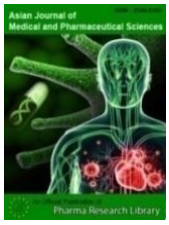

Asian Journal of Medical and Pharmaceutical Sciences
Home Page: https://pharmaresearchlibrary.org/journals/index.php/ajmps
ISSN (Online): 2348-0165 | Publisher: Pharma Research Library
A. J. Med. Pharm, Sci., 2025, 13(1): 01-08
DOI: https://doi.org/10.30904/j.ajmps.2025.4742

Formulation and Evaluation of Microparticle Controlled Release Solid Dosage Form of Lobeglitazone

Akkamgalla Sony[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 research work focuses on the advancement & evaluation of Lobeglitazone controlled-release (CR) tablets, specifically assessing their pre- & post-compression characteristics, alongside dissolution profiles in 6.8 phosphate buffer. A standard CC graph for Lobeglitazone was established by measuring absorbance at 231 nm, confirming compliance with the conc. extent of 2 to 10 µg per ml, with a regression value of 0.999 indicating high correlation. Pre-compression evaluations revealed good flow properties, with bulk & tapped densities being nearly uniform across formulations. Post-compression studies showed that the tablets maintained an acceptable weight variation, thickness (5.80 to 5.90 mm), & hardness (5.9 to 6.3 kg per cm²), with friability under 1%. The in-vitro disso studies demonstrated that the tablets released the drug effectively over 12 hours. Kinetic analysis of the dissolution data suggested a combination of zero-order and first-order release mechanisms, contributing to the formulation's potential for controlled drug delivery.
Keywords: Lobeglitazone, zero-order, hardness, controlled drug delivery, first-order

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 : 30 Sept 2024
Revised : 19 Oct 2024
Accepted : 31 Oct 2024
Published : 02 Jan 2025

Citation: Vijay Kumar Gampa, *et al. Formulation and Evaluation of Microparticle Controlled Release Solid Dosage Form of Lobeglitazone*. *A. J. Med. Pharm, Sci.*, 2025, 13(1): 01-08.

C o n t e n t s

1. Introduction

Lobeglitazone is a novel antidiabetic drug belonging to the thiazolidinedione class, primarily used in the management of type 2 diabetes mellitus. It works by improving insulin sensitivity in peripheral tissues and inhibiting hepatic glucose production, thereby helping to control blood glucose levels2. Despite its efficacy, the conventional oral dosage forms of lobeglitazone have limitations such as short duration of action and the need for frequent dosing, which can lead to poor patient compliance. To address these challenges, the development of controlled-release (CR) formulations has gained significant attention. Controlled-release systems are designed to release the drug at a predetermined rate, maintaining therapeutic drug levels over an extended period and reducing the frequency of dosing. Microparticle-based controlled-release systems, in particular, offer several advantages, including improved drug stability, reduced side effects, and enhanced patient adherence. This study focuses on the formulation and evaluation of a microparticle controlled-release solid dosage form of lobeglitazone. The objective is to develop a

CR formulation that can provide sustained release of lobeglitazone, thereby improving its therapeutic efficacy and patient compliance. The formulation process involves the selection of appropriate polymers and excipients, followed by the preparation of microparticles using techniques such as solvent evaporation, emulsion-solvent evaporation, or spray drying. The resulting microparticles are then incorporated into solid dosage forms, such as tablets or capsules.

The evaluation of the CR formulation includes various tests to assess its physicochemical properties, drug release profile, and stability. Key parameters such as particle size, morphology, drug loading, and encapsulation efficiency are analyzed to ensure the quality and consistency of the microparticles. In vitro drug release studies are conducted to determine the release kinetics and mechanism of the CR formulation, while stability studies are performed to evaluate the shelf-life of the product.

2. Materials and Methods

Table1: Ingredients & Manfactures

S.no	Ingredients	Supplier
1	Lobeglitazone	Supplied By Qualychrome
2	Hpmc K 100m	Qualychrome research lab pvt Ltd
3	Na Alginate	Qualychrome research lab pvt Ltd
4	Guar Gum	Qualychrome research lab pvt Ltd
5	Avicel Ph102(Mcc)	Qualychrome research lab pvt Ltd
6	Aerosil	Qualychrome research lab pvt Ltd
7	Mg Stearate	Qualychrome research lab pvt Ltd

Table 2: Equipment& Companies

S.No.	Name of the Equipment	Model
1.	Weighing mechine	KD 200
2.	Friability tester	EF-2W
3.	Oven	Dtc-00r
4.	Punching machine	VM-LWPM-1
6.	hardness tester	HR-1
7.	UV	CM-700d
8.	Dissolution tester	DT-8
9.	Verniercallipers	727HD

Making of Standard CC graph for Lobeglitazone:
Reagents: Buffer Solution
Buffer solutions making
Making buffer of 6.8 pH KH2PO4 solution:
27.22 g monobasic KH2PO4 was diluted to 1000 mL, 8 g NaOH was make to 1L, then 50 mL of the phosphate medium and 22.4mL of the NaOH medium were combined &make to 200 mL with water.

