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DEVELOPMENT AND CHARACTERIZATION OF SUSTAINED RELEASE SODIUM ALGINATE MICROSPHERES OF SITAGLIPTIN PHOSPATE FOR EFFECTIVE MANAGEMENT OF TYPE II DIABETES

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Abstract:

Sodium Alginate in Combination with other natural Polymers like HPMC, Eudragit, Carbopol, and Gelatine, Microspheres loaded with Sitagliptin Phospate have been selected as the basis of the research work because of Biocompatabilty,Low Toxicity Biodegradability and Sustainability. Sodium Alginate microspheres are investigated in control release system as vehicles for the delivery of therapeutic agent to local sites. As they are natural polymers which are biodegradable, lack toxicity and are non- antigenic in nature. Therefore, the use of them as a carrier system is the targeting of anti-diabetic drugs in the treatment of, diabetes. In this study, microspheres of an anti-diabetic drug will be developed using Sodium Alginate and other polymers. Sitagliptin Phospate is an anti-diabetic drug that belongs to a class of drugs known as dipeptidyl peptidase-4 (DPP-4) inhibitors that works by inhibiting the DPP-4 enzyme. By doing so, it prolongs the action of incretin hormones, primarily GLP-1. This prolongation enhances the release of insulin and suppresses the release of glucagon, resulting in improved blood sugar control in people with type 2 diabetes.To develop microspheres, certain preparation methods like the Ionic Gelation method have been adopted. The selection of best formulation will be based on the results demonstrating the particle size, surface morphology, loading efficiency, % yield value, physical characteristics, swelling properties, and the invitro release profile.

Index Terms - Sitagliptin Phospate, Microspheres, HPMC, Eudragit, Carbopol, Gelatine, Biocompatabilty, Biodegradability , Anti-diabetic and Antigenic.

I. INTRODUCTION

Microspheres are small spherical particles with dimensions ranging from one micron (m) to hundreds of microns. They are widely employed in a variety of scientific and technological sectors, including medicine, biotechnology, and materials research. Microspheres can be manufactured from a variety of materials such as polymers, ceramics, metals, and even biological compounds.

Oral pharmaceutical dose forms are the standard, convenient, and pleasant method of delivering medications to the body. Oral controlled release systems are the most widely used drug delivery methods. They have various advantages over conventional systems, such as:

- Increase patient convenience and compliance as fewer drug doses are required.
- Decrease in the constant variation of the plasma level, which will improve management of the illness state.
- Utilizing the drug to its maximum potential in order to minimize the total amount given.

➢ Lowering the cost of healthcare by using better therapy, shorter treatment periods, and dose regularity.

A medicinal chemical can be delivered to the target place in several ways with controlled release. The use of microspheres as medication carriers is one of these techniques. Therefore, a patient-friendly oral medication system needs to be created.Oral drug delivery systems were made with natural polymers (sodium alginate, gelatin, and HPMC). A significant difficulty with the formula is the regulated release of drugs, which can increase therapeutic efficacy through prolong in vivo action, controlled blood concentration, and local tissue-driven release.

Types of Microspheres

- **Drug-Loaded Polymer Microspheres**
- **Lipid Microspheres (Liposomes)**
- **Magnetic Microspheres**
- **Radioactive microspheres**
- **Mucoadhesive Microspheres**
- **Targeted Drug Delivery Microspheres**

MATERIALS AND METHODS:

Materials :

Sitagliptin Phospate obtained from NOSCH LABS PVT-LTD(100%EOU) , Sodium Alginate e (Finer Limited) , Hydroxypropyl Methyl cellulose(Finer Limited), Eudragit (s d fine-chem limited), Carbopol (SDFCL Fine Chemical Limited), Gelatin , Calcium Chloride (SDFCL Fine Chemical Limited) , Distilled Water were the materials used for the formulation of Microspheres .

Solubility studies :

Sitagliptin phosphate's solubility in different solvents is assessed by adding extra medication to glass vials holding one gram of vehicle and mixing the mixture with a cyclomixer.To reach equilibrium, the combination was left at room temperature for 72 hours. Following a 72-hour period, the equilibrated solutions were centrifuged for 15 to 20 minutes at 3000 rpm in order to separate the dissolved medication from the sediment phase. A micropipette was used to remove 0.1 ml of the supernatant, which was then filtered through 0.45µ filters.The supernatant aliquot were diluted using solvents, and the drug concentrations in each excipients were measured using spectrophotometer at λmax 242 nm.

UV Spectrophotometric analysis of Sitagliptin Phospate:

❖ Calibration Curve of Sitagliptin Phospate:

Callibration curve of Sitagliptin Phospate was Constructed using Methanol, 0.1N HCL and 6.8 pH Phospate Buffer

✧ Calibration curve of Sitagliptin Phospate in 0.1 N HCl

Standard stock solution Preparation:

Weigh and transfer about 10mg of Sitagliptin Phospate and 10ml 0.1NHcl in a 10ml volumetric flask

Preparation of test solution from stock solution:

From the standard stock solution, concentrations of 5,10,15,25 and 30ppm were prepared using 0.1N HCL then the UV scan was performed in the wavelength range of 400-200nm.

✧ Calibration curve of Sitagliptin Phospate in Methanol:

Standard stock solution Preparation:

The standard stock solution was prepared by transferring 10mg of Sitagliptin Phosphate into a 10ml volumetric flask containing methanol and the volume is made up to the mark using methanol.

◆ Preparation of test solution from stock solution:

From the standard stock solution, concentrations of 5,10,15,25 and 30ppm were prepared using methanol. The UV scan was performed in the wavelength range of 400-200nm.

✧ Calibration curve of Sitagliptin Phospate in 6.8 pH Phospate Buffer:

Standard stock solution Preparation:

The standard stock solution was prepared by transferring 10mg of Sitagliptin Phosphate into a 10ml volumetric flask containing 6.8 pH Phospate Buffer and the volume is made up to the mark of 6.8pH Phospate Buffer.

◆ Preparation of test solution from stock solution:

From the standard stock solution, concentrations of 10, 20, 30, 40 and 50ppm were prepared using 6.8 pH Phospate buffer . The UV scan was performed in the wavelength range of 400-200nm.

❖ Drug-excipients compatability studies by FT-IR Spectroscopy:

Studies on the compatibility of pharmaceutical medications with polymers used in therapeutic formulations evaluate interactions between the two.These investigations are essential to guarantee that the drug's stability, bioavailability, and other qualities are not compromised by polymers.

Using an FT-IR spectrometer and the KBr pellet method, the study was conducted in the wavelength range of 4000 to 400 cm-1. Sitagliptin Phospate and polymers were subjected to FT-IR spectra analysis. The spectrum was examined to look for particular drug and polymer peaks.

◆ Preparation of Sitagliptin Phosphate Microspheres:

Using the ionotropic gelation process, sodium alginate, hydroxypropyl methyl cellulose, eudragit, Carbopol, gelatin, distilled water, and calcium chloride were used to make Sitagliptin phosphate microspheres. Using a mechanical stirrer, an initial weighed quantity of sodium alginate in combination with other individual polymers was mixed with the necessary amount of water. Weighed amounts of medication and polymer were added to sodium alginate solution using a mechanical stirrer. The final solution was added drop-wise to 100 ml of Calcium Chloride Solution , agitated for 60 minutes, and dried for 12 hours at 40°C.

Formulation Table

Ingredients	Formulation Code								
	FS1	FS2	FS3	FS4	FS5	FS6	FS7	FS8	FS9
Sitagliptin Phosphate(mg)	100	100	100	100	100	100	100	100	100
Sodium Alginate(mg)	1000	1000	1000	1000	1000	500	500	500	500
Hydroxypropyl Methyl cellulose(mg)	--	500	--	--	--	350	--	--	--
Eudragit(mg)	--	--	500	--	--	--	350	--	--
Carbopol(mg)	--	--	--	500	--	--	--	350	--
Gelatin(mg)	--	--	--	--	500	--	--	--	350
Calcium Chloride(%)	2%	2%	2%	2%	2%	2%	2%	2%	2%
Distilled Water(ml)	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S

❖ Evaluation of Sitagliptin phosphate Microspheres:

◆ Solubility study:

When compared to methanol, acetone and Chloroform Sitagliptin Phosphate was discovered to have more solubility in Distilled Water and Ethanol.

