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FABRICATION AND EVALUATION OF GLIMEPIRIDE

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ABSTRACT

Nano suspension is a part of nanotechnology which is a submicron colloidal dispersion of pharmaceutical active ingredients in a liquid phase having size range below 1 um, and which is stabilized by surfactants and polymers. Most of the newly developed drugs are water insoluble, shows poor bioavailability. Glimepiride is an anti-diabetic drug belongs to sulfonylurea class, which is used to treat type II diabetes mellitus. Glimepiride increases the insulin secretion by acting on β-cells of the pancreas. Glimepiride binds to sulphonylurea receptors which are present on β-cell on the plasma membrane, which close the ATP-sensitive potassium channel leading to depolarization of cell membrane. So there is the opening of voltage-gated calcium channel due to which there is an influx of calcium ions causes secretion of the preformed insulin molecule. It is categorized under biopharmaceutical classification system class II drug, having poor solubility and high permeability. The present study is done on glimepiride nanosuspension.The major problem with the drug is having poor solubility when given through oral route. To overcome this problem it is formulated as Nano suspension by using the best solvent like acetone by solvent evaporation method. The prepared glimepiride Nano suspension was evaluated for Density, Viscosity, PH, Particle size, Zeta potential, and Diffusion studies. Among all the formulations of glimepiride, F4 formulation shows maximum drug release at the end of 12 hrs. (98%).

Key words: Glimepiride, Nano suspension,Density, Viscosity, PH, Particle size, Zeta potential, and Diffusion studies.

1.INTRODUCTION

Solubility is one of the major problems in case of Bio-pharmaceutics classification system (BCS) class II which are highly permeable and low soluble E.g. glimepiride and Paracetamol.

IMPORTANCE OF SOLUBILITY:

Solubility is the property of a solid ,liquid ,or gaseous chemical substance called solute to dissolve in a solid ,liquid ,or gaseous solvent to form a homogeneous solution of the solute in solvent .The solubility of a substance fundamentally depends on the solvent used as well as on temperature and pressure. However major

problem with oral dosage form is poor solubility. The poor solubility and low dissolution rate ofpoorlywater-soluble drugs in the aqueous GI fluids often cause inadequate bioavailability.

METHODS OF ENHANCING SOLUBILITY[1,12,14,16]:

1. Enhancement of drug solubility:
a.Microionisation
b.Nano ionization
c.Use of surfactants
d. Molecular encapsulation with Cyclodextrins
2.Enhancement of drug permeability:
a.Lipid technologies
b.Ion pairing
c.PenetrationEnhancers
3.Enhancement of drug stability:
a.Enteric coating
b.Complexation
c. Use of metabolism inhibitors
4. Enhancement of gastro intestinal retention:
a. Gastro retentive drug delivery system

NANOIONISATION:

Nano ionisation is defined as the process of reducing the average diameter of the solid particle Usually Nano ionisation term is used when the particle that are produced only a few micrometres in diameter .In pharmaceutical industry the modern application requires average particle diameter to be in Nanometer scale. Nano ionisation has advantages of better solubility assay for less soluble drugs.

USE OF SURFACTANTS:

Surfactants can be added as an extra granular excipient or can be incorporated during the solid dispersion manufacturing process internally. Studies shows that surfactants like SLS and polaxomeradded extra granularly to the solid dispersion, have minimal effect on the drug release. However, when the surfactants are intimately mixed with solid dispersion i.e. when surfactant,-drug, and polymer are dissolved in common solvent and dried toyield solid dispersion, they have shown a positive effect on drug release.

MOLECULAR ENCAPSULATION WITH CYCLODEXTRINS:

Cyclodextrins (EU), or CDs, is cyclic oligosaccharides with a defined ring size that are used in foods, cosmetics, home care products, and pharmaceuticals for active encapsulation and delivery. There are three basic types of natural CDs (alpha, beta, and gamma), which are produced from starch by enzymatic conversion. The bucket-shaped molecule has a hydrophilic exterior and a hydrophobic cavity and is able to form inclusion complexes with many organic guest compounds. Alpha has the smallest cavity, gamma the largest, and beta has an intermediate size. Alpha works the best with low MW materials and gamma for those with high MW. C log P and molecular weight usually determine which CD will form the best complex with the highest binding constant. Complexion and Release mainly depend on temperature and moisture conditions. Beta CD is the most frequently used CD. It has a water solubility of 1.9% and is normally used to make insoluble complexes. Hydroxypropyl (EU) Beta Cyclodextrin is typically used to form water soluble complexes.

Commercially Available CDs:

Hydroxypropyl alpha, beta, and gamma cyclodextrins.

NANOTECHNOLOGY[6]:

Nanotechnology is commonly considered to deal with particles in the size range <100 nm, and with the Nanomaterials manufactured using nanoparticles. The approaches to the toxicology testing, and assessment of the human and environmental risks are undergoing rapid development. One risk assessment area of strong interest is the extent to which nanoparticle and nanomaterial toxicity can be extrapolated from existing data for particles and fibres.

NANOSUSPENSION[2]:

Nano suspensions are aqueous suspensions containing one or several submicron sized drug substances and appropriate stabilizers. Stabilizers include excipients that enable Nano grinding of the drug particles, prevent crystal growth or Nano particle aggregation during storage, pH-buffering substances, preservatives, and other

components that may be needed for further processing (e.g., transforming into a solid form) or administration to patients (e.g., sweeteners, colorants) . The term Nano sizing, as used in this work, describes the reduction of suspended drug particles down to the submicron size range. The main challenge in Nano suspension technology isprevention of particle agglomeration or aggregation and crystal growth. At the nanometre scale, attractive Vander Waals and dispersive forces between particles come into play. Such attractive forces increase dramatically as particles approach each other, which ultimately results in irreversible aggregation.

Major Advantages of Nano suspensions:

- Its general applicability to most drugs and its simplicity.
- Can be applied for the poorly water-soluble drugs.
- Can be given by any route.
- Reduced tissue irritation in case of subcutaneous/intramuscular administration
- Rapid dissolution and tissue targeting can be achieved by IV route of administration.
- Oral administration of Nanosuspensions provide rapid onset, reduced fed/fasted ratio and improved bioavailability.
- The absorption from absorption window of the drugs can be increased, due to reduction in the particle size.
- Higher bioavailability and more consistent dosing in case of ocular administration and inhalation delivery.
- Drugs with high log P value can be formulated as Nanosuspensions to increase the bioavailability of such drugs.
- Improvement in biological performance due to high dissolution rate andsaturation solubility of the drug.
- Ease of manufacture and little batch-to-batch variation.
  Long term physical stability (Due to absence of Ostwald ripening).
- Nanosuspensions can be incorporated in tablets, pellets, hydrogel and suppositories are suitable for various routes of administration.
- Increasing the amorphous fraction in the particles, leading to a potentialchange in the crystalline structure and higher solubility.
- Possibility of surface-modification of Nanosuspension for site specific Delivery.
- Possibility of large-scale production, the pre-requisite for the introduction of a delivery system to the market.

DIABETES MELLITUS[4]:

Diabetes mellitus is a chronic life- long endocrine and metabolic disorder which occurs due to the defect in insulin secretion and insulin action .Insulin is a hormone which is produced by a specialised cell called as beta cells present on organ pancreas. Normally our body break down the carbohydrates and sugars which convert into glucose molecules and act as fuel for our body, but for utilisation of glucose, hormone insulin is required. Deficiency of insulin leads to increased blood glucose level in a body along with disturbances in the metabolism of carbohydrates, fats and proteins. If diabetes is uncontrolled then it leads to severe diabetic complications like Retinopathy, Neuropathy and various cardiovascular complications.

METHODS

Preformulation studies:

Preformulation is a group of studies that focus on the physicochemical properties of a new drug candidate that could affect the drug performance and the development of a dosage form. This could provide important information for formulation design or support the need for molecular modification. Every drug has intrinsic chemical and physical properties which has been consider before development of pharmaceutical formulation. This property provides the framework for drugs combination with pharmaceutical ingredients in the fabrication of dosage form. Objective of preformulation study is to develop the elegant, stable, effective and safe dosage form by establishing kinetic rate profile, compatibility with the other ingredients and establish Physico-chemical parameter of new drug substances. Among these properties, drug solubility, partition coefficient, dissolution rate, polymorphic forms and stability are plays important role in preformulation study.

FT-IR STUDIES:

FT-IR spectroscopy studies were carried out for identification of pure drug and compatibility study of physical mixture of nanosuspension. Solid admixtures were prepared by mixing the drug with each formulation excepients separately in the ratio of 1:1. FT-IR spectroscopy was conducted using a shimadzu FT-IR 8400 spectrophotometer and spectrum was recorded in the wave length region of 4000-400 cm-1.

