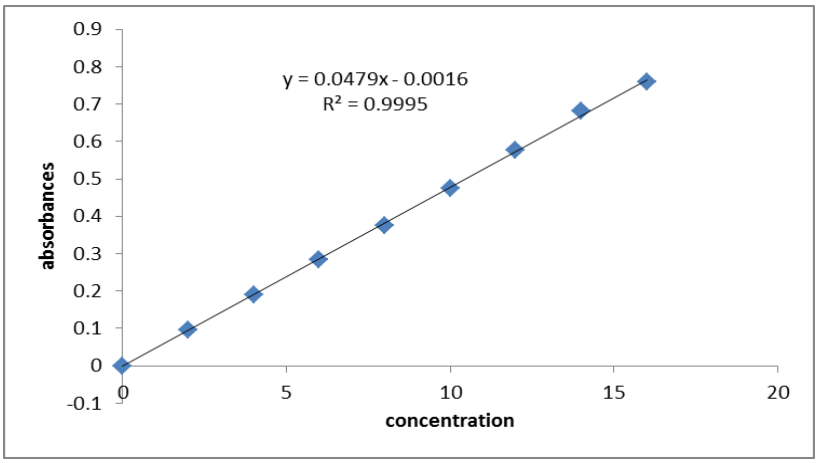
F.Code	F1	F2	F3	F4	F5	F6	F7	F8	F9
API (mg)	8	8	8	8	8	8	8	8	8
Xanthum	100	-	-	-	-	50	50	50	-
Guar gum	-	100	-	-	-	-	-	-	50
Eudragit	-	-	100	-	-	50	-	-	50
HPMC K100M	-	-	-	100	-	-	50	-	-
CMC	-	-	-	-	100	-	-	50	-
Mg.stearate(mg)	2	2	2	2	2	2	2	2	2
MCC	90	90	90	90	90	90	90	90	90
Total (mg)	200	200	200	200	200	200	200	200	200