Solubility Data of Sitagliptin Phospate in Various Solvents	
Solvent	**Concentration (mg/ml)**
Distilled Water	380.7
Ethanol	210.9
Methanol	166.3
Cholo-form	26.1
Acetone	79

❖ Micromeritic properties of Sitagliptin Phospate microspheres:

Formulation Code	Angle of Repose {degrees (°)}	Bulk density (g/ml)	Tapped density (g/m	Carr's Compressibility index (%)	Hausner's ratio (g/cm³)
FS1	22.56 ±0.702	0.42 ±0.066	0.73 ± 0.053	42 ± 0.075	1.7± 0.023
FS2	28.68 ±0.27	0.43 ±0.057	0.67 ± 0.041	5 ± 0.111	1.1±0.041
FS3	30.54 ±0.402	0.54±0.090	0.63 ± 0.046	14 ± 0.046	1.1±0.021
FS4	34.54 ±0.518	0.68 ± 0.09 7	0.71 ± 0.065	24 ± 0.065	1±0.085
FS5	35.37 ±0.873	0.51 ± 0.10	0.65 ± 0.078	17 ± 0.053	1.2±0.77
FS6	35.52 ±0.21	0.65 ± 0.11 2	0.78 ± 0.085	6 ± 0.045	1.2±0.345
FS7	38.3 ±0.351	0.73 ±0.120	0.79 ± 0.111	27 ±0.345	1±0.023
FS8	36.5 ±0.190	0.50 ±0.056	0.62 ± 0.773	19 ±0.021	1.2±0.0214
FS9	31.4 ±0.577	0.53 ± 0.06 5	0.58 ± 0.075	8 ± 0.032	1±0.034
standard deviation n=3					

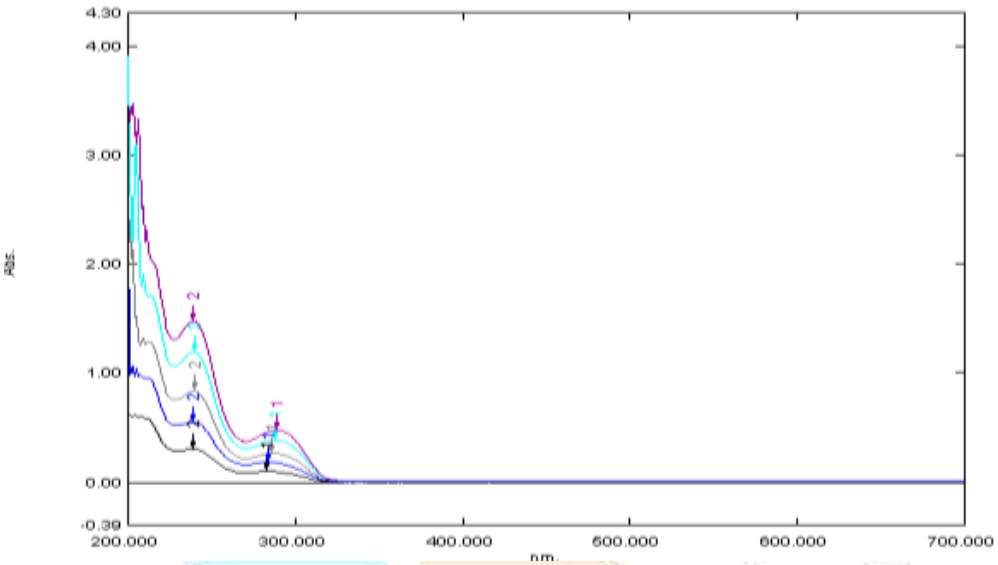
Discussion:

- Flow properties such as Angle of repose, Bulk density, tapped density, Compressibility index and Hausner's ratio are determined and it was found that prepared microspheres showed "Good" flow properties results
- The angle of repose of the formulations FS1,FS2 are between 25-30 degrees, which states that these formulations are exhibiting good flow and the angle of repose of F3-F9 are between 30-35 degrees, which indicates moderate flow.

- The Carr's compressibility index of formulations F2, F6 and F9 are between 5-15 g/cm³ that shows excellent relative flow-ability and the remaining formulations exhibited fair to poor flow-ability..
- The Hausner's ratio of all the formulations are between 1-1.2 which shows fair flow-ability.

UV SPECTRUM OF SITAGLIPIN PHOSPATE

Determination Of λmax And Calibration Curve Of Sitagliptin Phosphate in Methanol

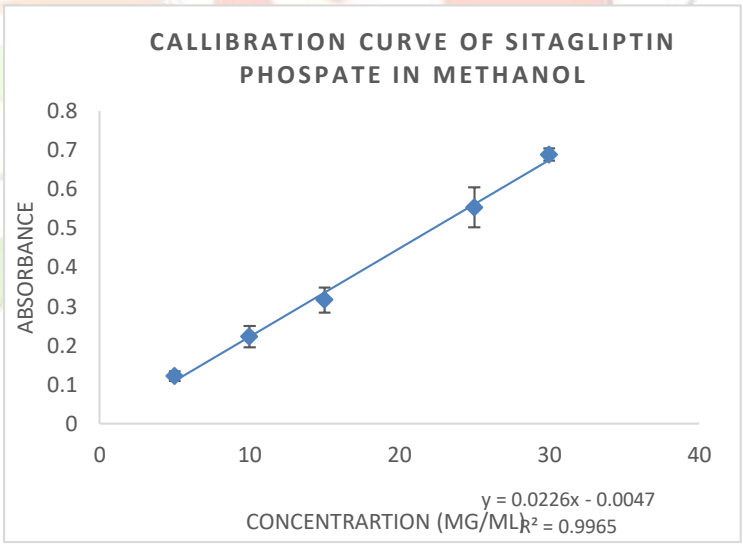


Discussion:

239nm is the maximum absorbance of Sitagliptin Phospate in Methanol.

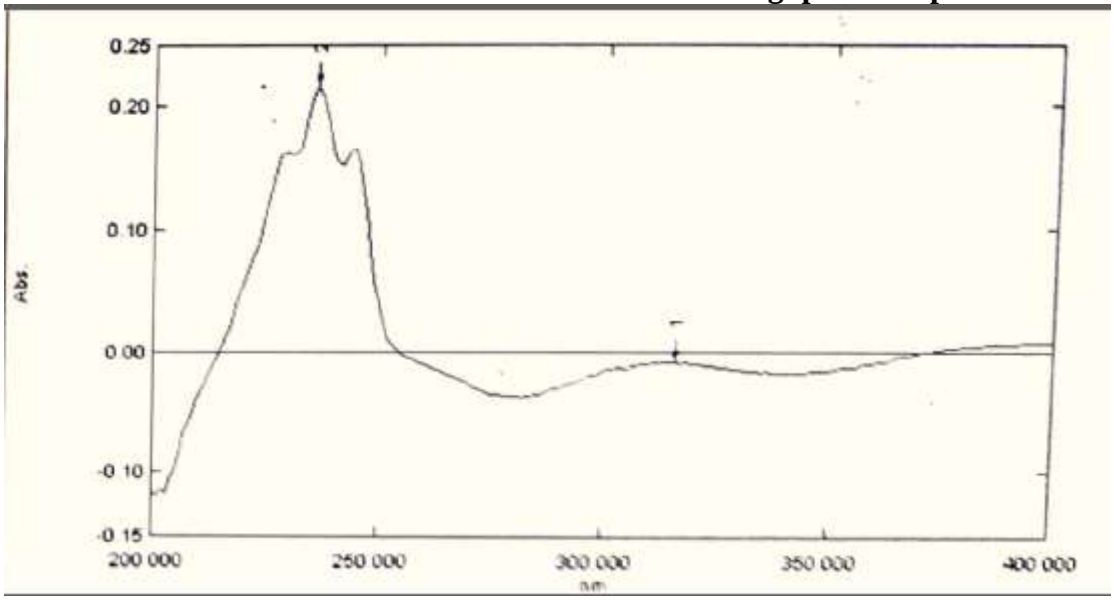
Sitagliptin Phospate Calibration Curve in Methanol:

Conc. (mg/ml)	Absorbance
5	0.121 ± 0.012
10	0.222 ± 0.027
15	0.316 ± 0.032
25	0.553 ± 0.051
30	0.688 ± 0.016
Standard Deviation n = 3	



The Regression Coefficient R2 for Calibration curve of Sitagliptin Phospate in methanol is 0.9965 , which is acceptable.

