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FORMULATION AND EVALUATION OF SUSTAINED RELEASE TABLETS OF VILDAGLIPTIN

[1]Deepak Lovevanshi, [2]Sunita Patidar, [3]Apurva Pagare, [4]Rajat Pawar

Swami Vivekanand College of Pharmacy, Indore (M.P)
Correspondence address: deepaklovevanshi2@gmail.com
Deepak Lovevanshi

ABSTRACT:

This study aimed to The Present research endeavor is directed towards the developmentof Once daily sustained release Tablets of vildagliptin 100mg. The different concentration of polymer was used to control the drug release from the dosage form. This sustained release tablet is effective in improving the type II diabetic glucose control. Sustained release System was based on Natural polymer was selected for sustaining the drug release. Different polymers toget the desired release profile over a period for 12 hours. Different batches of sustained release were prepared by direct compression method respectively. All the formulations were evaluated for physical characteristics, pre- compression properties, in vitro dissolution study, kinetic study andstability. Following conclusions have been made from the present study. The physical characteristics of all the blended formulations were satisfactory. The prepared tablets evaluated for Assay, weight variation,thickness and Friability were found to be within the official limits. The *in vitro* dissolution studies were performed for all the SR formulations *In Vitro* Dissolution study of SR formulations F8 showed release profile were satisfactory with respect to drug compared with another 8 formulation

Keywords: Vildagliptin, sustained release, *in vitro* dissolution, Type II diabetic glucose ,Stability studies

INTRODUCTION :

1.1. SOLID DOSAGE FORMS

Oral ingestion is the preferred route for administration of therapeutic agents, providing a convenient method of effectively achieving both local and systemic effects. Routes of drug administration that can be utilized in order to achieve systemic delivery of a drug include: parenteral, oral, buccal, transdermal, nasal and pulmonary. No single route matches all the physiological requirements of an"ideal" absorption site. But, considering surface area, low metabolic activity, contact time, blood supply, accessibility, lack of variability and permeability, relatively oral route is having more suitable characteristics for absorption of drugs.

Among the pharmaceutical dosage forms, oral dosage forms are having maximum attribute of ideal dosage forms Patients are usually accustomed to orally delivered drugs and find the method non invasive. Today it is estimated that around 80% of all medications used utilize the oral route, in which tablets, capsules and granules continue to remain the dosage form of first choice. It istherefore important that oral drug delivery technology continues to advance and improve the safety and efficacy of treatment.

Oral dosage forms represent the vast majority of the drug-delivery market because of the safety, efficacy, economic, and consumer compliance advantages they possess over alternative routes of delivery. Transdermal, injectable, and inhalation routes possess significant regulatory, technical and compliance barriers to their economical application towards a wide a range of compounds

MATERIALS AND METHODS :

Preformulation Studies:

Pre-formulation studies are the first step in the rational development of dosage form. It is an investigation of physical and chemical properties of a drug substance alone and when combined with excipients. Pre-formulation investigations are designed to identify those physicochemical properties and excipients that may influence the formulation design, method of manufacture, and pharmacokinetic- biopharmaceutical properties of the resulting product. Following are the test performed for the pre-formulation study.

Description

Appearance of the material was noted compared with specifiedmonograph or with standard materials.

Identification

Identification is the important parameter for Qualitative Analysis ofmaterials. Material was identified by chemical and FT-IR method.

Solubility Analysis:

Solubility is an important parameter for preformulation studies because affects the dissolution of drug. Bioavailability of drug is directly affected by dissolution and absorption of drug by oral administration. Particle size, shape, surface area may affects the dissolution characteristics of drug hence it should be determined during Preformulation.

Table No.1: Solubility description

Descriptive Term	Approximate volume of solute in milliliters per gram of solute
Very Soluble	Less than 1
Freely soluble	From 1 to 10
Soluble	From 10 to 30
Sparingly soluble	From 30 to 100
Slightly soluble	From 100 to 1000
Very slightly soluble	From 1000 to 10000
Practically insoluble	More than 10000

Method: Appropriate quantity of drug was weighed and added to the suitable volume of solvent.