Principle:
Std solution of Lobeglitazone by 6.8 Buffer Solution:
A solution was made by mixing 100 mg drug in 100 mL MeOH, diluting 10 mL of this in 100 mL pH 6.8 buffers, and further diluting to various concentrations for analysis at 270 nm using a blank buffer as reference.

III. Making of matrix tablets by non aqueous wet granulation technique:

1. Lobeglitazone, polymers, and diluent are sieved using a 60# sieve and combined in a bag of poly for 10 minutes.
2. This blend is then granulated with isopropyl alcohol. The granules are dried in a oven at 60°C about 1 hour.
3. The granules which are dried are passing through a sieve 30#.
4. These granules are lubricated using a 60# sieve. Colloidal SiO2 (Aerosil-200) and magnesium stearate are sieved together and combined in a bag of poly for 5 minutes.
5. The lubricated granules are compressed with the help of a rotary machine with round concave-shaped punches, aiming for an Avg wt of 500 milligram& a minimum strength of 5-6 kg per cm².

A) Study of Pre Compressibility:
Repose Angle:
The Angle of Repose, identified using the method of funnel, is calculated by quantifying the diameter of the cone of powder formed when the powder freely flows from a funnel, with its tip touching the apex of the cone.

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

Density:
Bulk density (BD):
Bulk density is defined as the fractions of the complete wt's of a powder to its BV9 bulk volume). To measure it, accurately weigh 25 g of granules that have been earlier passed through a 22 sieve & transfer them into a 100 mL cylinder. Spread the powder smoothly without compacting it, and note the observed volume. Use the following formula to find the BD in g per mL.

BD = powder Wt / volume in Bulk.

$$\mathbf{D_b} = \frac{M}{V_0}$$

Tapped density (TD):
Tapped density is described as the ratio of the total mass of a powder to its volume tapped. To determine it, accurately weigh 25 g of granules that have been sieved through a 22# sieve and transfer them into a 100 mL cylinder of a tap density apparatus. Operate the tester for a fixed no. of taps until the powder volume reaches its minimum. The tapped density can then be calculated using the appropriate formula.

TD = powder wt / Tapped volume

Dt = (*M*) / (*V f*).

Index of Carr's:

Index is utilized to identification the compressibility of a po wder combined. It evaluates both BD & TD to assess how well the powder packs down. This index is a straight forward test, and the equation is as follows:

Ratio of Hausner's:

$$\textbf{Hausner's Ratio} = \frac{\text{Tapped Density}}{\text{Bulk Density}}$$

Post compressibility investigation:

General appearance:

The tablets are evaluated based on their overall appearance, with observations made regarding their shape, color, texture, & odor.

Avg wt/Weight difference:

20 tablets were chosen & wt individually. From the total wt, the avg wt was determined. Every tablet's wt is compared to the avg to ensure it met acceptable limits. For 300 mg tablets, no > two individual wts deviated from the avg by > 7.5%, & none deviated by > double that %. Acceptance limitations for tablet wt variation (USP 29-NF 34)

Table 3: Wt different tolerance for uncoated tablets

Avg wt of tablet(mg)	% variance allowed
130 or <	± 11
131-325	± 7.4
> 325	± 4

Hardness test:

To determine the strength of a tablet

Friability test: To determine the % of drug loss

It should be preferably between 0.5 to 1.0%.

Assay Procedure.

Take a atlest 20 tablets, weigh, & finely powder them. Transfer an weighed portion of the powder, equal10 mg of the drug, into a 10 mL VF. Add 6 mL of 0.1N HCl, then rotate & sonicate for 10 mins to ensure total extraction. Dilute to the mark with MeOHl & mix thoroughly. Pipette a 1 mL into a 10 mL VF, dilute to volume with the MP, mix, and filter. Finally, withdraw 1 mL and make up till the margin using buffer. Calculate the quantity in mg of model drug Hcl in the portion taken by the formula

Dissolution Study of In-vitro:

drug distribution in In-vitro studies:

In vitro disso studies were performed using a USP 24 dissolution tester paddle method at a speed of 100 rpm. The test lasted for 12 hours with a 6.8 KH2PO4 buffer solution (1000 mL). At regular intervals, 10 mL sample is taken & replaced with an same volume of fresh dissolution , pre warmed to 37 °C. filtered The samples through a 0.45 µm filter, and the drug in every sample was studied after appropriate dilution using a UV-Visible spectroscopy at the respective λ max of each dissolution medium.

In-vitro distribution Kinetics investigation:

Analyzing the drug distribution function from a dosage form is crucial yet complex, especially for matrix systems. The release order from FDDS can be described using either kinetics of zero or 1stt-order. The drug distribution MOA from FDDS is examined using the eqn Higuchi& the Peppas-Korsmeyer eqn.