Determination Of λmax And Calibration Curve Of Sitagliptin Phosphate in 0.1N HCL

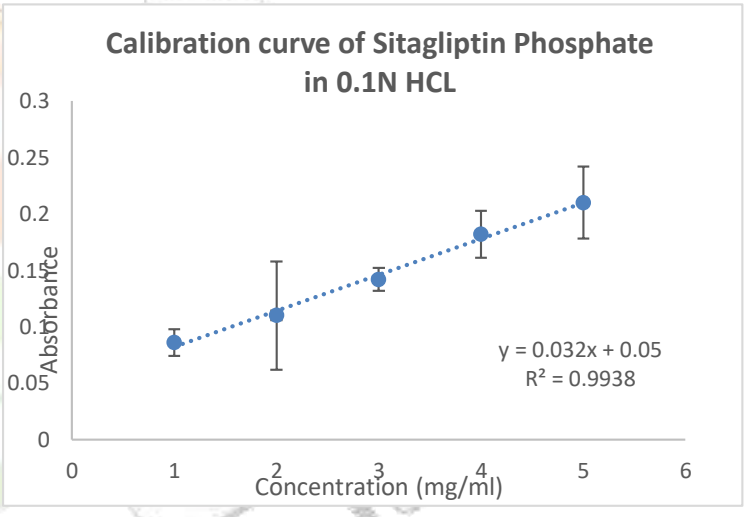


Discussion:

236nm is the maximum absorbance of Sitagliptin Phospate in 0.1N HCL.

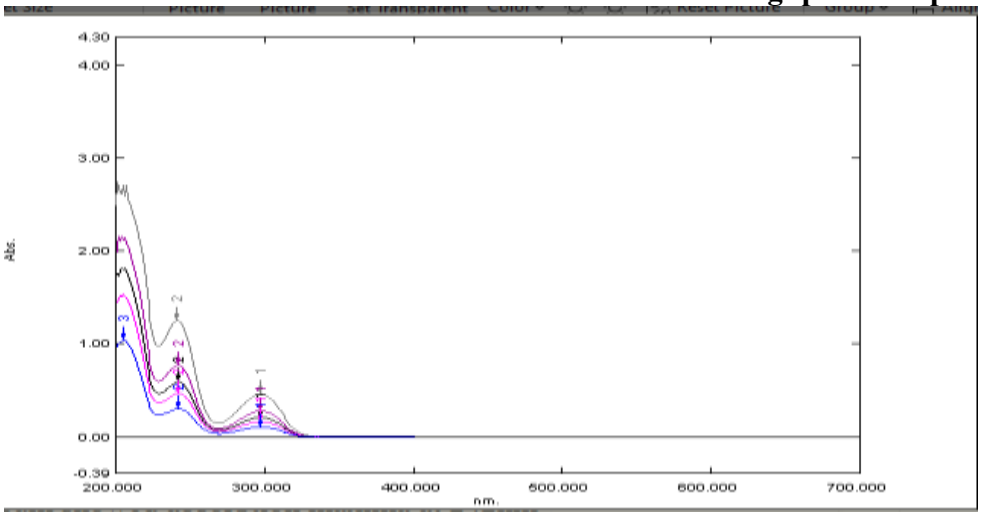
Sitagliptin Phospate Calibration Curve in 0.1N HCL:

Conc.(µg/ml)	ABSORBANCE
1	0.086 ± 0.012
2	0.11 ± 0.048
3	0.142 ± 0.010
4	0.182 ± 0.021
5	0.21 ± 0.032
Standard Deviation n=3	



The Regression Coefficient R2 for Calibration curve of Sitagliptin Phospate in 0.1N HCL is 0.9938 , which is acceptable.

Determination Of λmax And Calibration Curve Of Sitagliptin Phosphate in 6.8 Phosphate Buffer

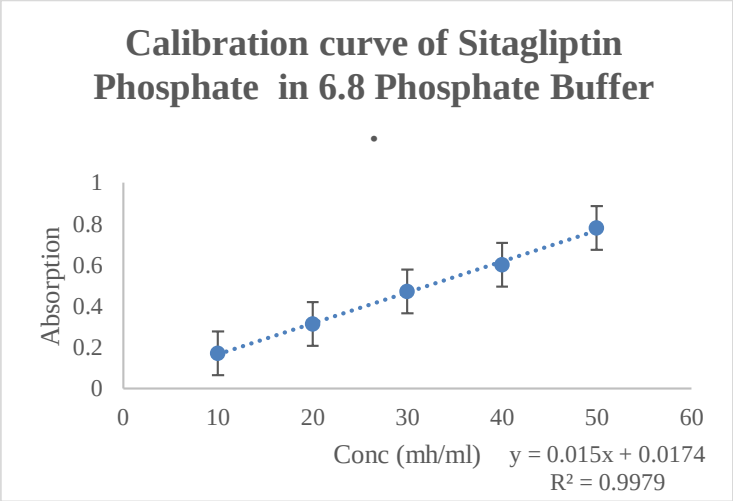


Discussion:

242nm is the maximum absorbance of Sitagliptin Phospate in 6.8 Phosphate Buffer .

Calibration curve of Sitagliptin Phosphate in 6.8 Phosphate Buffer:

Conc. (m g/ml)	Abs.
10	0.173 ± 0.045
20	0.313 ± 0.023
30	0.471 ± 0.027
40	0.601 ± 0.013
50	0.779 ± 0.074
Standard Deviation n=3	



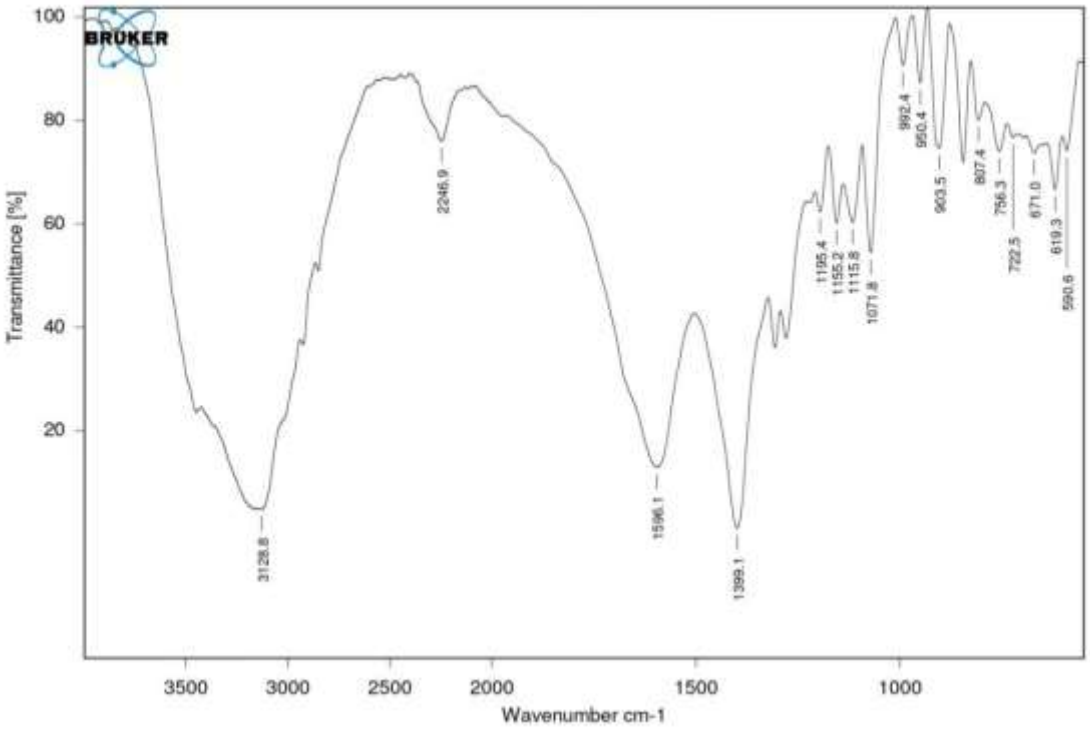
The Regression Coefficient R2 for Calibration curve of Sitagliptin Phospate in 6.8 pH Phosphate Buffer is 0.9979 , which is acceptable.