Construction of standard calibration curve for Glimepiride:

Stock solution:

5 mg of glimepiride was dissolved in 10 ml of phosphate buffer 6.8 to get a solution of 50 mcg/ml concentration.

Standard concentration:

Aliquot of standard drug solution ranging from 1ml, 2ml, 3ml, 4ml, 5ml were transferred in to 10 ml volumetric flask and were diluted up to the mark with 6.8 phosphate buffer. Thus the final concentration range from 5-25 mcg/ml. Absorbance of each solution was measured at 227 nm against 6.8 phosphate buffer as a blank. A plot of concentration of drug versus absorbance was plotted.

Preparation of phosphate buffer 6.8:

place 125 ml of 0.2 M potassium dihydrogen phosphate in 500ml volumetric flask Add 56 ml of 0.2 M sodium hydroxide and then add water to make up the volume.

Preparation of GlimepirideNanosuspension by solvent evaporation method[6,8]:

- Glimepiride nanosuspension was prepared by solvent evaporation method.
- P-188 is taken in specified quantity and mixed with specified amount of water and mix thoroughly (aqueous phase).
- specified amount of drug and HPMC[E_{50}] of different concentrations (200mg,400mg, 600mg) were dissolved in acetone (organic phase)
- Organic phase is added to aqueous phase under ultra sonication for specified time.
- This solution is allowed for magnetic agitation (one hour)
- The obtained solution is cooled and the nanosuspension is lyophilized by using Lyophilized.
- The freeze dried samples were used for characterization studies.

Table3: Ingredients used in formulation table:

S.no	Name of the formulation	Drug(mg) Glimepiride	Polymer(mg) HPMC[E_{50}]	Solvent(ml) Acetone	Surfactant(mg) Poloxamer-188	Drug/Polymer Ratio	Agitation time
1	F1	20	200	10	500	1:10	1
2	F2	20	200	10	500	1:10	2
3	F3	20	400	10	500	1:20	1
4	F4	20	400	10	500	1:20	2
5	F5	20	600	10	500	1:30	1
6	F6	20	600	10	500	1:30	2

CHARACTERIZATION OF GLIMEPIRIDE NANOSUSPENSION[15,17,36]:

Particle size:

Horiba scientific sz-100 with dynamic laser light scattering technique was employed in assessing the mean particle size and polydispersity index (PDI).Measurements were obtained at an angle of 173.

Zeta potential[4]:

Horiba scientific sz-100 was employed for the determination of the ZP of different formulations with the help of a laser light scattering technique. The formulations were diluted approximately with double distilled water and measurements were obtained with an angle of 173.

Fourier Transform infra red spectroscopy:

The FT-IR spectra of Glimepiride, HPMC[E_{50}], Poloxamer-188, and Glimepiride nano suspension particles were recorded on Agilent technologies carry 630 FTIR .IR absorbance scans of samples were analyzed in range of 4000 to 400cm^{-1} for changes in the intensity of sample peaks.

pH[28]:

The pH values of suspensions were examined with the help of pH meter.

1. Preparing for Calibration
   - Turn on your pH meter.
   - Clean your electrode.
   - Prepare your buffers
2. Calibrating Your pH Meter
   - Place your electrode in the buffer with a pH value of 7 and begin reading.
   - Set the pH.
   - Rinse your electrode with distilled water.
   - Place your electrode in the appropriate buffer for your sample and begin reading.
   - Set the pH a second time.
   - Rinse your electrode.
3. Using Your pH Meter
   - Place your electrode in your sample and begin reading.
   - Set your pH level.
   - Clean your electrode after use.

Viscosity:

Viscosity of formulated suspensions was determined by using Brooke Field Viscometer.
A sample of 400 - 600ml in a suitable container is placed under the viscometer which is then lowered to dip the spindle into the sample up to an immersion mark on the spindle shaft. The dip-in spindle is suitable for comparative testing of the viscosity of free-flowing fluids.

Selection of spindle: When the viscosity of a fluid is not known

If the reading is below 10% at the highest speed, the next largest spindle should be used. To test a fluid at multiple speeds, choose a spindle that will produce readings between 10% and 100% for at least three speed settings.

Density:

Density of formulated Nano suspension was determined by using specific gravitybottle (25mL).

- Weight of clean dry specific gravity bottle=W1
- Weight of specific gravity bottle + Distilled water = W2
- Weight of specific gravity bottle + Sample liquid = W3
- Weight of water in specific gravity bottle = W4 (W2-W1)
- Weight of sample liquid in specific gravity bottle = W5 (W3-W1)
- Volume of specific gravity bottle = Mass(W4)/ Density of distilled water
- Density of sample liquid = W5/Volume of specific gravity bottle

Entrapment efficiency:

Take 10 ml of GlimepirideNano suspension and separated by using cooling centrifuge (Remi,Mumbai)at 14500rpm for 60 min at 4°C.Glimepiride concentration was measured by using UV spectrometer at 227nm from the collected clear supernatant sample .

Following equation was used to calculate %EE

$$\%\text{Entrapment efficiency} = \frac{\text{Weight of initial drug} - \text{Weight of final drug}}{\text{Weight of initial drug}} \times 100$$

%drug loading (%d)was calculated using:

%DL= (amount of entrapped drug/total amount of polymer)×100

Invitro drug release studies (diffusion studies)[13,19,34]:

Diffusion parameters:

6.8M Phosphate buffer

RPM: 50

Diffusion medium: 100ml

Procedure:

Invitro drug release study of Glimepiride nano suspension (F_1-F_6) was studied by the dialysis bag diffusion method.5ml of Glimepiride nano suspension was taken in a dialysis bag and tied at both ends. The dialysis bag was immersed in a dissolution medium containing 100ml of Phosphate buffer,pH6.8 and stirred at 50rpm.1ml of samples were withdrawn at various time intervals(1,2,3,4,5,6,8,10 and,12 hr)and replaced by a fresh dissolution medium with the same volume. Each withdrawn sample was diluted to 10ml.The drug concentrations were measured by uv-visible spectrophotometer at 227nm .The percent cumulative drug release (%CDR) from the different formulation was calculated using an equation obtained from a standard curve.

7.RESULTS

In order to achieve the increase in solubility of Anti diabetic agents, Glimepiride was used as a model drug for the treatment of Type-II Diabetes mellitus, which was formulated by solvent evaporation method employing different ratios of polymer (HPMC[E_{50}]) and agitation time.

In the present study 6 Formulations(F1-F6) with variable polymer(HPMC[E_{50}]) ratios and agitation time were prepared and evaluated for various parameters such as particle size, Zeta potential, FTIR, P^H, Density, Viscosity, Encapsulation efficiency and Invitro drug release studies. On the basis of invitro release studies the best formulation (F4) was selected.

To know the mechanism of drug release from this formulation the data were treated according to first order release, Higuchi and korsemeyerPeppa's model equation along with zero order(cumulative drug release Vstime)

Preformulation studies (compatibility studies):

Compatibility studies were performed by using FT-IR spectrophotometer. The IR spectrum of pure Glimepiride drug was compared with the spectrum of physical mixture of Glimepiride (HPMC[E_{50}], Polaxomer-188).

There is no appearance or disappearance of any characteristics peaks. This shows that there are no chemical interactions between the drug and excipients.

The presence of peaks at the expected range confirms that the materials taken for the study are confirmed.

Table 5: Characteristic peaks of drug in FT-IR spectra:

S.no	Name of the compound	Wave number	Functional group
1	Glimepiride	3270	N-H
		2930	C-H
		1703	C=O
		1671	N-C=O
		1343	O=S=O
2	HPMC[E_{50}]	2899	C-H
		1458	C-C
		1374	C-O
		943	OH
3	Polaxomer-188	1341	OH
		2880	C-H
		1097	C-O
4	Glimepiride+ HPMC[E_{50}]	2842	C-H
		1442	C-C
		950	OH
		3368	N-H
		1703	C=O

		1671	N-C=O
5	Glimepiride+ Polaxomer-188	1342	O=S=O
		2861	C-H
		1040	C-O
		3369	N-H
		1670	N-C=O
		2930	C-H

FTIR:

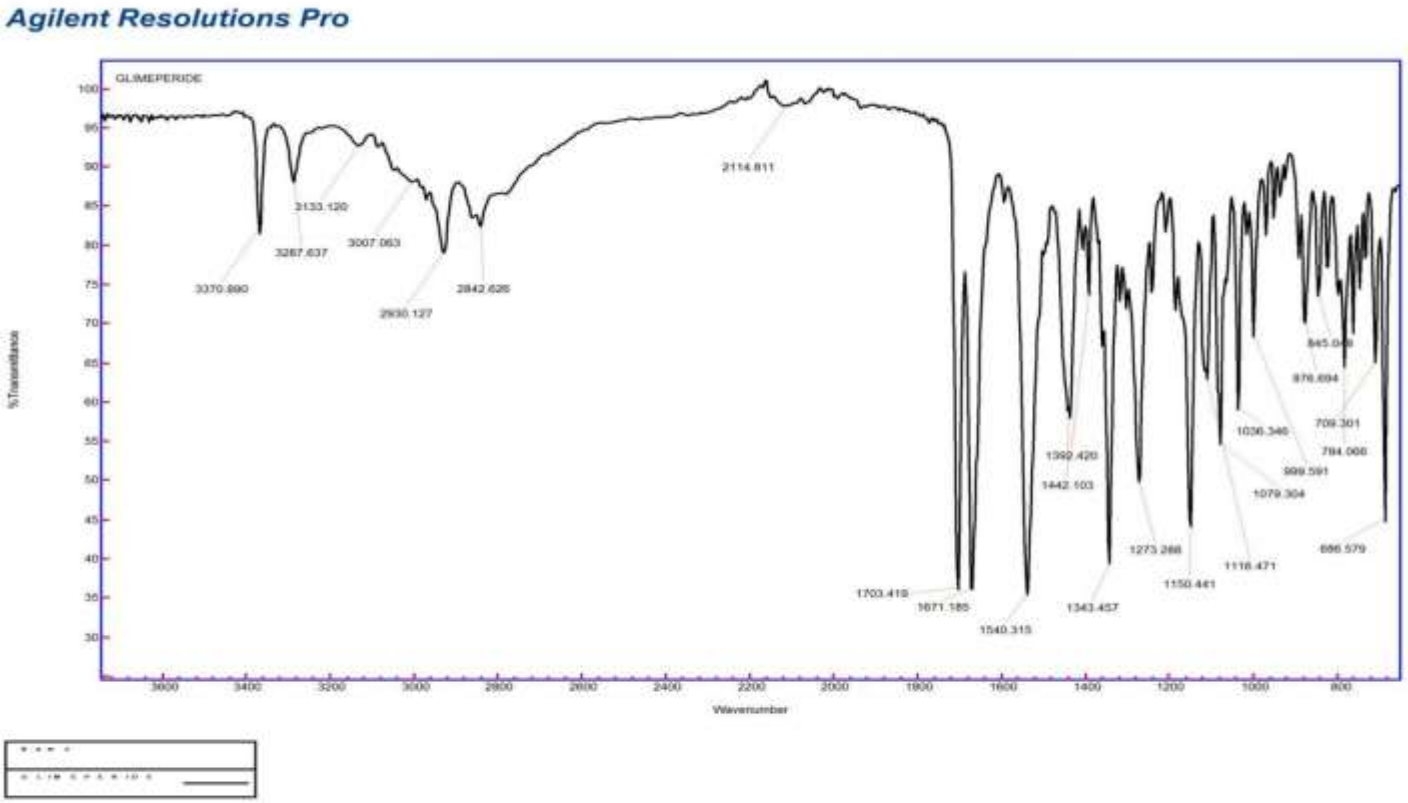

Figure 4: FTIR Spectra of Glimepiride

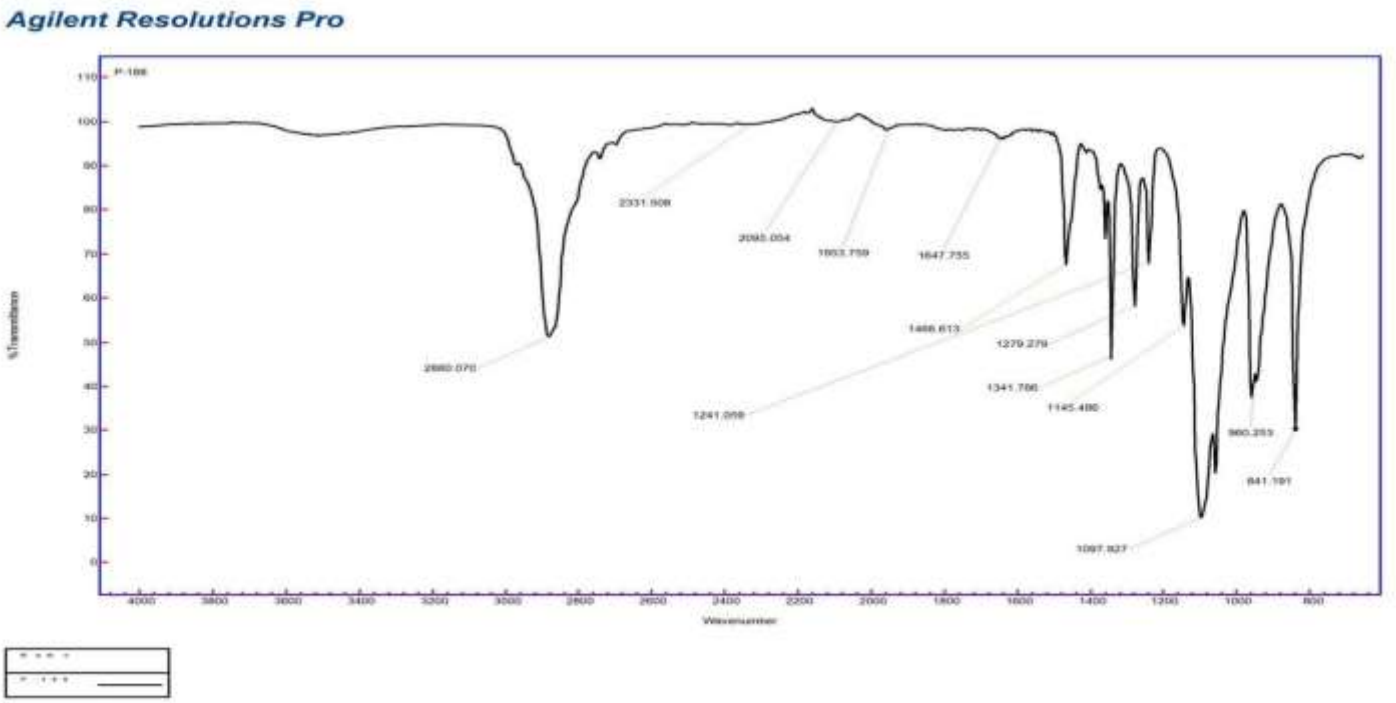

Figure 5: FTIR Spectra of Polaxomer-188

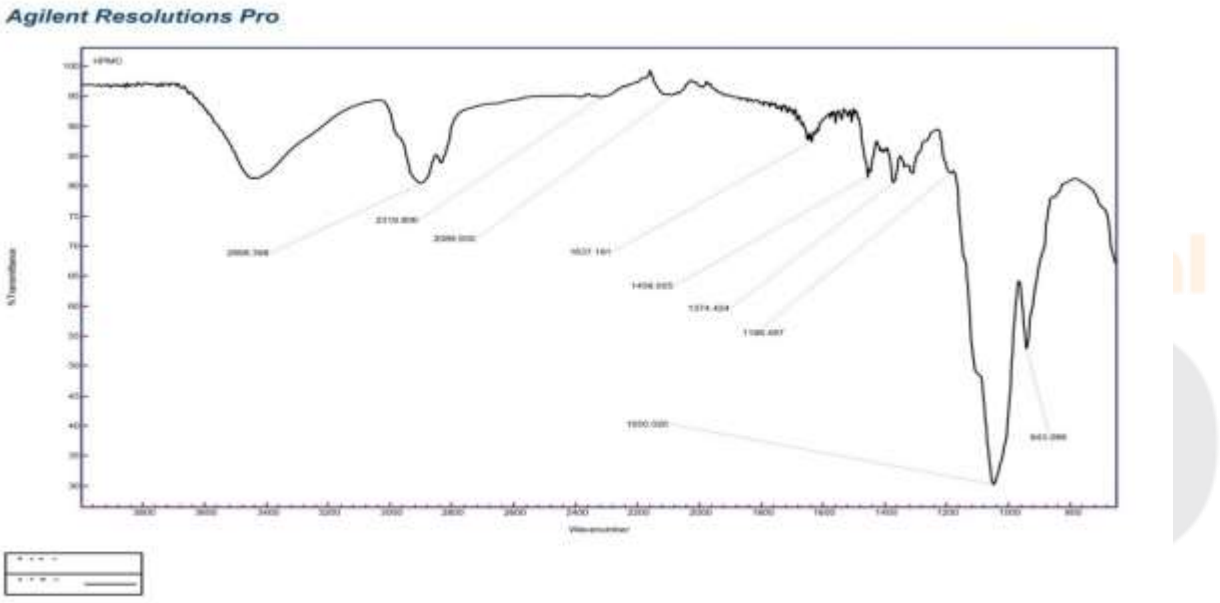

Figure 6: FTIR Spectra of HPMC[E_{50}]