Zero Order Release Kinetics:

It describes a parallel relationship b/w the ratios of drug released & time. If the release follows 0-order kinetics, a graph of the ratios of drug distributed versus Tin linear.

First Order Release Kinetics:

Wagner state that drug distribute from slow-release dosage forms follows first-order kinetics, as the exposed tablet surface area decreases exponentially over time. A plot of log percentage of remain drug vs time will yield a straight line if the distribute follows 1st-order kinetics.

Higuchi equation:

It describes a linear relationship between the ratios released / unit surface area (Q) and the square root of time.

Peppa's-Korsemeyer equation: To identify a model that better fits the synthesis, the disso data was further analyzed using the Peppas-Korsmeyerequn.

Table 4: Drug distribute kinetics mechanism

Diffusion exponent (n)	Mechanism
0.46	Fickian diffusion
0.46 < n <0.88	Anomalous (Non- Fickian) diffusion
0.88	Case II transport
n > 0.88	Super Case II transport

3. Results and Discussion

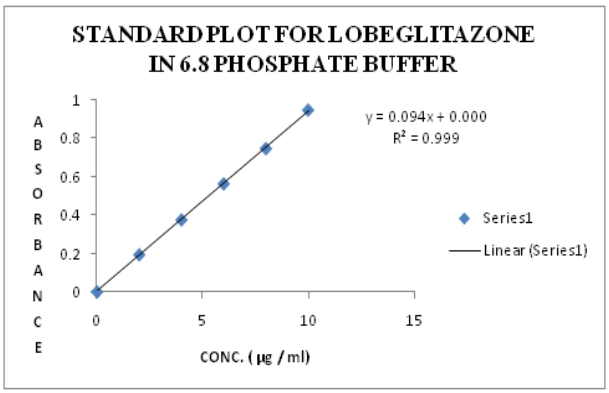

Figure 1: Standard CC graph of Lobeglitazone in 6.8 KH2PO4 buffer at λMax = 231 nanometers