Drug polymer interaction (FTIR) study:

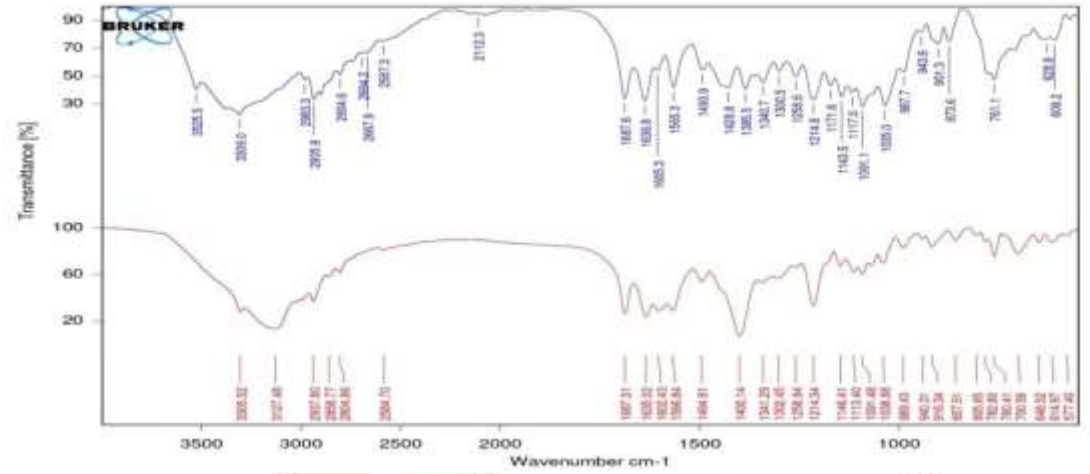
All of the distinctive peaks of Sitagliptin Phospate were found in the combination spectrum, demonstrating the compatibility of the Sitagliptin Phospate and polymer physical mixture.

Sitagliptin Phospate microspheres, and blank microspheres.Polymer and Sitagliptin Phospate. IR spectra are displayed in the ensuing figures.

IR Spectra of Pure Drug Sitagliptin Phospate:



IR Spectra of Optimized Formulation:



We observed from the drug excipients compatibility research that there are no interactions between the optimized formulation (Sitagliptin Phospate +excipients) and the pure drug (Sitagliptin Phospate), suggesting that no physical modifications have occurred.

Percentage Yield (%), Drug Entrapment Efficiency(%) Studies and % Swelling Index:

Formulation Code	Percentage Yield(%)	Drug Entrapment Efficiency(%)	% Swelling Index
FS1	82.42 ± 0.549	61.7 ± 0.75	89.01 ±0.574
FS2	92.4 ±0.503	89.2 ± 023	93.11 ±1.480
FS3	77.3 ±0.802	76.8 ±0.602	62.04 ±1.055
FS4	85.3 ± 0.208	72.4 ±0.312	57.9 ±0.550
FS5	81.4 ±1.36	78.4 ±0.360	80.09 ±0.807
FS6	88.18 ±0.521	87.8 ±0.642	87.4 ±0.896
FS7	57.9 ±0.416	57.8 ±1.418	65.03 ±1.00
FS8	76.2 ±0.713	64.6 ±0.737	75.7 ±0.472
FS9	72.7 ±1.153	79.6 ±0.450	69.34 ±0.851
standard deviation n=3			

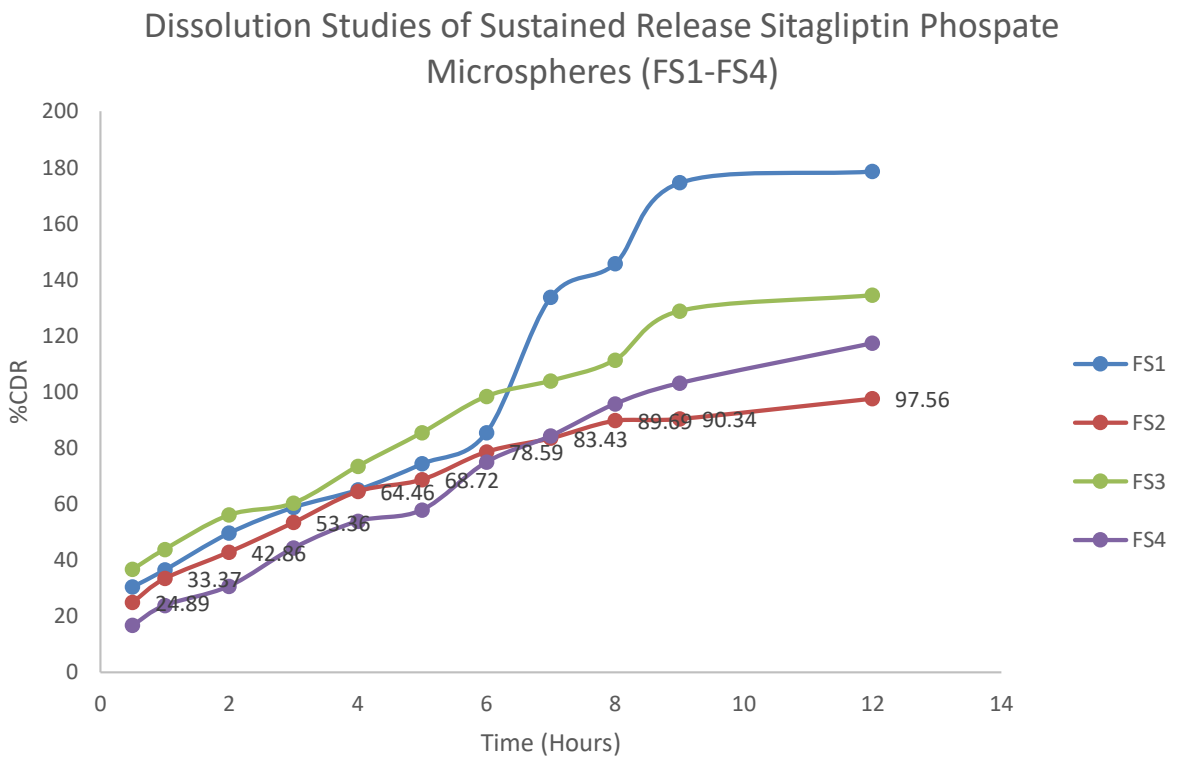
Discussion:

- The % percentage yield of formulations FS2, FS6 and FS4 are found as 92.4%, 88.8% and 85.3% respectively, which is maximum when compared to other formulations.
- Drug entrapment efficiency(%) of formulations FS2, FS6 is 89.2% and 88.18% respectively maximum when compared to the remaining formulations
- The %Swelling index of formulations FS2, FS1, and FS6 is found to be 93.1%, 89.01% and 87.4%, which is high when compared to the rest of the formulations .