5. RESULTS AND DISCUSSION

5.1 Glibenclamide Standard curve in 6.8pH phosphate buffer.

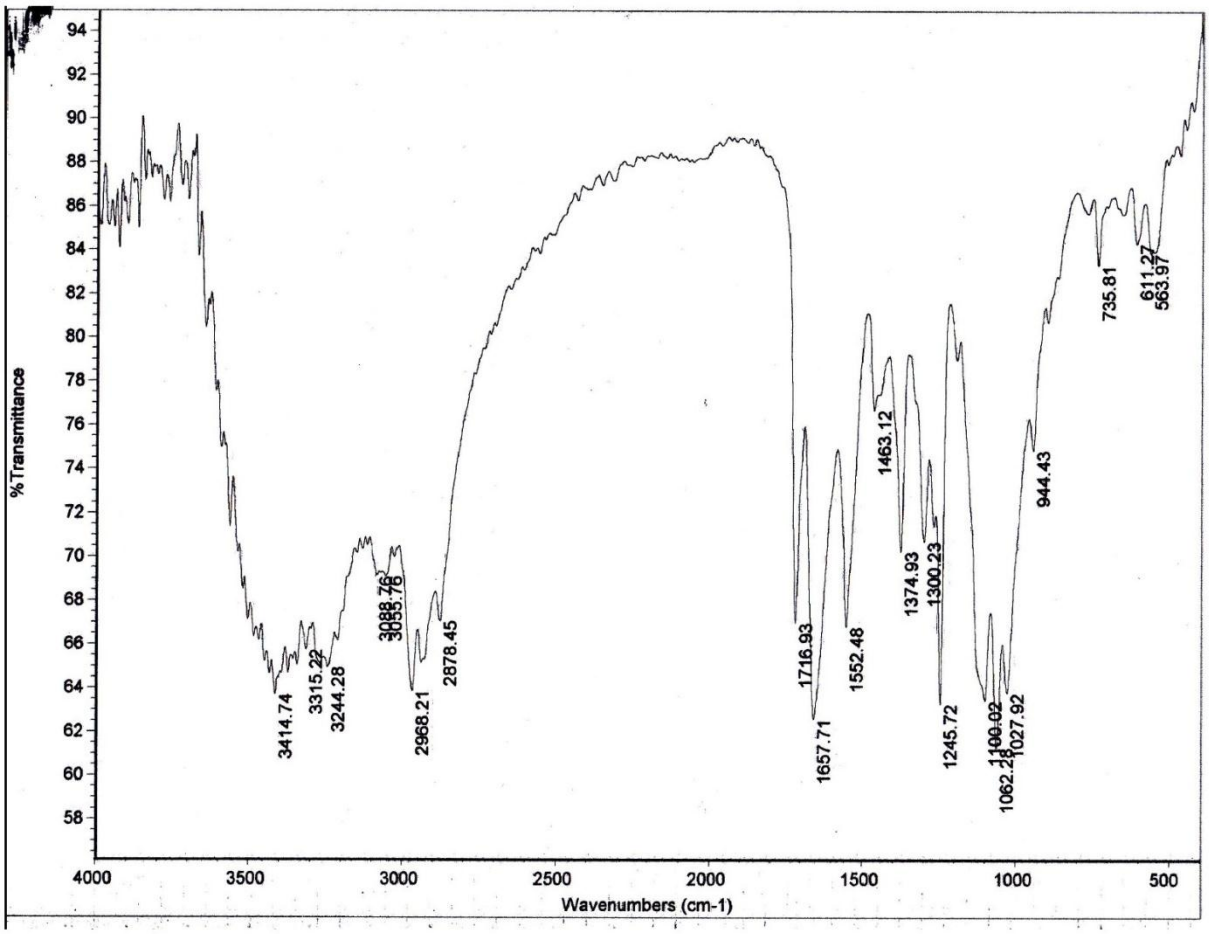


5.2 Glibenclamide standard curve in 0.1N HCL.



5.3 Compatability Studies

The spectrum of the standard and the samples were then superimposed to find out any possible interactions between the drug and the polymers. All the characteristic peaks of GLIBENCLAMIDE were also found in the spectrum formulations. The results suggest that the drug is intact in the formulations and there is no interaction found between the drug and the excipients.



5.4 PRE COMPRESSION PARAMAETRS

Table No.2

Formulations	Angle of Repose (θ)	Loose Bulk Density (g/ml)	Tapped Bulk Density (g/ml)	%Compressibility	Hausner's ratio
F1	27.5	0.33±0.01	0.38±0.01	13.16	1.15
F2	25.3	0.37±0.02	0.43±0.03	13.95	1.16
F3	28.1	0.34±0.01	0.39±0.06	12.82	1.15
F4	26.8	0.38±0.03	0.44±0.04	13.64	1.16
F5	27.4	0.34±0.04	0.39±0.07	12.82	1.15
F6	25.9	0.32±0.02	0.37±0.02	13.51	1.16
F7	26.4	0.36±0.03	0.41±0.01	12.20	1.14
F8	29.1	0.30±0.04	0.35±0.02	14.29	1.17
F9	28.7	0.34±0.06	0.38±0.01	10.53	1.12