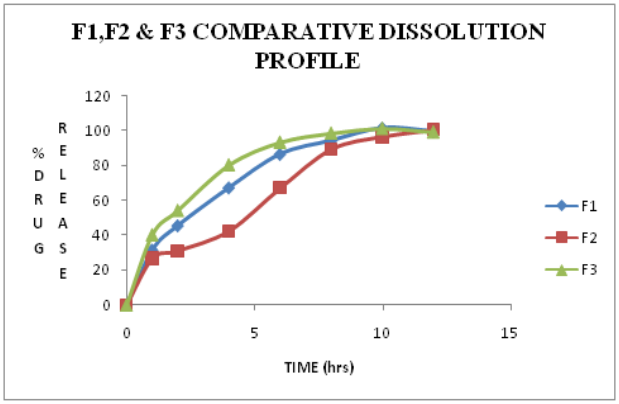

Figure 2: Comparative dissolutionF1, F2 and F3 formulations of Lobeglitazone

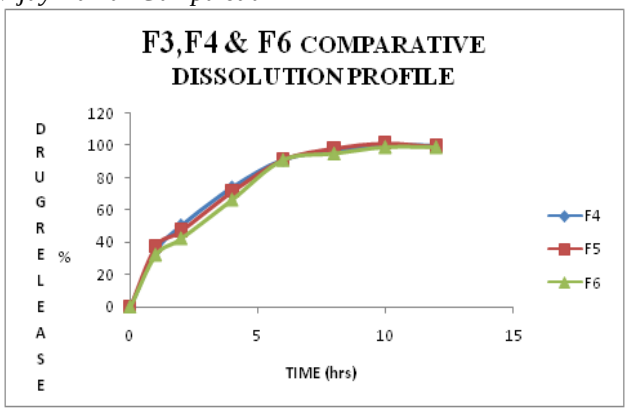

Figure 3: Comparative dissolutionF4, F5 and F6 formulations of Lobeglitazone

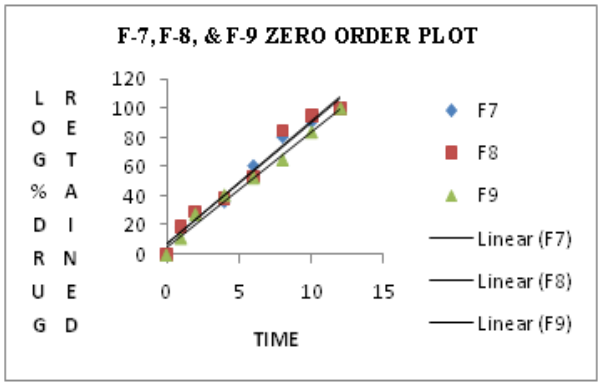

Figure 4: Comparative dissolutionF7, F8 and F9 formulations of Lobeglitazone

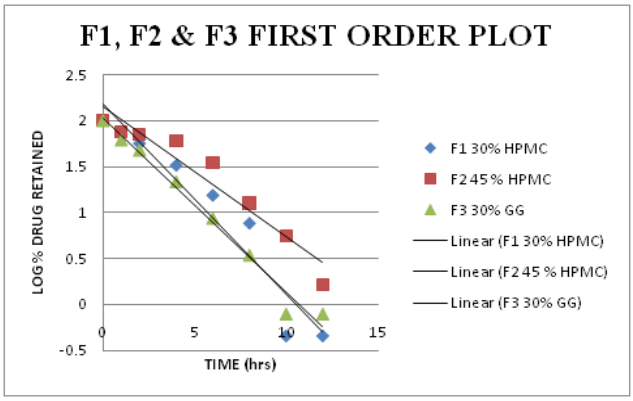

Figure 5: F1, F2 and F3 First order plot

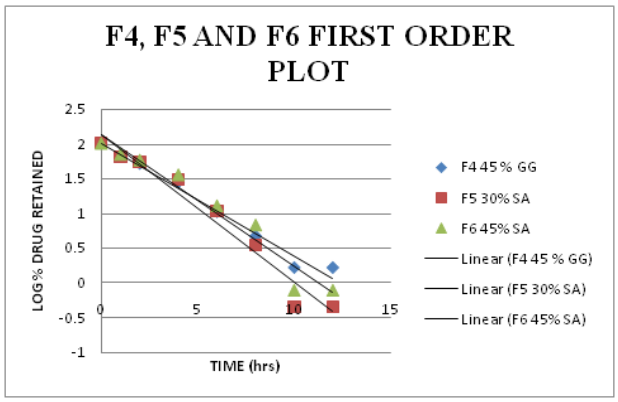

Figure 6: F4, F5 and F6 First order plot

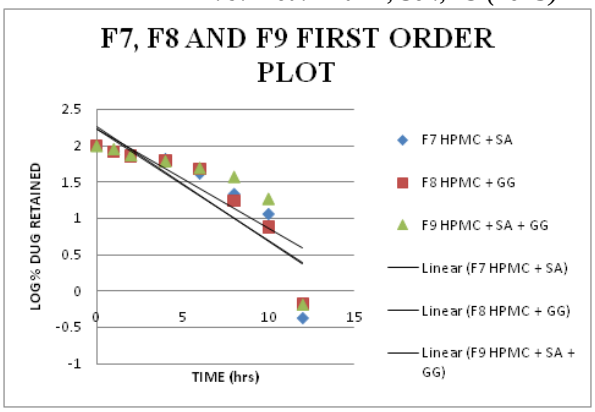

Figure 7: F7, F8 and F9 First order plot

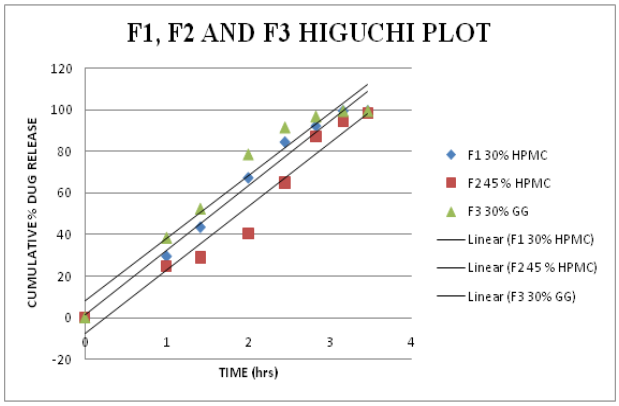

Figure 8: F1, F2 and F3 higuchi plot

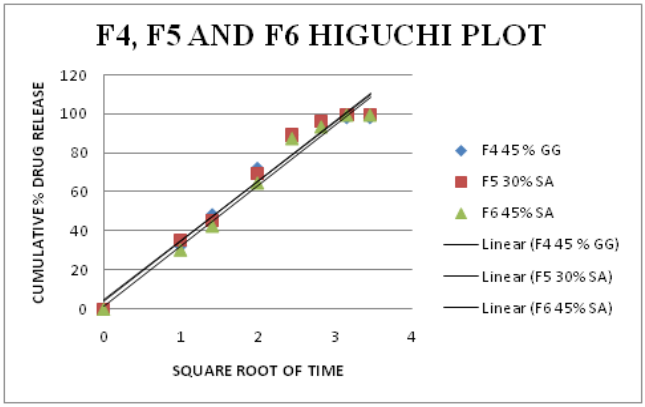

Figure 9: F-4, F-5 & F-6 higuchi plot

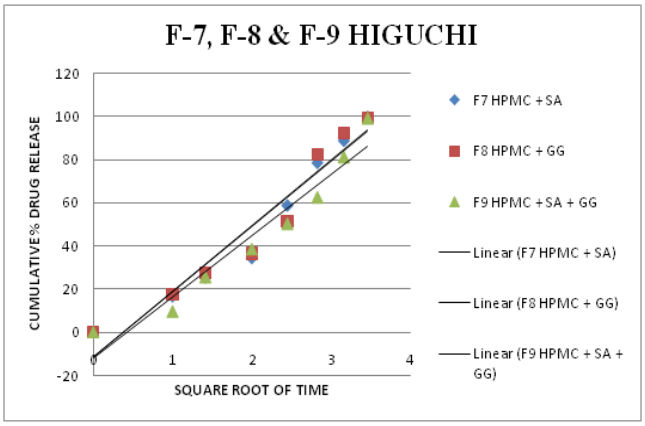

Figure 10: F7, F8 and F9 higuchi plot

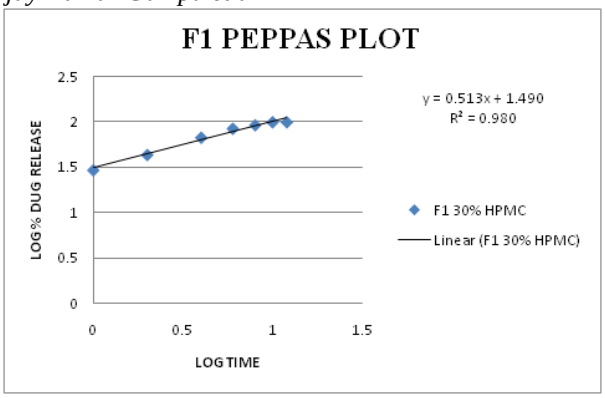

Figure 11: korsmayerspepas plot for formulation F1

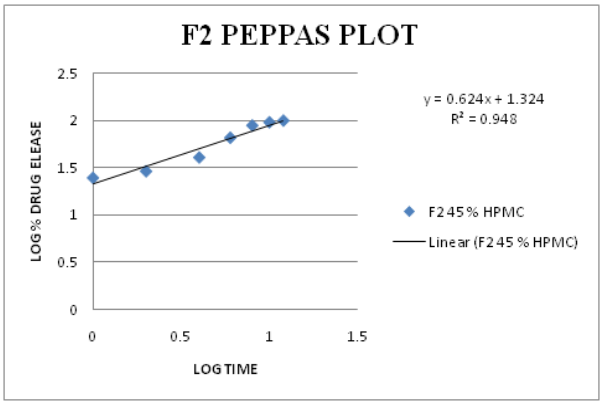