❖ **IN VITRO RELEASE DATA OF SITAGLIPTIN PHOSPATE MICROSPHERES:**

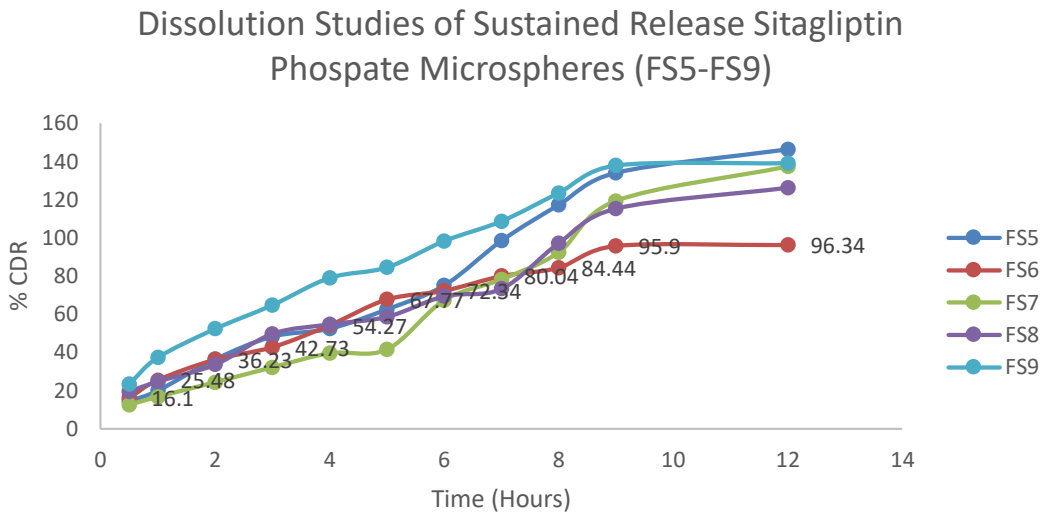
Dissolution Studies of Sustained Release Sitagliptin Phospate Microspheres (FS1-FS4)

In-vitro dissolution values of Sitagliptin Phospate				
Time (hrs)	**FS1**	**FS2**	**FS3**	**FS4**
0.5	30.429 ± 0.28	24.89 ±0.611	36.64 ± 0.35	16.7 ± 0.19
1	36.45 ± 0.66	33.37 ±0.71	43.79±0.37	23.84 ± 0.17
2	49.599 ± 0.35	42.86 ±0.15	56.02 ±0.60	30.7 ± 054
3	58.779 ± 0.77	53.36 ± 0.32	60.27 ±0.44	44.3 ± 0.35
4	65.07 ± 0.64	64.46 ±1.16	73.42 ±0.48	53.84 ± 0.26
5	74.331 ± 0.28	68.72 ±0.51	85.41 ±0.42	57.89 ± 0.17
6	85.401 ±0.41	78.59 ±0.21	98.34 ±0.37	74.94 ± 0.29
7	133.65 ± 0.28	83.43 ±0.50	103.91 ±0.35	84.31 ± 0.24
8	145.719 ± 0.46	89.69 ±0.40	111.3± 0.54	95.71 ± 0.39
9	174.501 ± 0.54	90.34 ±0.75	128.73 ±0.64	103.1 ± 0.33
12	178.61 ±0.37	97.56 ±0.50	134.37 ± 0.52	117.34 ± 0.56
Standard Deviation n =3				



❖ **Dissolution Studies of Sustained Release Sitagliptin Phospate Microspheres (FS5-FS9)**

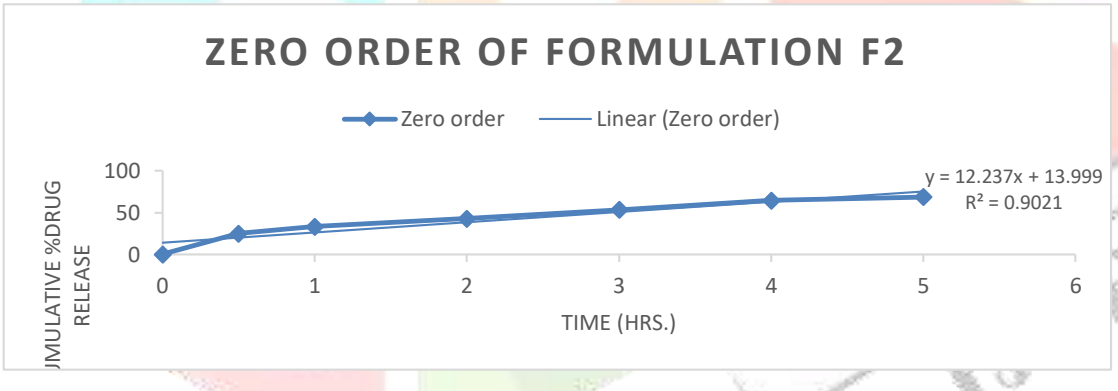
Time (hrs)	FS5	FS6	FS7	FS8	FS9
0.5	14.57 ± 0.36	16.1 ± 0.37	12.51 ± 0.68	19.52 ±0.34	23.45 ±0.36
1	20.04 ± 0.45	25.48 ± 0.46	16.74 ± 0.32	24.75 ±0.57	37.34 ±0.33
2	34.04 ± 0.32	36.23 ± 0.28	24.34 ±0.17	33.62 ±0.72	52.34 ±0.24
3	48.34 ± 0.26	42.73 ± 0.34	32.17 ±0.72	49.73 ±0.97	64.78 ±0.54
4	52.46 ± 0.54	54.27 ± 0.58	39.54 ±0.57	54.71 ±0.31	79.03 ± 0.19
5	62.62 ± 0.17	67.77 ± 0.74	41.52 ±0.89	58.67 ±1.3	84.54 ±0.35
6	75.12 ± 0.29	72.34 ± 0.1	67.32 ± 1.45	69.47 ±0.17	98.32 ±0.29
7	98.55 ± 0.19	80.04 ± 1.2	78.24 ±0.39	73.34 ±0.64	108.74 ±0.64
8	117.3 ± 0.67	84.44 ± 0.97	92.37 ±0.74	97.32 ±0.79	123.54 ±0.79
9	134.1 ± 0.73	95.9 ± 0.34	119.34 ±0.31	115.42 ±0.69	137.89 ± 0.93
12	146.34 ±0.54	96.34 ± 0.54	137.34 ±0.16	126.34 ±1.75	139.09 ± 0.57
Standard deviation n=3					



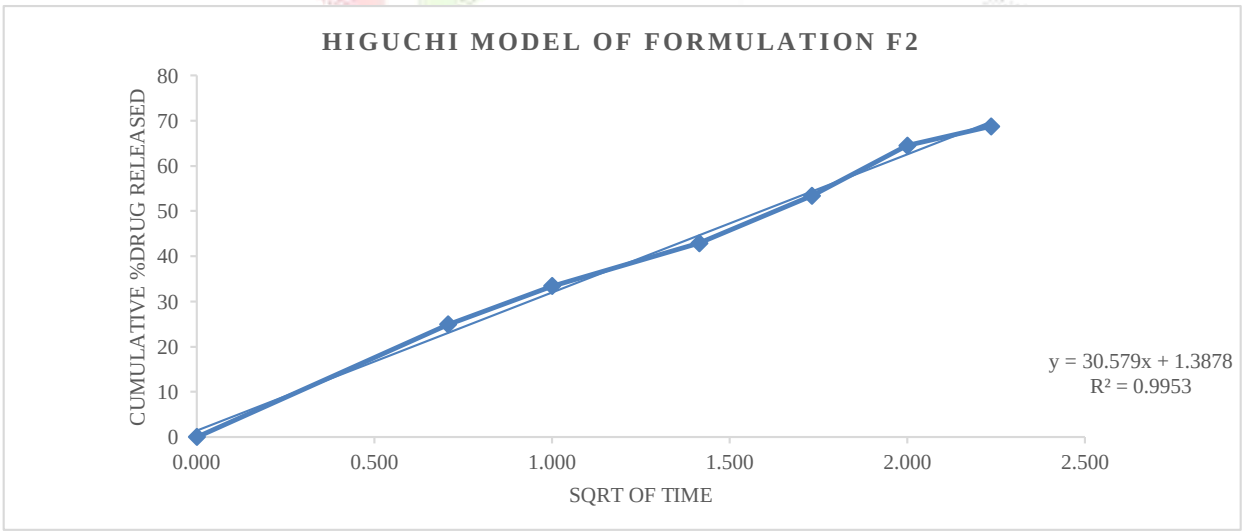
Kinetics of dissolution data:

The drug release data obtained was extrapolated to Zero, first, Higuchi and Korsemeyer order to know the mechanism of action, as a result the optimized FS2 and FS6 has shown the drug release which is independent of concentration and the results are shown in below graphs.