Post Compression Parameters

Tablet No.3

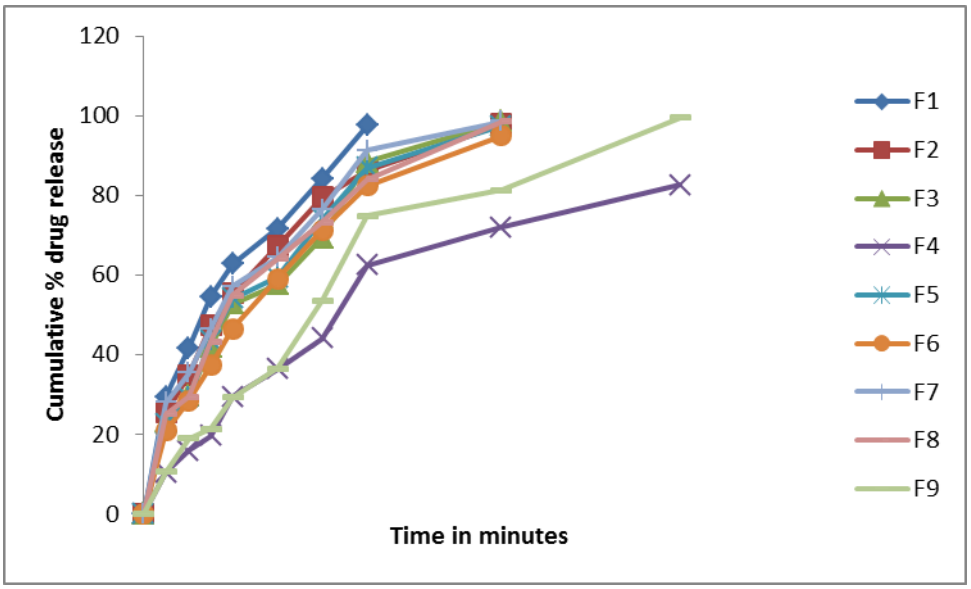
SrNo	Hardness	Thickness	Friability	Drug content	Wt uniformity
F1	6.51±0.01	3.22±0.07	0.34±0.01	98.10±0.07	200 ±0.01
F2	6.53±0.03	3.19±0.01	0.35±0.02	98.39±0.03	202±0.02
F3	6.55±0.02	3.15±0.03	0.40±0.05	99.10±0.04	199 ±0.04

F4	6.64±0.06	3.09±0.04	0.29±0.04	99.12±0.03	201±0.04
F5	6.30±0.08	3.31±0.05	0.53±0.09	99.24±0.01	198±0.07
F6	5.10±0.01	3.45±0.02	0.55±0.07	99.10±0.04	201±0.09
F7	5.21±0.04	3.40±0.03	0.63±0.04	98.39±0.07	200 ±0.01
F8	6.43±0.06	3.27±0.04	0.34±0.03	97.48±0.09	197±0.01
F9	6.65±0.04	3.04±0.01	0.46±0.01	99.04±0.01	201 ±0.03

In-Vitro Drug Release Studies for SR tablets

Table no.4

Time	F1	F2	F3	F4	F5	F6	F7	F8	F9
Dissolution medium 0.1N HCL									
1	29.4 ±0.1	25.2 ±0.5	23.3 ±0.2	10.4 ±0.6	22.4 ±0.3	20.9 ±0.6	27.9 ±0.4	25.0 ±0.6	10.5 ±0.2
2	41.7 ±0.2	34.9 ±0.4	29.6 ±0.1	15.9 ±0.3	29.2 ±0.5	28.4 ±0.2	35.4 ±0.3	29.4 ±0.1	18.9 ±0.2
6.8pH phosphate buffer									
3	54.5 ±0.5	47.2 ±0.4	41.9 ±0.2	19.5 ±0.1	43.5 ±0.3	30.1 ±0.	46.4 ±0.3	43.2 ±0.1	21.4 ±0.4
4	62.7 ±0.3	55.4 ±0.1	52.8 ±0.4	29.4 ±0.6	54.1 ±0.1	46.4 ±0.4	57.1 ±0.4	54.9 ±0.7	29.2 ±0.6
6	71.6 ±0.7	67.3 ±0.6	57.6 ±0.2	36.3 ±0.1	59.3 ±0.3	59.0 ±0.4	64.3 ±0.5	64.1 ±0.7	36.4 ±0.6
8	84.2 ±0.1	79.5 ±0.5	69.3 ±0.4	44.1 ±0.6	74.1 ±0.2	71.3 ±0.5	76.4 ±0.4	73.2 ±0.3	53.5 ±0.4
10	97.5 ±0.5	86.3 ±0.3	88.4 ±0.2	62.4 ±0.4	86.9 ±0.5	82.4 ±0.4	91.3 ±0.3	84.1 ±0.2	74.9 ±0.1
16	-	97.9 ±0.1	98.5 ±0.5	71.9 ±0.3	97.4 ±0.2	94.9 ±0.1	98.5 ±0.3	98.5 ±0.4	81.3 ±0.4
24	-	-	-	82.5 ±0.4		-	-	-	99.5 ±0.4