Figure 12: korsmayerspepas plot for formulationF2

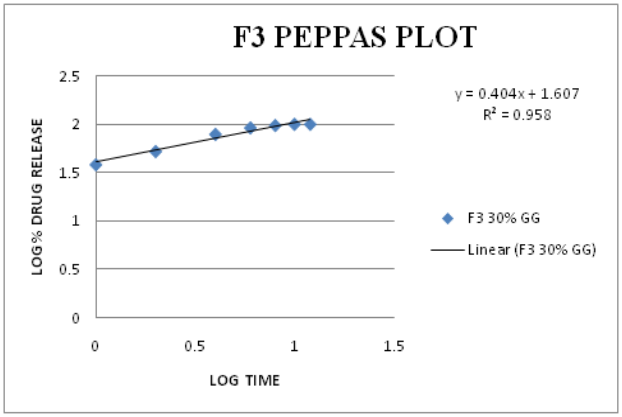

Figure 13: korsmayerspepas plot for formulation F3

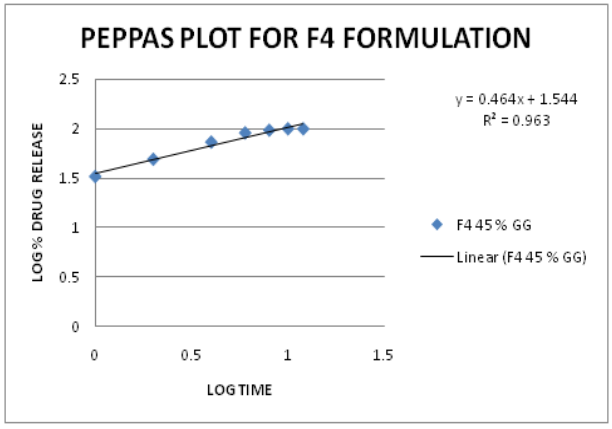

Figure 14: korsmayerspepas plot for formulation F4

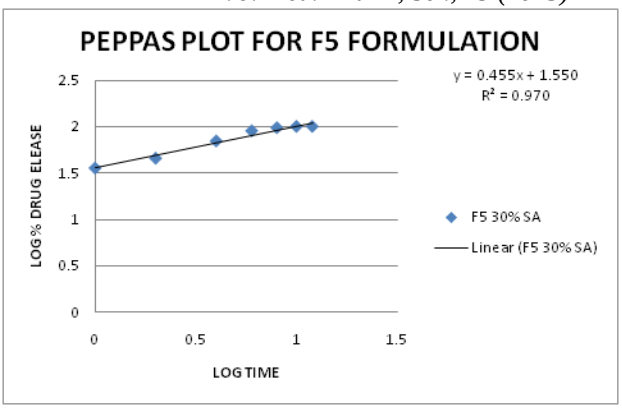

Figure 15: korsmayerspepas plot for formulationF5

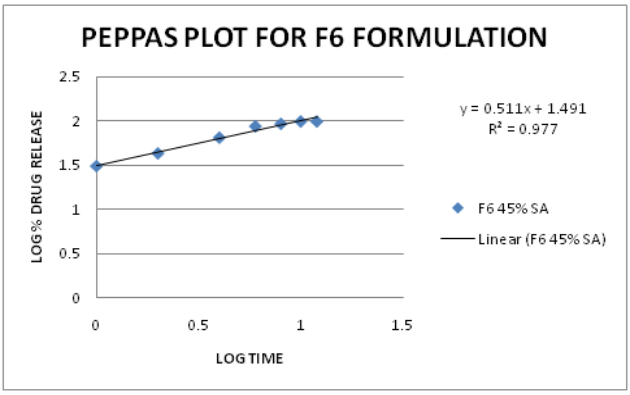

Figure 16: korsmayerspepas plot for formulationF6

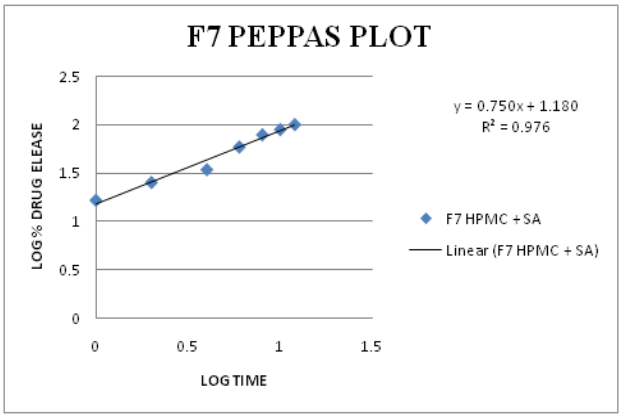

Figure 17: korsmayerspepas plot for formulationF7

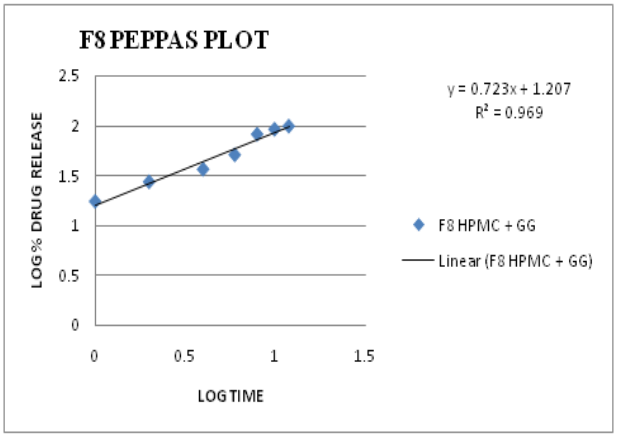

Figure 18: F8 korsmayerspepas plot

Table 5: Lobeglitazone f1–f6 table

S.no	Ingredients	F-1 30% HPMC	F-2 45 % HPMC	F-3 30% GG	F-4 45 % GG	F-5 30% SA	F-6 45% SA
INTRAGRANULAR							
	Lobeglitazone	0.5	0.5	0.5	0.5	0.5	0.5
	HPMC K100M	20	20	--	--	--	--
	Sodium Alginate	--	--	--	--	15	30
	Guar gum	--	--	15	30	--	--
	Avicel PH 102	70	70	75	60	75	60
Extra granular							
	Aerosil	5	5	5	5	5	5