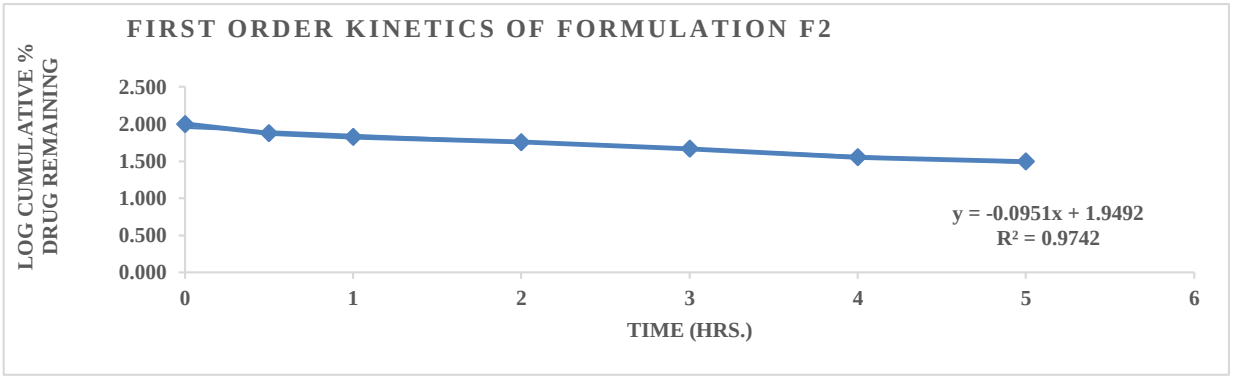
Zero order of Optimized Formulation F2



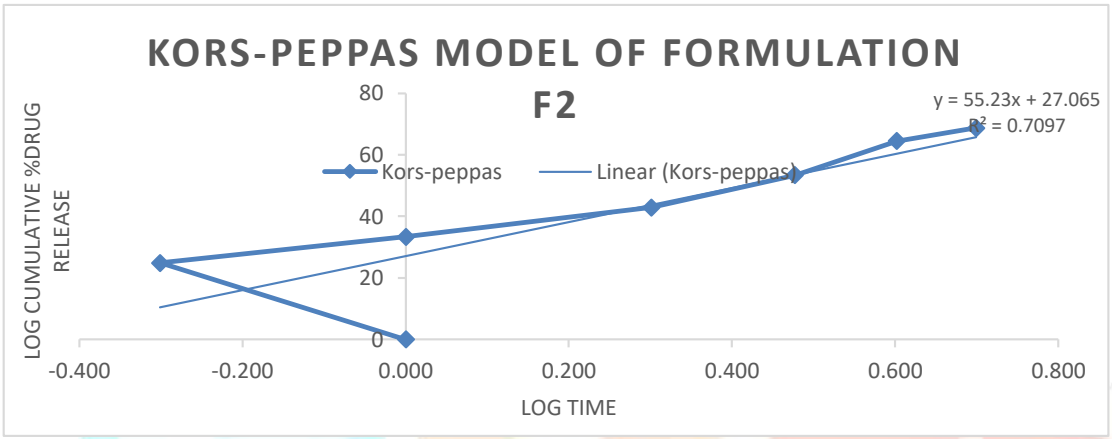
Higuchi and First order of Optimized Formulation F2



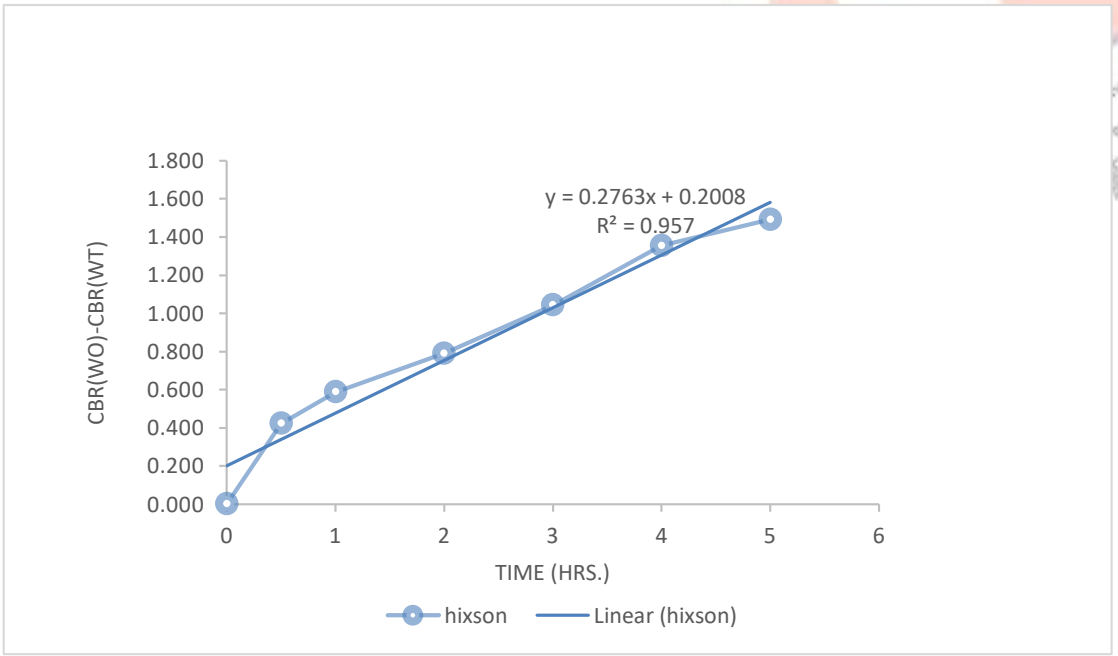
First order kinetics of formulation F2



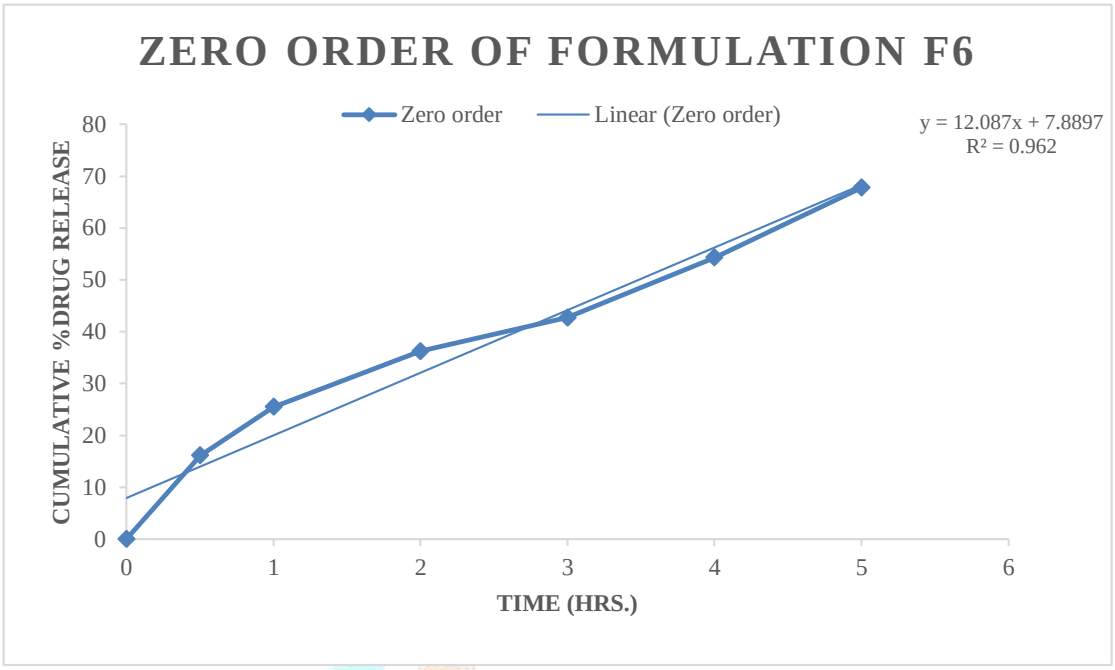
Korsemeyer order for Optimized Formulation F2