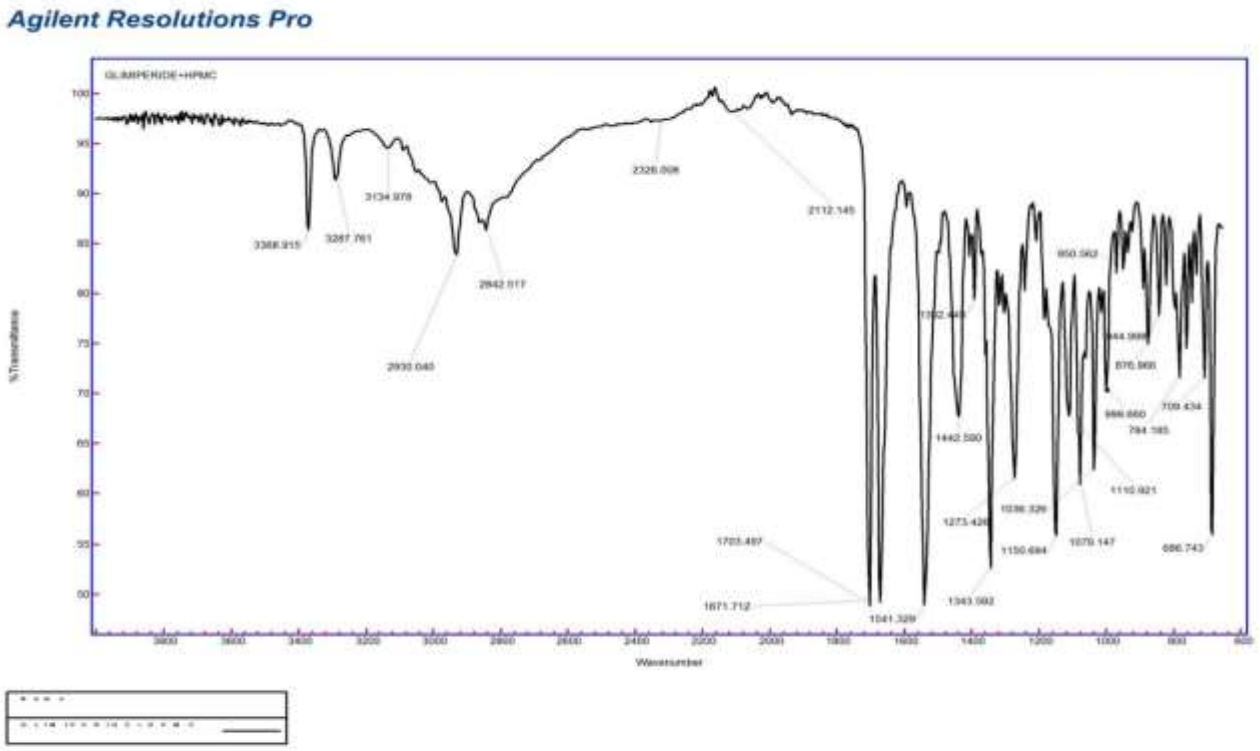

Figure 7: FTIR Spectra of Glimepiride+HPMC[E_{50}]

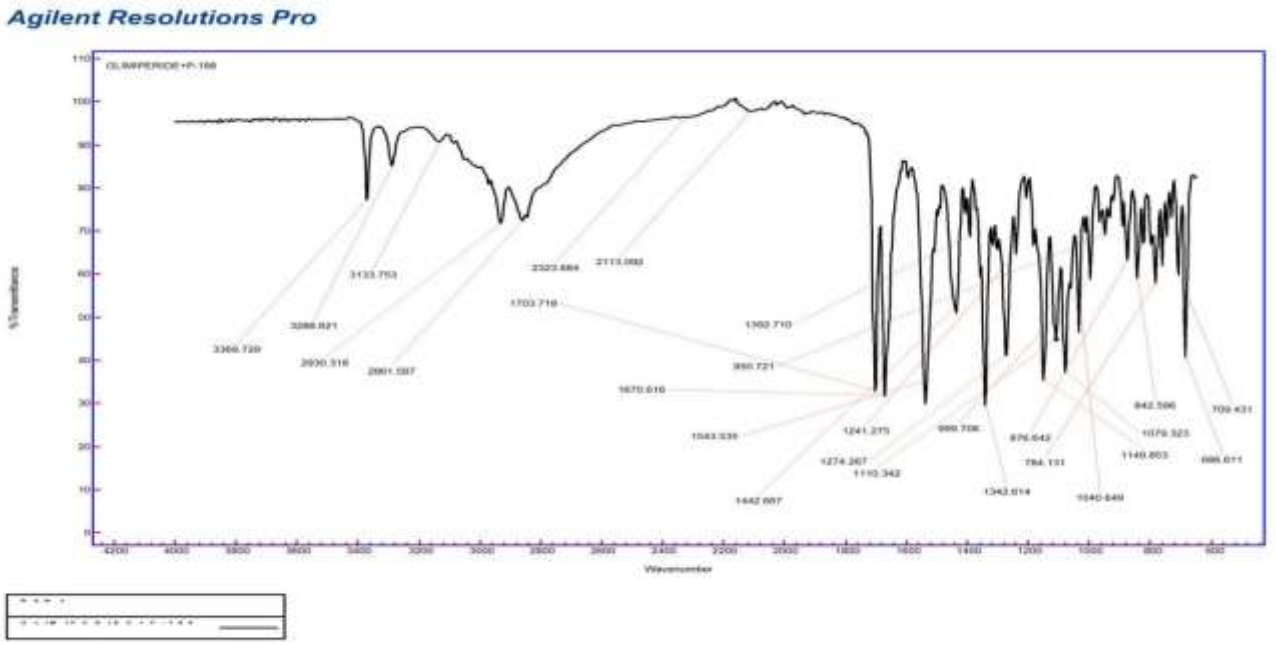

Figure 8: FTIR Spectra of Glimepiride+P-188

Standard calibration curve ofGlimepiride:

Standard curve of Glimepiride was determined by plotting absorbance vsconcentration (µg/mL) at 227nm. The results were obtained are as follows.

Table 6: Calibration curve of Glimepiride in 6.8 phosphate buffer:

S.no	Concentration(µg/ml)	Absorbance at 227nm
1	0	0
2	5	0.0550
3	10	0.0849
4	15	0.1122
5	20	0.1599
6	25	0.1828

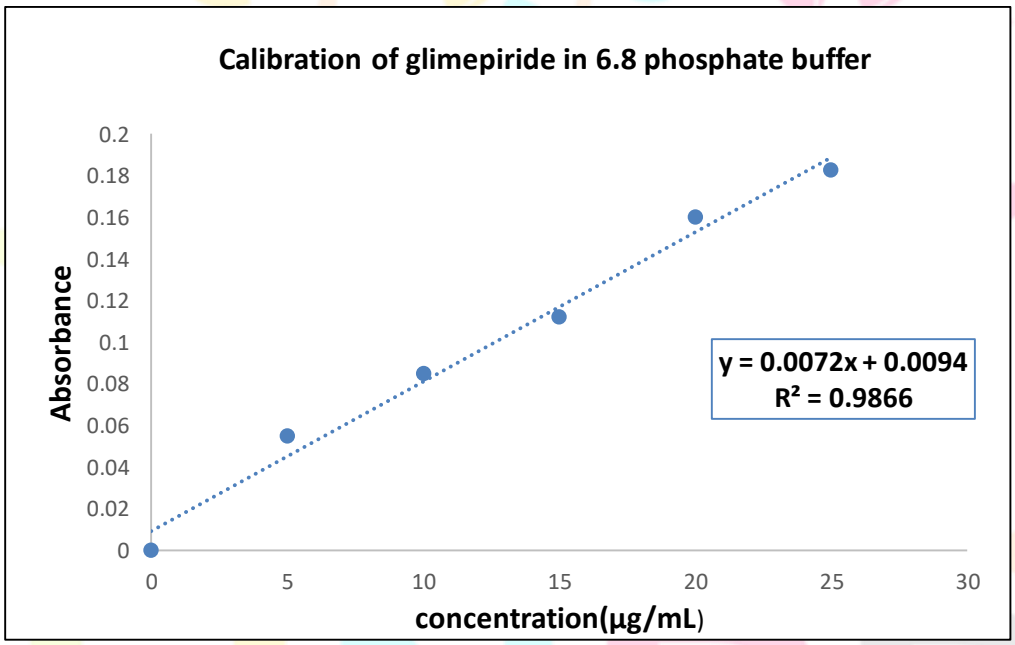

Figure 9: Standard calibration curve of Glimepiride in 6.8 phosphate buffer

PH:

Table 7: PH of different formulations:

S.no	Name of the formulation	PH
1	F1	7.11
2	F2	7.32
3	F3	7.37
4	F4	6.70
5	F5	6.45
6	F6	7.30

DENSITY:

Table 8: Density of different formulations:

S.no	Name of the formulation	Density(gm/ml)
1	F1	0.936
2	F2	0.938
3	F3	0.975
4	F4	0.972
5	F5	1.0029
6	F6	1.0034

VISCOSITY:

Table 9: Viscosity of different formulations:

S.no	Name of the formulation	Stress	Viscosity(cp)
1	F1	2.5%	7.5
2	F2	2.5%	7.3
3	F3	2.5%	8.4
4	F4	2.5%	8.2
5	F5	2.5%	10.2
6	F6	2.5%	10.0

Particle size of Glimepiride:

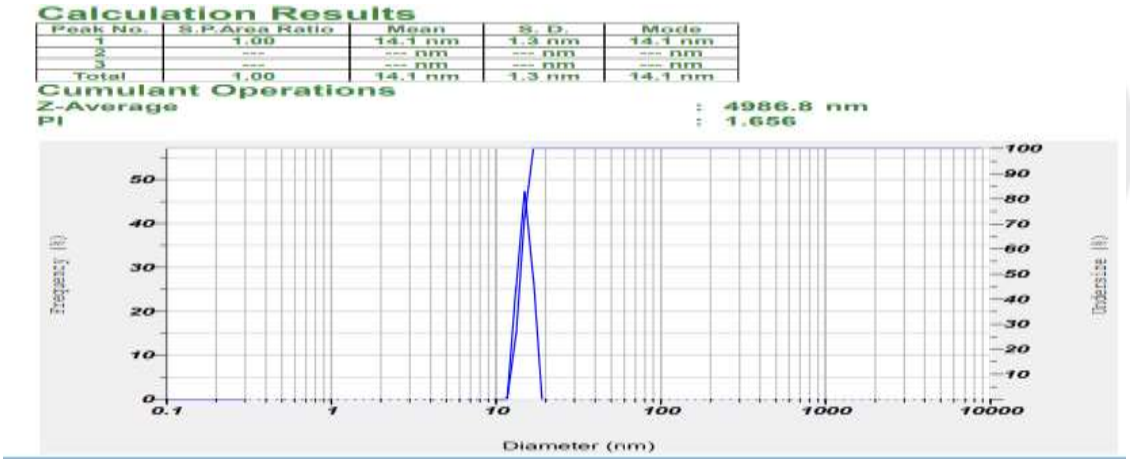

Figure 10: Particle size for F4 Formulation

Zeta Potential:

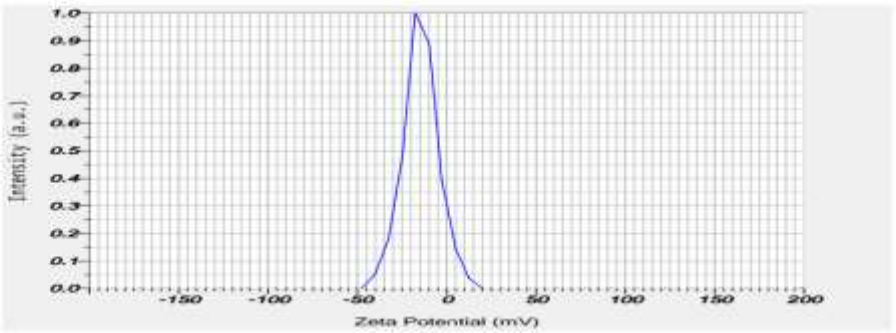

Figure 11: Zeta Potential for F4 Formulation

Entrapment efficiency:

The highest % entrapment efficiency (%EE) values were found to be 91% respectively for the F4 formulation which was found to be better compared to the other formulations (F1, F2, F3, F6.) the results reveals the drug was successfully entrapped in the nanoparticle and the encapsulated drug loaded into unit wait of Nanoparticle. Hence F4 formulation was optimized based on evaluation parameters.

Table 10: Entrapment efficiency values

S.no	Name of the formulation	%Entrapment efficiency
1	F1	75%
2	F2	80.5%
3	F3	83%
4	F4	91%
5	F5	85%
6	F6	85.13%

IN-VITRO DRUG RELEASE FOR GLIMEPIRIDE NANOSUSPENSION:

The Glimepiride Nanosuspensionwasprepared (F1-F6) by using HPMC, Polaxomer-188.In-vitro drug release study of Glimepiride Nanosuspension (F1-F6) was studied by diffusion method. Nanosuspensiondispersionequivalent to 5ml of Glimepiride Nanosuspension was taken in a dialysis bag and tied at the both ends. The dialysis bag was immersed in a dissolution medium containing 100ml of 6.8 phosphate buffer and stirred at 50rpm. 1ml of sample was withdrawn at various time intervals (1, 2, 3, 4, 5, 6, 8, 10,12hrs) and replaced by the fresh dissolution medium with the same volume to maintain sink condition. Each withdrawn sample was diluted to 10ml. The drug concentration was measured by UV-visible

spectrophotometer at 227nm. The %cumulative drug release (%CDR) from the different formulations was calculated.

Table 11: In-vitro release profile for Glimepiride Nanosuspension Formulations:

Time(hrs)	Formulation percentage drug release (%)					
	F1	F2	F3	F4	F5	F6
1	9	8	11	13	9	11
2	14	15	23	26	22	25
3	28	30	35	37	34	40
4	32	43	42	50	48	49
5	48	55	53	65	53	55
6	55	62	64	74	62	66
8	69	75	72	82	78	79
10	77	80	83	91	86	87
12	82	87	92	98	89	90

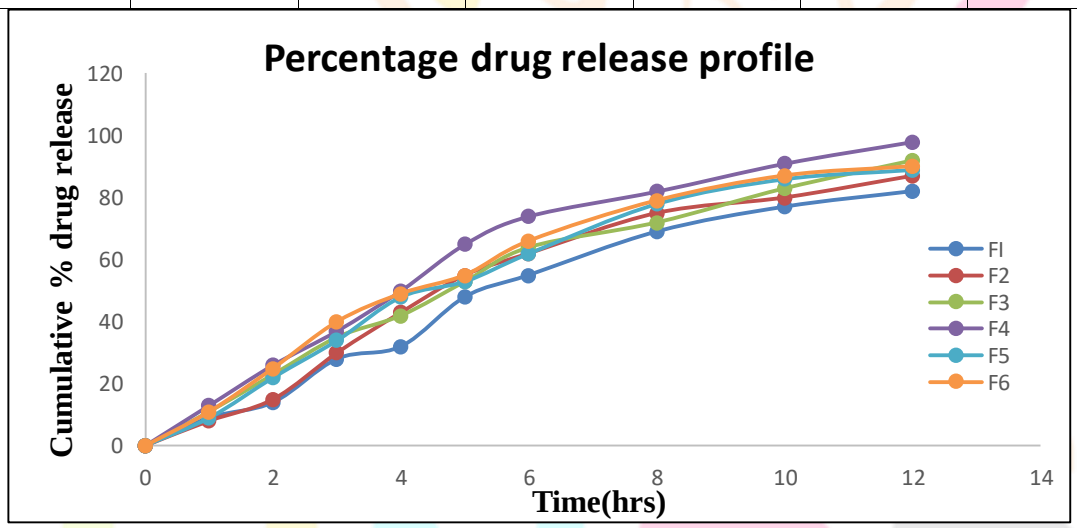

Figure 12: Percentage drug release for different formulations

Table 12:In-vitro Release Profile for Glimepiride Nanosuspension-Formulation (F1)

Time (hrs)	Absorbance at 227nm	Concentration (µg/ml)	Amount of Drug Release(mg/100ml)	Cumulative % Drug Release
0	0	0	0	0
1	0.0130	1.8056	1.8056	9
2	0.0202	2.8056	2.8056	14
3	0.0403	5.5972	5.5972	28
4	0.0461	6.4028	6.4028	32
5	0.0691	9.5972	9.5972	48

6	0.0792	11.00	11.00	55
8	0.0994	13.80	13.80	69
10	0.1109	15.4028	15.4028	77
12	0.1181	16.4028	16.4028	82