	Mng Stearate	4.5	4.5	4.5	4.5	4.5	4.5
	Total	100	100	100	100	100	100

Table 6: Lobeglitazone f7 – f9 formulations table

Sno	Chemical constituents	Qty per Tablet (mg)			Purpose
		F7 HPMC+SA	F8 HPMC+GG	F9 HPMC+SA+GG	
Intragranular					
1	Lobeglitazone	0.5	0.5	0.5	API
2	HPMC K100M	10	30	10	Synthetic CR Polymer
3	Sodium Alginate	10	--	10	Natural CR Polymer
4	Guar gum	--	10	10	Natural CR Polymer
5	Avicel PH 102	70	50	70	diluent
Extra granular					
6	Aerosil	5	5	5	glidant
7	Mng Stearate	4.5	4.5	4.5	lubricant
	Total	100	100	100	

Table 7: Limits in Repose Angle

Flow ability	Degree of Angle of Repose
Very good	24–31
Good	30–36
Fair	35–41
Passable	40–46
Poor	45–56
Very poor	55–66
Very, very poor	>66

Table 8: Compressibility Index Limitations

Compressibility Index (%)	Flow Character	Hausner's Ratio
≤ 11	Very good	1.01-1.12
10-16	Good	1.13-1.19
15-21	Fair	1.18-1.24
20-26	Passable	1.27-1.35
25-32	Poor	1.36-1.46
31-38	Very Poor	1.45-1.58
> 39	Very, very Poor	> 1.61