Loss on drying (%)

1g of drug was accurately weighed and dried in an oven at 105°Cfor 3 hours. By gentle sidewise shaking, the sample was distributed atthe specified temperature for constant weight.

The drug sample was allowed to come to room temperature in a desiccator before weighing.(69) The difference between successive weights should not be more than 0.5mg The loss on drying is calculated by theformula:

$$\% \text{ LOD} = \frac{W3 - W2}{W2 - W1} X\ 100$$

Where, $W1$ – Weight of empty weighing bottle $W2$ – Weight of weighing bottle + sample

$W3$ – Weight of weighing bottle + dried sample

Melting point determination :

The melting point of Active ingredients were determined by capillary method, using definite quantity of Active ingredients were taken and placed in apparatus and melting point was determined and matched with standards.

Angle of repose:

The flow characteristics are measured by angle of repose. Improper flow of powder is due to frictional forces between the particles. These frictional forces are quantified by angle of repose. Angle of repose is defined as the maximum angle possible between the surface of a file of the powder and the horizontal plan.

$$\text{Ø} = \text{Tan}^{-1}\, h/r \quad \text{Where, } h = \text{height of file}$$

R = radius of the base of the pile Ø = angle of repose

Flow properties and corresponding Angle of Repose:

Table.No: 2 Flow properties and corresponding Angle of Repose

Flow property	Angle of Repose (Degree)
Excellent	25-30
Good	31-35
Fair-aid not needed	36-40
Passable- may hang up	41-45
Poor- must agitate, vibrate	46-55
Very poor	56-65
Very, very poor	> 66

The ideal characteristics of a tablet that make it a popular and acceptable dosage form are compactness, physical stability, rapid production capability, chemical stability and efficacy. In general above characteristics of tablet are dictated by the quality of the granulation from which it is made. Many formulation and process variables involved

in the granulation step can affect the characteristics of the granulation produced. Therefore various methods to measure certain granulation characteristics have been developed to monitor granulation suitability for tablet formulation. The main characteristics required to be monitored in granulation are flow properties and compressibility.

Compressibility index :

The compressibility Index and Hausner ratio are measures of the property of a powder to be compressed. As such, they measure the relative importance of inter particulate interactions. In a free flowing powder, such interactions are generally less significant, and the bulk and tapped densities will be closer in value. For poorer flowing materials, there are frequently greater inter particle interactions, and a greater difference between the bulk and tapped densities will be observed. These differences are reflected in the compressibility index and the Hausner ratio.

The compressibility index and Hausner ratio are calculated by measuring the values for bulk density (P_{bulk}) and tapped density (P_{tapped}) as follows:

$$\text{Compressibility index} = P_{tapped} - P_{bulk}/P_{tapped} \times 100 \qquad \text{Hausner ratio} = P_{tapped} / P_{bulk}$$

Table.No.3. Scale of flowability

Compressibility index (%)	Flow character	Hausner Ratio
≤ 10	Excellent	1.10-1.11

11-15	Good	1.12-1.18
16-20	Fair	1.19-1.25
21-25	Passable	1.26-1.34
26-31	Poor	1.35-1.45
32-37	Very poor	1.46-1.59
>38	Very, very poor	>1.60

Bulk density :

The powder sample (blend) under test was screened through sieve #18 and the sample equivalent to 20gm was accurately weighed and filled in a 100ml graduated cylinder and the powder was leveled and the unsettled volume (V_0) was noted.

Drug and Drug – Excipient Physical Compatibility Studies:

The Active ingredients and excipients were mixed and taken in 2 ml glass vials and sealed. These glass vials are kept at Room Temperature and 40°C / 75 % RH for about 1 month. At the interval of 10 days, the samples were withdrawn and analysed for colour change.

Drug and Drug – Excipient Compatibility Studies:

The successful formulation of a stable and effective dosage form depends on the careful selection of the excipients that are added to facilitate administration, promote the consistent release and Bioavailability of the drug and protect it from degradation. The excipients are selected by conducting compatibility studies with the APIs.