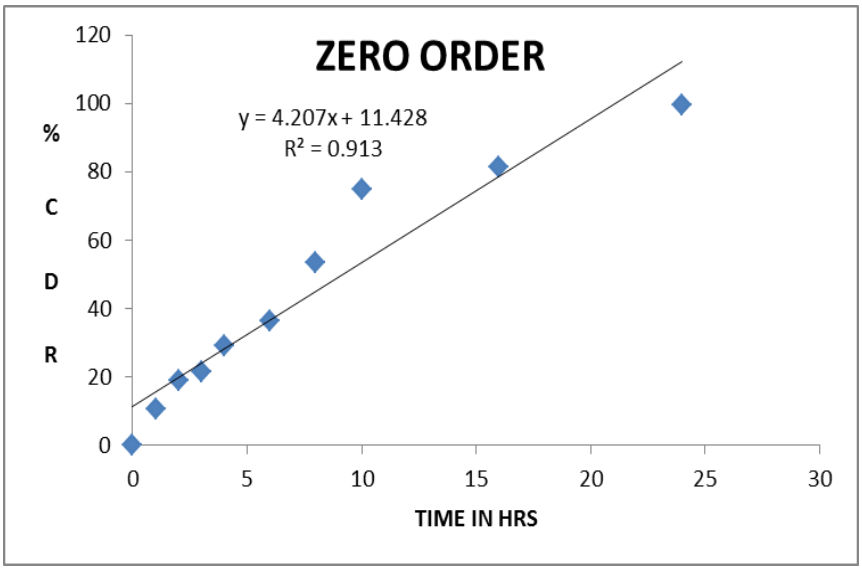


Dissolution profile graph for F1-F9: The results of release studies of formulations F1 to F9 are shown. The release of drug depends not only on the nature of matrix but also upon the drug polymer ratio. As the percentage of polymer increased, the kinetics of release decreased. Formulation F1, F2, F3, F5, F6, F7 and F8 were failed to sustain release beyond 16h.The formulation F9 was optimized because drug release was sustained up to 24hrs and followed USP guidelines.

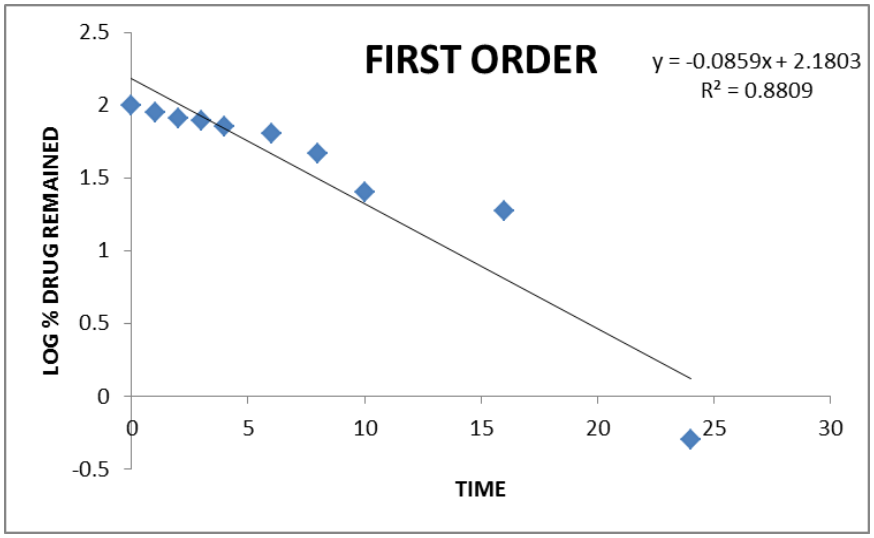
Kinetic analysis of dissolution data: The release rate kinetic data for the F9 is shown in Table respectively. As shown in Figures 14-18, drug release data was best explained by zero order equation, as the plots showed the highest linearity (r^2 = **0.947**) and Higuchi's equation (r^2= **0.97**). As the drug release was best fitted in zero order kinetics, indicating that the rate of drug release is independent of time.