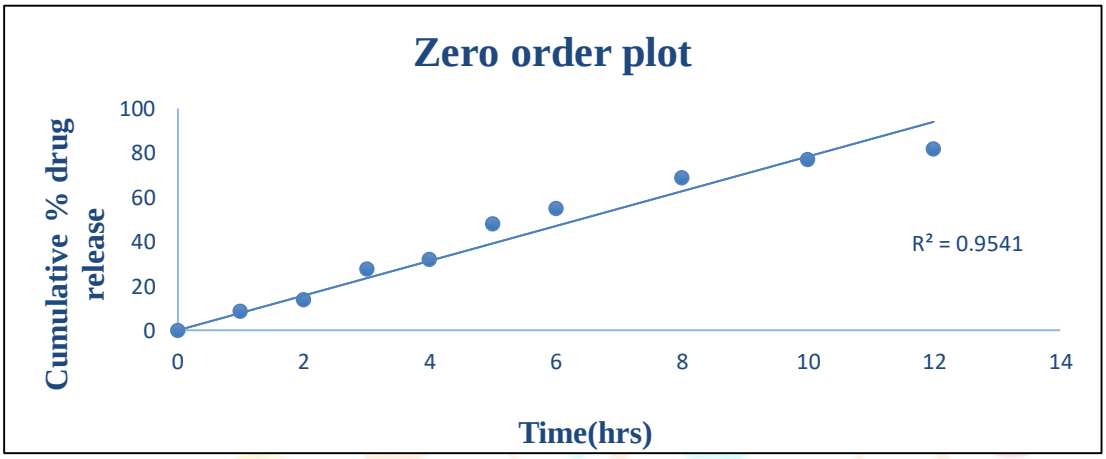

Figure 13: Zero order plot for F1

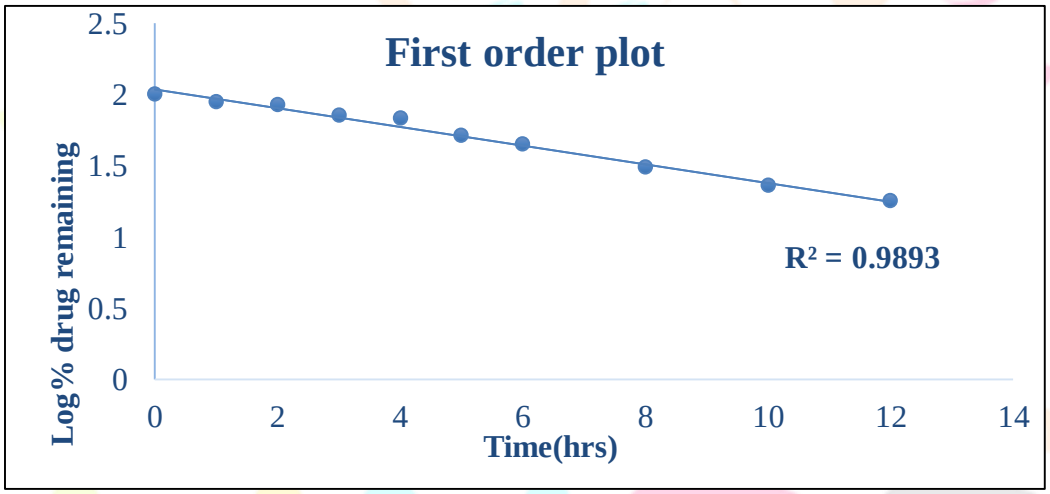

Figure 14: first order plot for F1

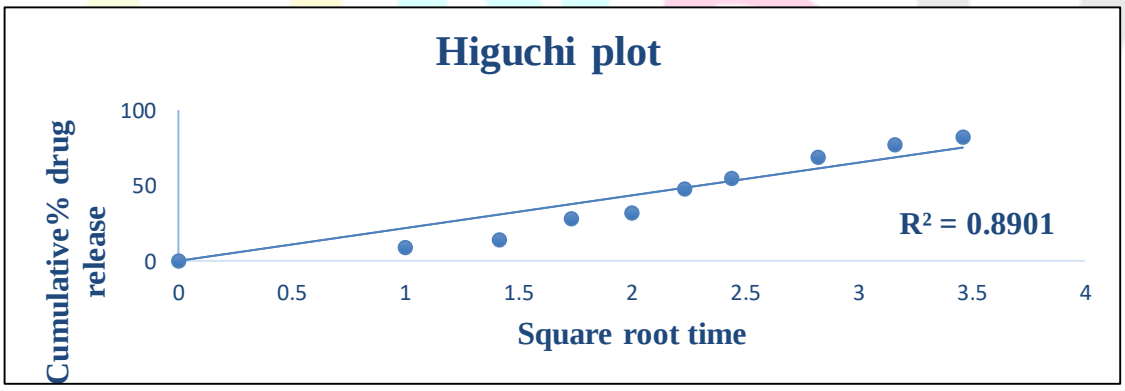

Figure 15: Higuchi plot for F1

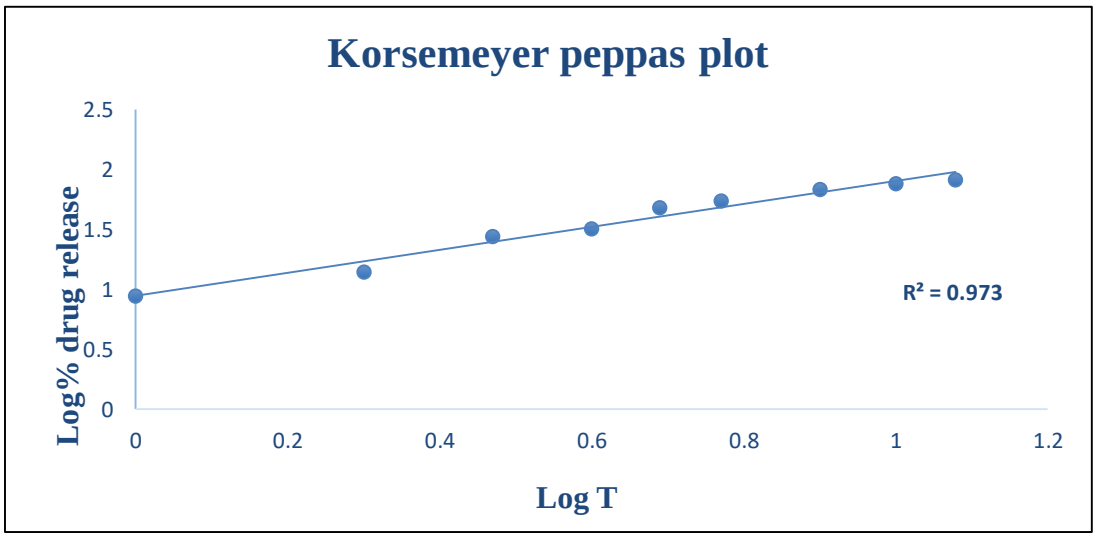

Figure 16: Korsemeyer plot for F1

Table 13: In-vitro Release Profile for Glimepiride Nanosuspension-Formulation (F2)

Time (hrs)	Absorbance (nm)	Concentration (µg/ml)	Amount of Drug Release(mg/100ml)	Cumulative % Drug Release
0	0	0	0	0
1	0.115	1.5972	1.5972	8
2	0.0216	3.00	3.00	15
3	0.0432	6.00	6.00	30
4	0.0619	8.5972	8.5972	43
5	0.0792	11.00	11.00	55
6	0.0893	12.4028	12.4028	62
8	0.1080	15.00	15.00	75
10	0.1152	16.00	16.00	80
12	0.1253	17.4028	17.4028	87