Table: 9: Pre compressibility studies of Lobeglitazone CR formulations *n=3

Formulation Code's	Pre compressibility studies*,*n=3				
	repose Angle (^{o})	BD (g/cc)	TD (g/cc)	Index Carr's (%)	Ratio Hausner's
F-1	32.17±0.16	0.517±0.015	0.525±0.009	1.52±1.05	1.015±0.08

F-2	41.11±0.12	0.474±0.012	0.477±0.013	0.63±0.24	1.006±0.12
F-3	35.71±0.14	0.506±0.006	0.528±0.016	4.17±0.66	1.043±0.32
F-4	33.31±0.12	0.525±0.022	0.527±0.023	0.38±0.27	1.04±0.24
F-5	41.11±0.12	0.475±0.012	0.479±0.013	0.84±0.24	1.008±0.12
F-6	35.71±0.14	0.507±0.006	0.524±0.016	3.24±0.66	1.034±0.32
F-7	33.31±0.14	0.524±0.024	0.534±0.023	1.87±0.27	1.019±0.24
F-8	41.11±0.12	0.474±0.012	0.478±0.013	0.84±0.24	1.008±0.12
F-9	41.11±0.12	0.473±0.012	0.476±0.013	0.63±0.24	1.006±0.12

Table 10: Post compressibility investigations of Lobeglitazone CR tablets

Formulation Code's	**Post compressibility investigation**				
	Mean. Wt (mg) (n=20)	**Thickness (mm) (n=3)**	**Hardness (kp) (n=3)**	***Friability%**	**Drug content% (n=3)**
F-1	500.4±0.6	5.80±0.35	5.10±0.26	0.79	97.98±0.19
F-2	502.3±0.4	5.89±0.24	6.3±0.25	0.88	100.21±0.21
F-3	499.8±0.4	5.82±0.2	6.2±0.21	0.68	98.67±0.13
F-4	499.0±0.3	5.86±0.2	5.9±0.23	0.69	100.32±0.15
F-5	499.7±0.4	5.82±0.2	6.3±0.21	0.68	98.67±0.13
F-6	502.3±0.4	5.90±0.24	6.2±0.25	0.78	100.21±0.21
F-7	500.5±0.6	5.80±0.35	5.9±0.26	0.69	97.98±0.19
F-8	502.6±0.4	5.90±0.24	6.3±0.25	0.78	100.21±0.21
F-9	499.7±0.4	5.82±0.2	6.2±0.21	0.68	98.67±0.13

Table 11: Dissolution profile

Variables	**Info.**
Disso apparatus	paddle
Buffer	6.8 Na2PO4 buffer
Volume taken	900 ml
RPM	100rpm
^{o}C	37^{o}C
volume taken	5mL
Intervals	1,2,4,6,8,10 &12hr
Analytical technique	UV
λ_{max}	271 nm

Table 12: In-vitro Disso outcomes of Formulation trails of Lobeglitazone

Time (hr)	**F-1**	**F-2**	**F-3**	**F-4**	**F-5**	**F-6**	**F-7**	**F-8**	**F-9**
	30	**45**	**30**	**45**	**30**	**45**	**HPMC+SA**	**HPMC+GG**	**HPMC+SA+GG**
0	0	0	0	0	0	0	0	0	0
1	31.52	26.6	40.32	34.52	37.5	32.32	18.54	19.38	11.52
2	45.51	30.9	54.25	50.57	47.32	42.54	27.28	29.38	27.6
4	67.32	42.32	80.35	74.32	71.55	66.54	36.24	38.57	40.52
6	86.54	67	93.32	91.54	91.32	91.24	60.58	53.22	52.32
8	94.32	89.32	98.55	97.32	98.47	95.23	80.32	84.34	64.58
10	101.54	96.45	101.21	100.34	101.54	99.21	90.54	94.35	83.35
12	99.54	100.34	99.21	100.34	99.54	99.21	99.58	99.32	99.35

Table 13: R^2 value and n outcomes table

Formulation code's	**R^2 value**				
	0 order	**1storder**	**plot Higuchi**	**Plot of Peppas**	**n value**
F-1	0.854	0.962	0.992	0.982	0.515
F-2	0.951	0.967	0.982	0.951	0.626
F-3	0.758	0.992	0.976	0.960	0.406
F-4	0.806	0.993	0.983	0.965	0.466
F-5	0.814	0.982	0.986	0.972	0.457
F-6	0.840	0.978	0.991	0.978	0.513

F-7	0.978	0.874	0.975	0.978	0.752
F-8	0.968	0.911	0.969	0.971	0.725
F-9	0.987	0.831	0.971	0.978	0.871

4. Conclusion

As the conc. of CR polymer increases the order of CR is also increasing F2 >F1 (HPMC), F4 > F3 (GG), F6 > F5 (SA). When the CR tablets with only natural CR polymers (SA & GG) were tried in both concs. (30% & 45%) no CR was obtained up to 12 hrs, hence there are not intended to use alone for CR. nIn all the CR polymers 45 % of HPMC (F2) is showing better CR, hence for further studies to know the effect of natural CR polymers (SA & GG) with HPMC, the 45% OF HPMC is kept constant.(F7,F8 & F9). Out of all formulations the 45% HPMC + 10%SA + 10% GG, (F9) is having better CR, due to combination of various release mechanism characters of all three polymers. The order of CR F9>f7>F8 From the dissolution data evident that the order of CR was It is evident that CR was better attained with combination of HPMC & the two natural polymers, than HPMC + single Natural polymer or HPMC alone.