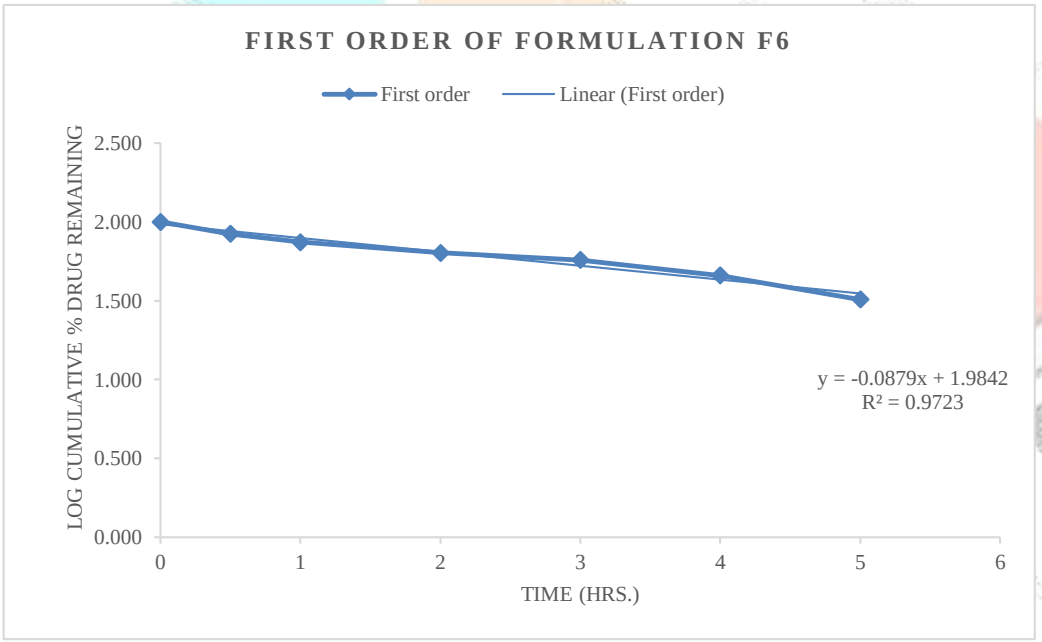
Hixson Crowel Model for Optimized Formulation F2



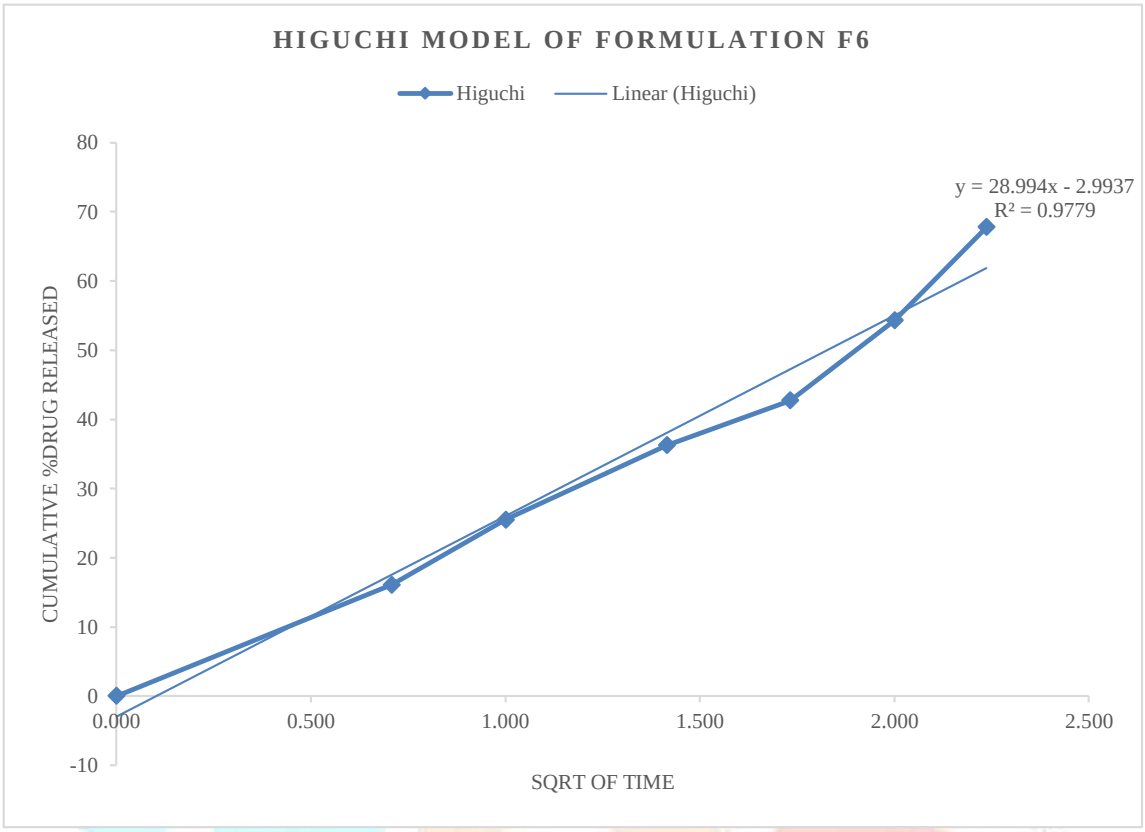
Zero Order for Optimized formulation F6



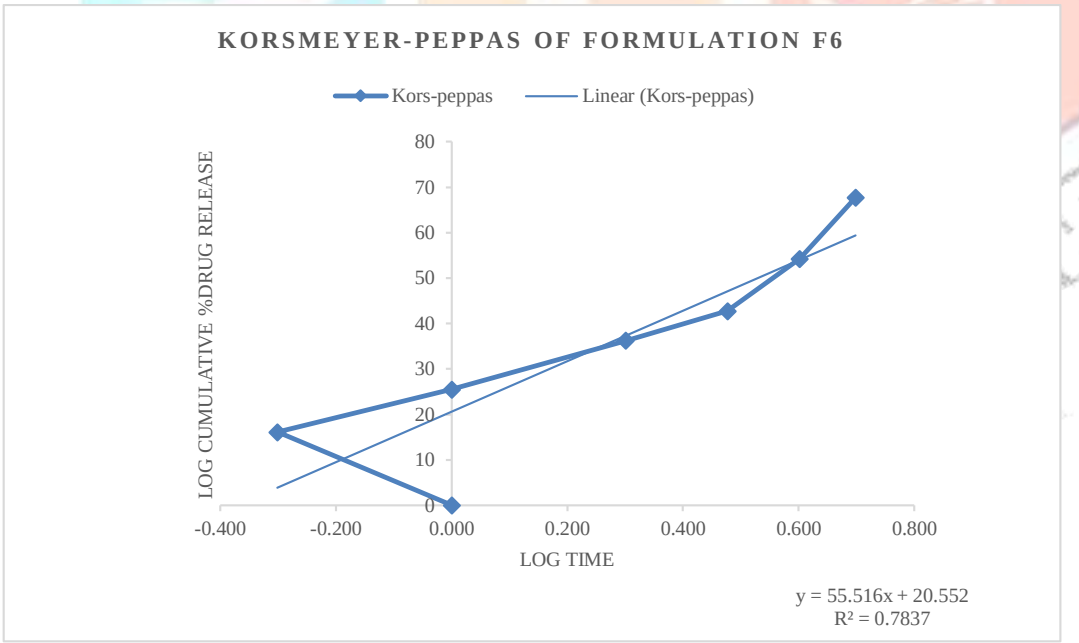
First order kinetics for Optimized formulation F6