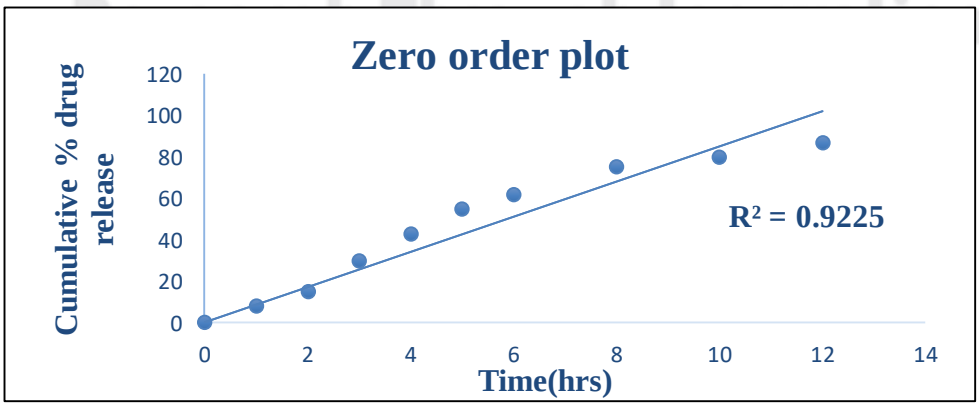

Figure 17: Zero order plot for F2

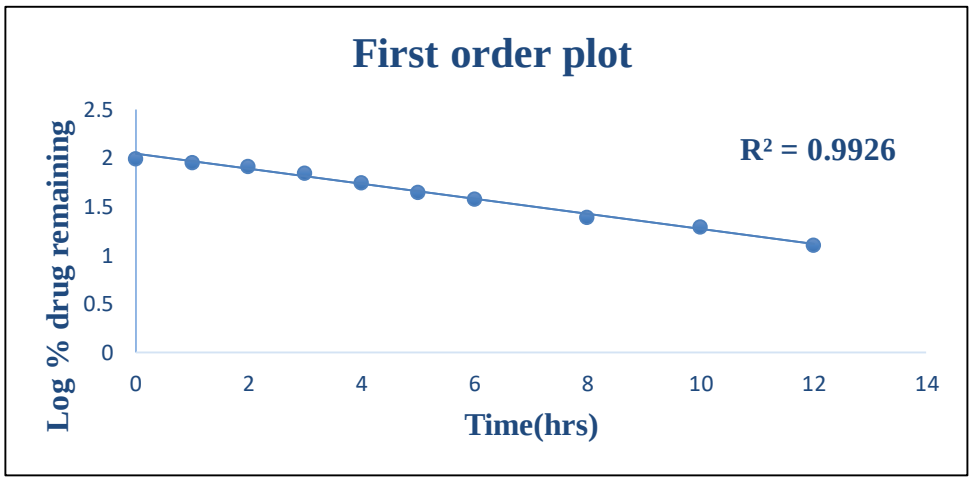

Figure 18: first order plot for F2

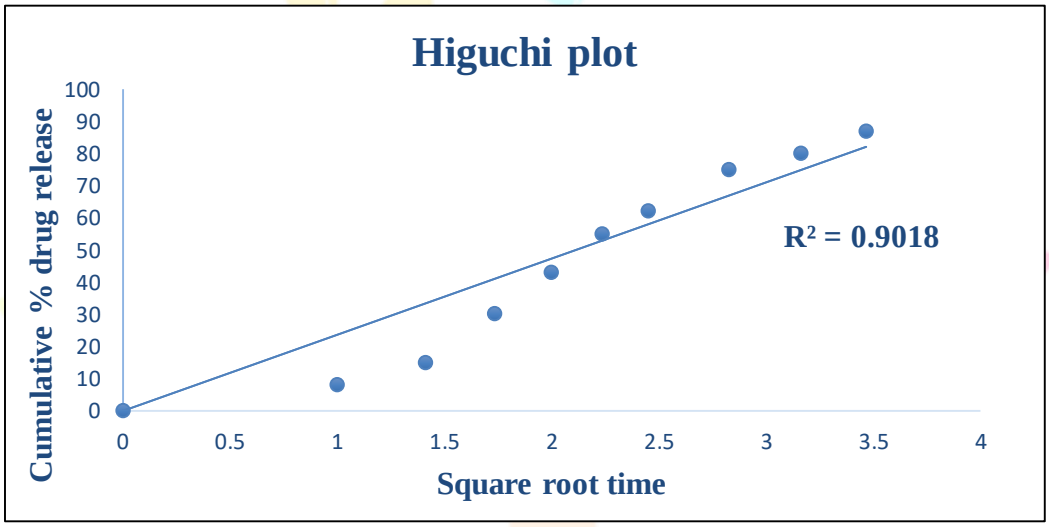

Figure 19: Higuchi plot for F2

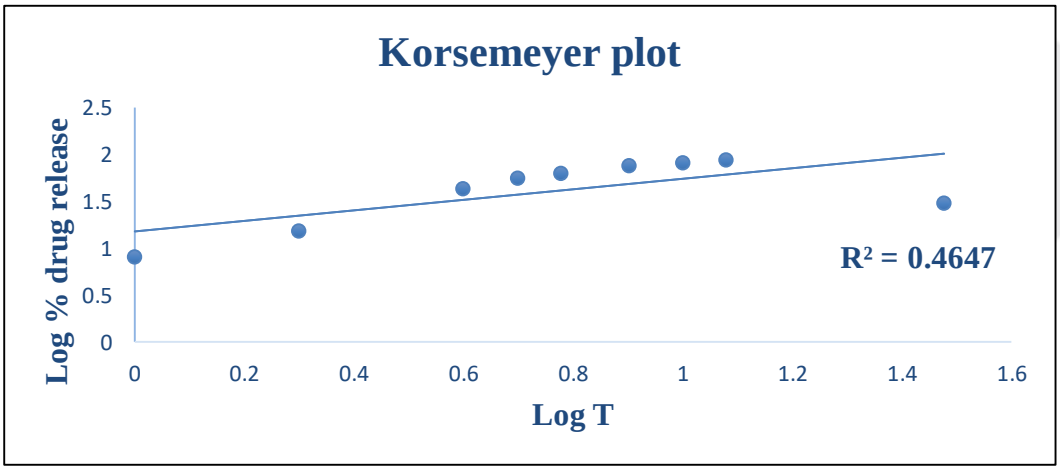

Figure 20: Korsemeyer plot for F2

Table 14: In-vitro Release Profile for Glimepiride Nanosuspension-Formulation (F3)

Time (hrs)	Absorbance (nm)	Concentration (µg/ml)	Amount of Drug Release(mg/100ml)	Cumulative % Drug Release
0	0	0	0	0
1	0.0158	2.1922	2.1922	11
2	0.0331	4.5972	4.5972	23
3	0.0504	7.00	7.00	35
4	0.0605	8.4028	8.4028	42
5	0.0763	10.597	10.597	53
6	0.0922	12.8056	12.8056	64
8	0.1037	14.4028	14.4028	72
10	0.1195	16.5972	16.5972	83
12	0.1325	18.4028	18.4028	92