5. References

[1] Yie.W.Chien, "Novel Drug Delivery System, 2ndedn, revised and expanded" pg 182.

[2] Robinson JR, and LeeVHI(eds)(22Edition),New York Controlled Drug Delivary Fundamentals and Applications,"1987.Pg.09

[3] D.M. Brahmankar and Sunil B.Jaiswal, Biopharmaceutics and Pharmacokinetics A Treatise",Pg.335-350.

[4] Robert E. Nortari, "Biopharmaceutics and pharmacokinetics An Introduction" 4th edn revised and expanded, pg no.208

[5] S.PVyas, Roop K.Khar, Controlled Drug Delivary Concepts and Advances"Pg.155-158.

[6] MiloGibaldi and Donald Perzier vol.15, Pharmacokinetics" 2ndedn,"revised and expanded Pg.185

[7] Lisa Brannan-Peppas, Polymers in Controlled Drug Delivary"nov.1997.

[8] Syed NisarHussain Shah , SajidAsghar , Muhammad Akram Choudhry , Muhammad Sajid Hamid Akash , "Formulation and evaluation of natural gum-based sustained release matrix tablets of flurbiprofen using response surface methodology "Drug Development and Industrial Pharmacy 2009, 35, (12), Pg 1470-1478.

[9] Vinayak Dhopeshwarkar, Janet C. O'Keeffe, Joel L. Zatz, Robert Deete and And Michael Horton. Development of An Oral Sustained-Release Antibiotic Matrix Tablet Using In-Vitro/In-Vivo Correlations, Drug Development and Industrial Pharmacy, 1994, 20, (11), Pg 1851-1867.

[10] John W. Skoug, , Martin V. Mikelsons, Cynthia N. Vigneronand Nick L. Stemm "Qualitative evaluation of the mechanism of release of matrix sustained release dosage forms by measurement of polymer release" Control Development, April-1993.

[11] AyhanSavaşer, YalçınÖzkan, and AşkınIşımer, "Preparation and in vitro evaluation of sustained release tablet formulations of diclofenac sodium" Department of Pharmaceutical Technology, Gülhane Military Medical Academy, Etlik, 06018 Ankara, Turkey.October-2008.

[12] P.G.Yeole, U.C.Galgatte, I.B.Babla, "Design and evaluation of xanthan gum based sustained release matrix tablets of diclofenac sodium" International Journal of pharmaceutical sciences.2006, pg 185-189.

[13] D.M. Morkhade, S.V. Fulzele, "Gum Copal and Gum Damar: Novel Matrix forming Materials for Sustained Drug delivery", International Journal of pharmaceutical sciences.2006, pg 53-58.

[14] Umit Gonullu, Melike Uner, Gulgun Yener, "introduction of sustained release Opipramol Di hydrochloride matrix tablets as a new approach in the treatment of depressive disorders", International Journal of Biomedical science, 2006, 2, (4), pg 337-343.

[15] A.K. Srivastava, Saurabhwadhwa, B.mishra, "oral sustained delivery of Atenolol from floating matrix tablets - formulation and in vitro evaluation." Drug development and industrial pharmacy, 2005, 31, (4-5), pg 367-374.

[16] Neal M.Davies, "sustained release and enteric coated NSAIDS: Are they really GI safe?", J pharm pharmaceutsci, 1999, 2, (1), pg 5-14.

[17] Mohammad Reza Siahi, Mohammad Barzegar-Jalali, Farnaz Monajjemzadeh, "Design and Evaluation of 1- and 3-Layer Matrices of Verapamil Hydrochloride for Sustaining Its Release". AAPS Pharm Sci Tech. 2005; 6(4): E626-E632.

[18] Mohammad Siahi, Mohammad Barzegar-Jalali, Farnaz Monajjemzadeh, Fatemeh Ghaffari Shirzad Azarmi , "Design and evaluation of 1- and 3-layer matrices of verapamil hydrochloride for sustaining its release", AAPS Pharm Sci Tech. 2005; 6(4): E626-E632.

[19] Giovanna Corti, Marzia Cirri, Francesca Maestrelli, Natascia Mennini, "Sustained-release matrix tablets of metformin hydrochloride in combination with triacetyl-β-cyclodextrin" Europian Journal of pharmaceutics and biopharmaceutics 2008, 68, (2), pg 303-309.