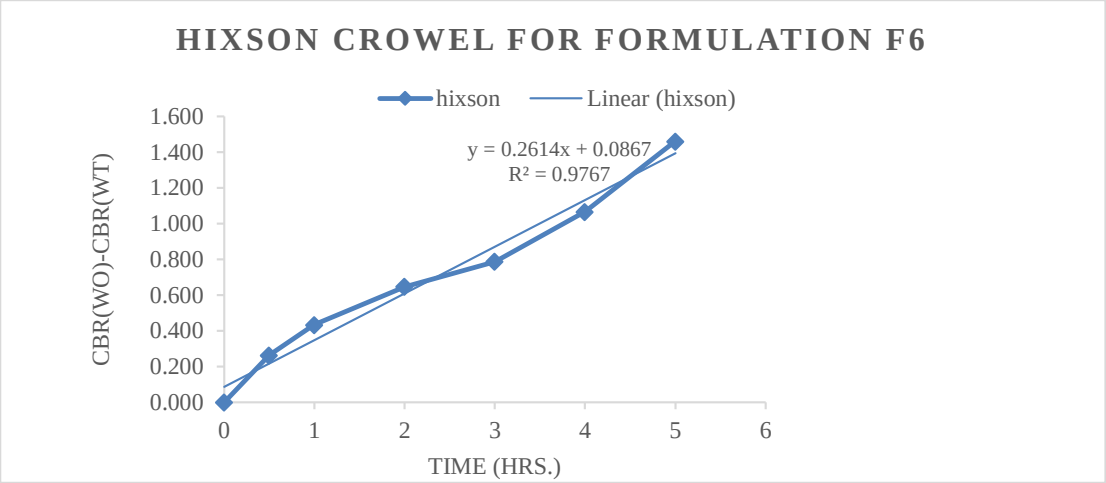
Higuchi Model of Optimized Formulation F6



Korsemeyer order of Optimized Formulation F6



Hixson Crowel Model for Optimized Formulation F6



The Drug release kinetics data were obtained for formulations (FS1 – FS6) by fitting the ,% CDR vs. Time values to various release kinetics models. The data revealed that two optimized formulations followed the zero order release kinetics, as R2 values for two formulations were higher than that of the first order release kinetics. Therefore, favoring controlled drug release. All formulations released drug predominantly by diffusion, and were diffusion controlled type systems, as the R2 value was higher for the Higuchi release model.

References:

1. N. K. Jain, Controlled and Novel drug delivery, 04 Edition, CBS Publishers New Delhi, India; 21, N236-237,

2. Chein YW. Oral Drug Delivery Systems: In Novel drug delivery systems. Vol.50, Marcel Dekker, Inc., New York. 1992, 139. 177.

3. Mathew Sam T., Devi Gayathri S., PrasanthV.V., Vinod B; NSAIDs as microspheres, The Internet Journal of Pharmacology.6(1), 2008, 67-73.

4. Li, S.P., Kowalski C.R., Feld K.M., Grim W.M. Recent Advances in Microencapsulation Technology and Equipment, Drug Dev Ind. Pharm. 14, 1988, 353-376.

5. P.M. Dandagi, VS. Mastiholimath, M.B. Patil, M.K. Gupta, Biodegradable microparticulate system of captopril. International Journal of Pharmaceutics. 307, 2006, 83- 88.

6. Chinna Gangadhar B. Shyam Sunder R., Vimal Kumar Varma. M., Sleeva Raju M., Sai Kiran M. Formulation and Evaluation of Indomethacin Microspheres using natural and synthetic polymers as Controlled Release Dosage Forms. International Journal of Drug Discovery, 2(1), 2010,8-16.

7. Rana mazumder, lila K. Nath, Anwarul, Haque, Tarasankar Maity, Prasant K. Choudhary, Bhupendra Shreshta, Formulation and in vitro evaluation of natural polymers based microsphere for colonic drug delivery, International journal of pharmacy and pharmaceutical sciences, 2(1), 2010, 211-219.

8. Kavitha K, Chintagunta Pavanveena, Anil Kumar S. N., Tamizh Mani T, Formulation and evaluation of trimetazine hydrochloride loaded gelatin microsphere. International Journal of Pharmacy and Pharmaceutical Sciences, 2(3), 2010, 67-70.

9. Lorenzo-Lamosa ML. Design of microencapsulated chitosan microspheres for colon drug delivery. J. Control. Release, 52(1-2), 1998, 109-118.

10. Sudha Mani T and Naveen Kumar K, At preparation and evaluation of ethyl cellulose microspheres of ibuprofen for sustained drug delivery. International Journal of Pharma Research and Development. 2(8), 2010, 120-121.

11. [10:12 am, 27/01/2024] Anusha Badde: Party Chan K. Kavid M. Rupesitiksumari, SD. Jagadeesh Singh Nawal Morphere for Drag Delivery: A Review International Journal of Antical Research Anal Developeme 407) 2012 31-37

12. Adulyade, Sadhana Shahi, M. Thube, Ankit S. Review un perial Jumal of Pharmaceutical Research Allied Sciences, 1(1), 2012.

13. Saravan Kumar K. Jayachandra Reddy P., Chandra Sekhar K.B. A Review on sphere for Novel drug delivery System. Journal of Pharmacy Research, 5(1), 2012. 100-424

14. Katana Sahil, Middla Akanksha, Sandhu Premjeet, Ajay Bilandi and Bhawana Kapoor, rosphere: A Review. International Journal of Research In Pharmacy and Chemistry, 1(4), 2011,1184-1198

15. Sipai Altaf Bhat. M. Vandana yadav, Mamatha Y, Prasanth V. V. Mucoadhesive Mizusphere An overview. American journal of Pharmtech Research, 2(1), 2012,237-258.

16. Shiv Shankar Hardenma, Ankit Jian, Ritesh Patel, Anu Kaushal, Formulation and evaluation of mucoadhesive microsphere of ciprofloxacin. Journal of Advanced Pharmacy Education and research. 1(4), 2011, 214-224.

17. Nalini M. Anandea, Sunil K. Jain a,, Narendra K. Jain, Con-A conjugated mucoadhesive microspheres for the colonic delivery of diloxanide furoate. International Journal of Pharmaceutics, 359, 2008,182-189.

18. Guojun Liu, Husheng Yang, Jiayun Zhou, Preparation of magnetic microsphere from waterin-oil emulsion stabilized by block copolymer dispersant, Biomacromolecules, 6, 2005, 1280-1288

19. P. Dutta, J.Struti, Ch. Niranajan patra, M.E. Bhaoji rao, Floating Microsphere: Recents Trends in the Development of Gastroretentive Floating Drug Delivery System. International Journal of Pharmaceutical Science and nanotechnology, 4(1), 2011, 1293-1306.

20. Y. Kawashima, T. Niwa, H. Takeuchi, T. Hino, Y. Ito, Preparation of multiple unit hollow microspheres (microbal loons) with acrylic resin containing tranilast and their drug

21. Kamila M. Nitamondal, Gosh L. Gupta B. Multiunit floating drug delivery system of Rosiglitazone maleate: Development, 21.characterization, stastistical optimization of drug release and in vivo evaluation. AAPS Pharm Sci Tech 2009;10(3):887-99

22. Senthilkumar SK, Jaykar B, Kavimani S. Formulation, Characterization and In vitro Evaluation of Floating Microsphere Containing Rabeprazole Sodium. JITPS2010;1(6):274-872

23. Barhate SD. Rupnar YS. Sonvane RM, Pawar KR, Rahane RD formulation and evaluation of floating microspheres of ketorolac trometamol. IUPRD 2009;1(9):1-8.