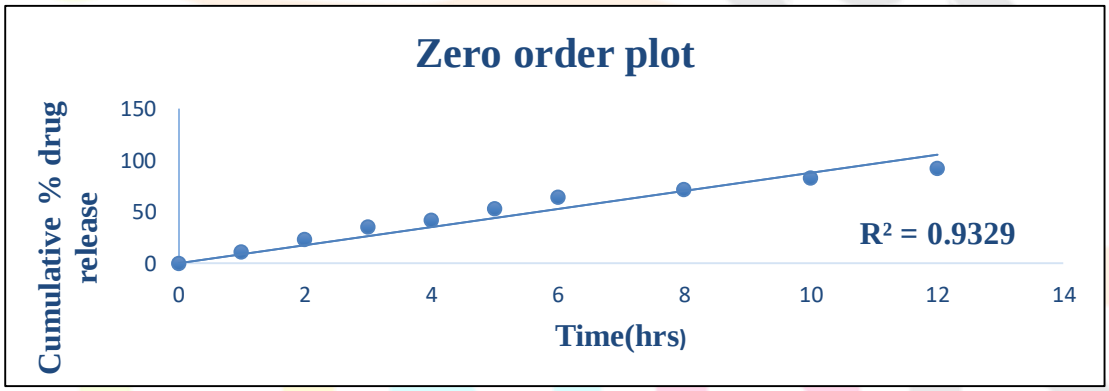

Figure 21: zero order plot for F3

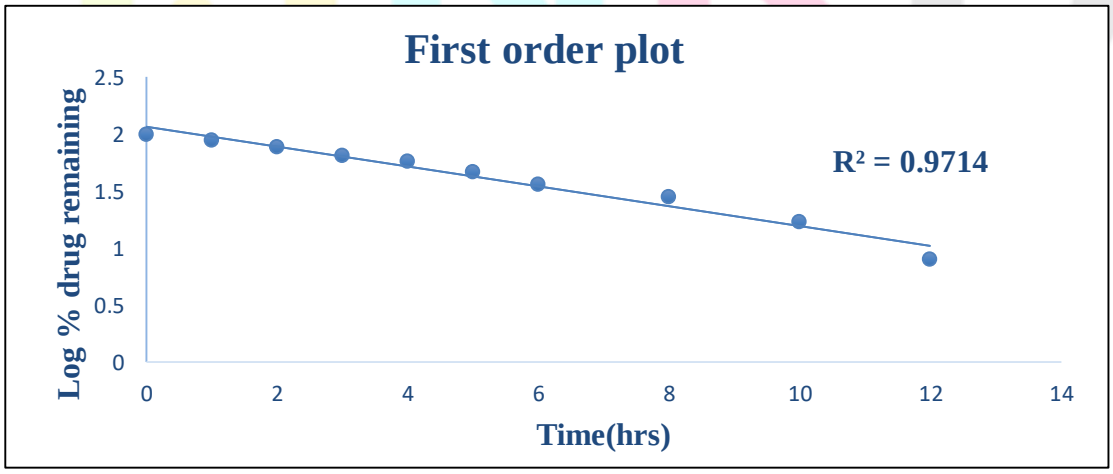

Figure 22: first order plot for F3

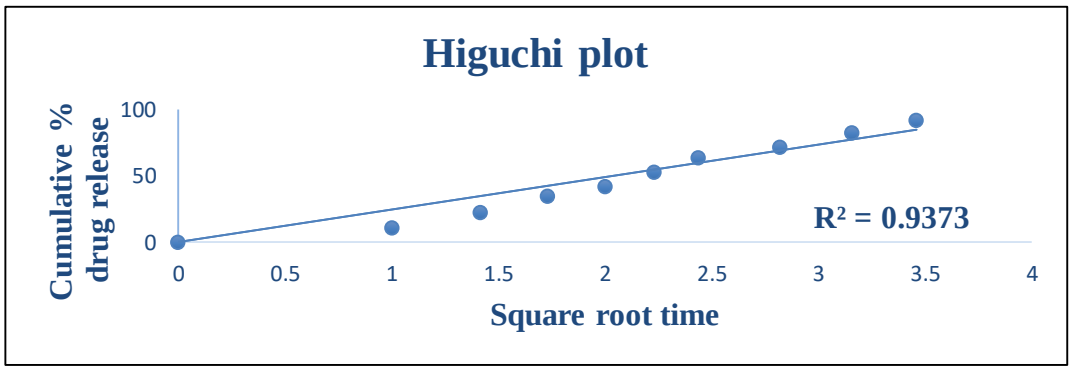

Figure 23: Higuchi plot for F3

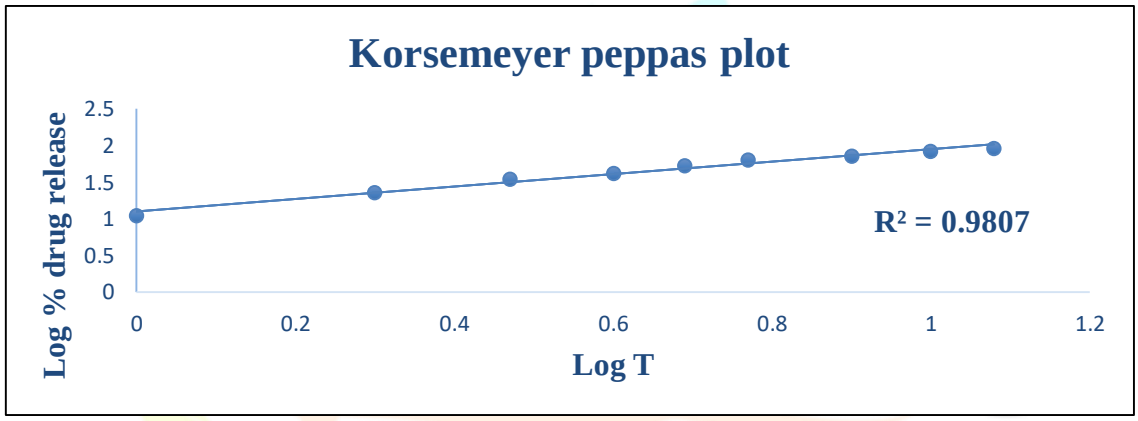

Figure 24: Korsemeyer plot for F3

8. DISCUSSION

Particle size:

The prepared Glimepiride nanosuspension wasanalyzed by particle size analysis. The particle size of Glimepiride nanosuspension was found to be 14.1nm. The colloidal nanoparticles size was ranging from 10-1000 nm .The Glimepiride nanosuspension particle size was within the permissible range.

Zeta potential:

Zeta potential of Glimepiride nanosuspension was measured by photon correlation spectroscopy (PCS). The zeta size (horiba-SZ-100 for window Z type version 2.0) was used at 173° fixed angle and 25.0°C for measurement. The mean zeta potential of Glimepiride nanosuspension of F4 formulation was found to be -14.6mV.The shift in the zeta potential to more negativevalue is mainly due to presence of negatively charged functional group of Glimepiride. Hence the value indicates successful loading of Glimepiride into the particles.

Fourier transforminfrared spectroscopy (FTIR):

FTIR Spectra of a pure Glimepiride with and its physical mixture (1:1 ratio wt/wt) with the excipients used in this study

The results revealed that functional groups of Glimepiride (wave number) were found interpretation of Glimepiridenanosuspension. They have been explained that Glimepiride is compatible with excipients which are used for Nanosuspensionformulation.

Entrapment efficiency:

The highest % entrapment efficiency (%EE) value was found to be 91% for F4 formulation. It was found to be better compared to the other formulations (F1, F2, F3, F5, and F6). the results reveals the drug was successfully entrapped in the nanoparticles and the encapsulated drug loaded into unit weight of the nanoparticles. Hence F4 formulation was optimized based on evaluation parameters.

P^H:

P^H tests were performed for all the six formulations by using P^H meter. The P^H value for F4 formulation was found to be 6.70 which is almost equal to intestinal P^H due to which it shows more solubility.

9.CONCLUSION

It is evident from the result of formulation F4 which is formulated with 400 mg of HPMC with 2 hrs of agitation shows maximum and better release at the end of 12 hrs., when compared with remaining formulations. This may be due to reduction in particle size, more agitation time, Polymer drug ratio and more entrapment efficiency. All the six formulations exhibited fickian drug release mechanism.

10. BIBLIOGRAPHY

1. Agrawal, Y., Patel, V., 2011. Nanosuspension: An approach to enhance solubility of drugs. J. Adv. Pharm. Technol. Res. 2, 81–87.
2. Arunkumar, N., Deecaraman, M., Rani, C., 2011. Nanosuspension technology and its applications in drug delivery. Asian J Pharm 3, 1–5.
3. Arunkumar, N., Deecaraman, M., Rani, C., Mohanraj, K.P., Venkateshkumar, K., 2010. Formulation development and in vitro evaluation of Nanosuspensions loaded with Atorvastatin calcium AmrutaPapdiwal*, K.S. and V.P., 2016. Formulation and evaluation of Irbesartannanosuspension by precipitation method. Der Pharm. Lett. 8, 502–510.
4. Kavitha, V.B., Neethu, C.S., Dineshkumar, B., Krishnakumar, K., John, A., 2014. Nanoscience and Nanotechnology : An International Journal ISSN : 2278-1374
5. Patil, M.S., Godse, S.Z., Saudagar, R.B., 2013. Solubility Enhancement By Various Techniques: an. World J. Pharm. Pharm. Sci. 2, 4558–4572.
6. Detroja, C., Chavhan, S., Sawant, K., 2011. Enhanced antihypertensive activity of candesartan cilexetilnanosuspension: Formulation, characterization and pharmacodynamic study. Sci. Pharm. 79, 635–651.
7. Kumar, B.P., Baig, A.A., 2010. Formulation and evaluation of Pitavastatinnanosuspension. J. Chem. Pharm. Sci. 7, 330–335.
8. Zhang, D., Tan, T., Gao, L., Zhao, W., Wang, P., 2007. Preparation of azithromycin Nano suspensions by high pressure homogenization and its physicochemical characteristics studies. Drug Dev. Ind. Pharm. 33, 569–575.
9. Kocbek, P., Baumgartner, S., Kristl, J., 2006. Preparation and evaluation of nanosuspensions for enhancing the dissolution of poorly soluble drugs. Int. J. Pharm. 312, 179–186.
10. Langguth, P., Hanafy, A., Frenzel, D., Grenier, P., Nhamias, A., Ohlig, T., Vergnault, G., Spahn-Langguth, H., 2005. Nanosuspension Formulations for Low-Soluble Drugs: Pharmacokinetic Evaluation Using Spironolactone as Model Compound. Drug Dev. Ind. Pharm. 31, 319–329. doi:10.1081/DDC-200052182
11. Patravale, V.B., Date, A. a, Kulkarni, R.M., 2004. Nanosuspensions: a promising drug delivery strategy. J. Pharm. Pharmacol. 56, 827–840. doi:10.1211/0022357023691
12. Ghosh I, Bose S, Vippagunta R, Harmon F, Nanosuspension for improving the Bioavailability of a poorly soluble drug and screening of stabilizing agents to inhibit crystal growth. International Journal of Pharmaceutics. 2011; 409: 260-268.
    Lei Gao, Dianrui Zhang, Minghui Chen, T.Z. and S.W., 2007. Preparation and characterization of an Oridonin Nanosuspension for solubility and dissolution velocity enhancement. Drug Dev. Ind. Pharm. 33, 1332–1339.