Table no.5

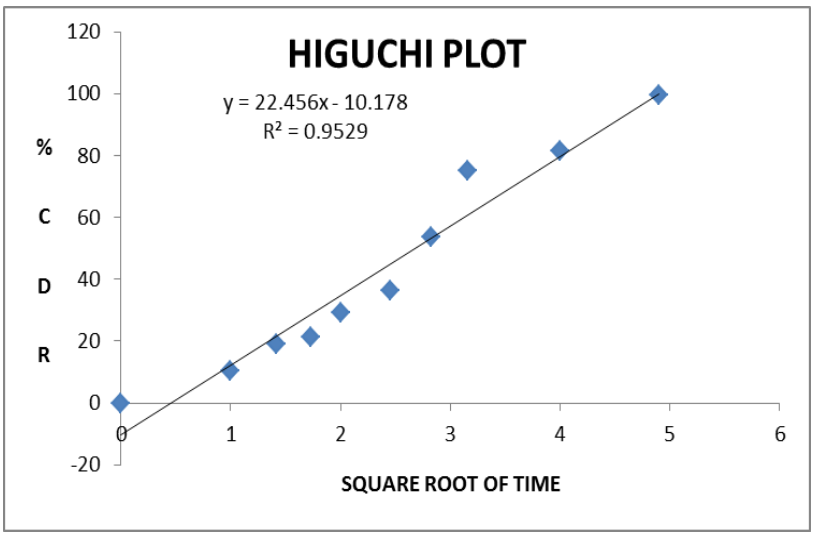
	ZERO	FIRST	HIGUCHI	PEPPAS
	% CDR Vs T	Log % Remain Vs T	%CDR Vs √T	Log C Vs Log T
Slope	4.206959565	-0.085876417	22.45556462	1.075857308
Intercept	11.42849922	2.180254996	-10.17787792	0.701538337
Correlation	0.95550852	-0.938588758	0.976156771	0.872534493
R 2	0.912996533	0.880948857	0.952882042	0.761316441



Zero order graph for F9 formulation



First order graph for F9 formulation



Higuchi model graph for F9 formulation

6. SUMMARY AND CONCLUSION

The Controlled released tablets containing Glibenclamide were successfully prepared by direct compression method. The physiochemical evaluation results for the dry blend of all trials pass the official limits in angle of repose, compressibility index. The prepared powdered blend were also maintained the physiochemical properties of tablets such as thickness, hardness, weight variation, friability and uniformity of drug content. The optimized formulation contains the average thickness of 3.55, average hardness of 6.8, average weight of 198, friability of 0.45 and drug content of 99.2% .The optimized formulation was F12 trial which releases the Glibenclamide in controlled manner in 1st hour it releases 11.3 % but the remaining drug release was controlled up to 24 hours.“Hence it may

be summarized that the trial F12 tablets prepared by direct compression method for controlled release layer might be a perfect and effective formulation to used with diet to lower blood glucose by increasing the secretion of insulin from pancreas and increasing the sensitivity of peripheral tissues to insulin.

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