Procedure:

The APIs were mixed with some of the excipients that can be used for the formulation in the ratio of Drug: Excipient (1:1, 1:0.5). These are placed in stability chambers at conditions 25°C / 60 % RH and 40°C / 75 % RH for 30 days. The samples that were placed in 40°C / 75 % RH chambers were analysed with IR spectroscopy after 30 days. For IR studies Shimadzu FTIR was used. The IR spectroscopy graphs obtained were compared with standard graphs. Any possible interactions can be detected from changes in graphs of IR studies. The excipient that is causing a change will not be used in the formulation.

PREPARATION OF STANDARD CURVE

Preparation of 0.1 M Hydrochloric acid:

Accurately measure 8.5 ml of hydrochloric acid and sufficient water to make upto 1000 ml.

Preparation of stock solution:

Accurately weigh 100 mg of Vildagliptin and transfer it to a 100 ml volumetric flask. Then make up the volume to 100ml with 0.1 M Hcl.

Preparation of standard solution:

Pipette out 10 ml of the above solution and transfer it to a 100 ml volumetric flask. Then make up the volume to 100 ml with 0.1 M Hcl. Then from the standard stock solution withdraw 5ml, 10ml, 15ml, 20ml, and 25ml into five 100 ml different volumetric flasks. Then make up the volume to 100 ml with 0.1M Hcl to get 5, 10, 15, 20, 25 µg/ml concentration.

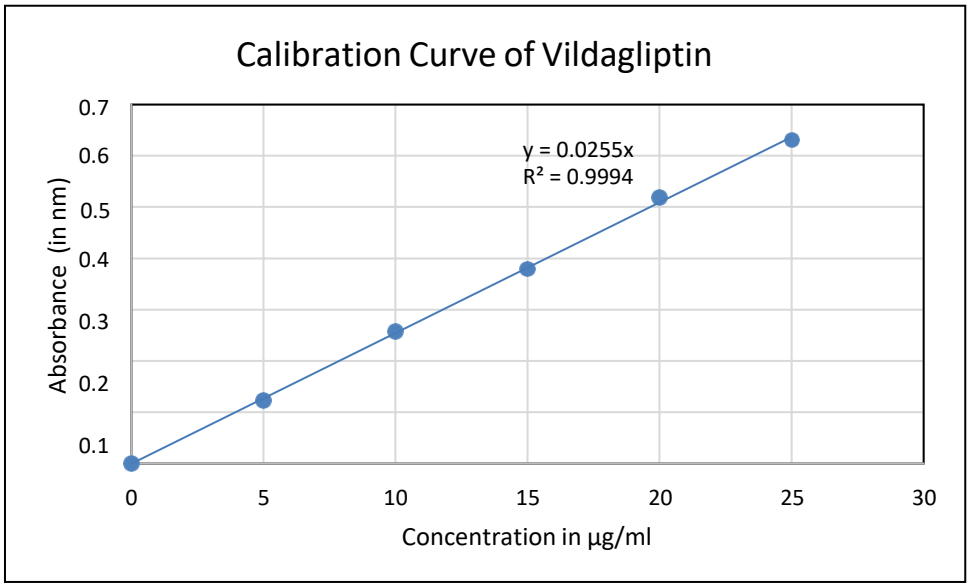
CALIBRATION CURVE OF VILDAGLIPTIN 0.1 N HCL:

The absorbance of the prepared stock solutions was measured at 232 nm in an UV spectrophotometer. Plot a graph between concentration (in µg/ml) vs absorbance (in nm) on X-axis and Y-axis respectively.

Table.No.:4. Calibration curve of Vildagliptin

S.no.	Concentration(in µg/ml)	Absorbance (in nm)
1.	0	0
2.	5	0.102
3.	10	0.201
4.	15	0.298
5.	20	0.403
6.	25	0.506
R^2	0.9999	

Figure.No.1 Calibration curve of Vildagliptin



CALIBRATION CURVE OF VILDAGLIPTIN 6.8 pH Phosphate Buffer:

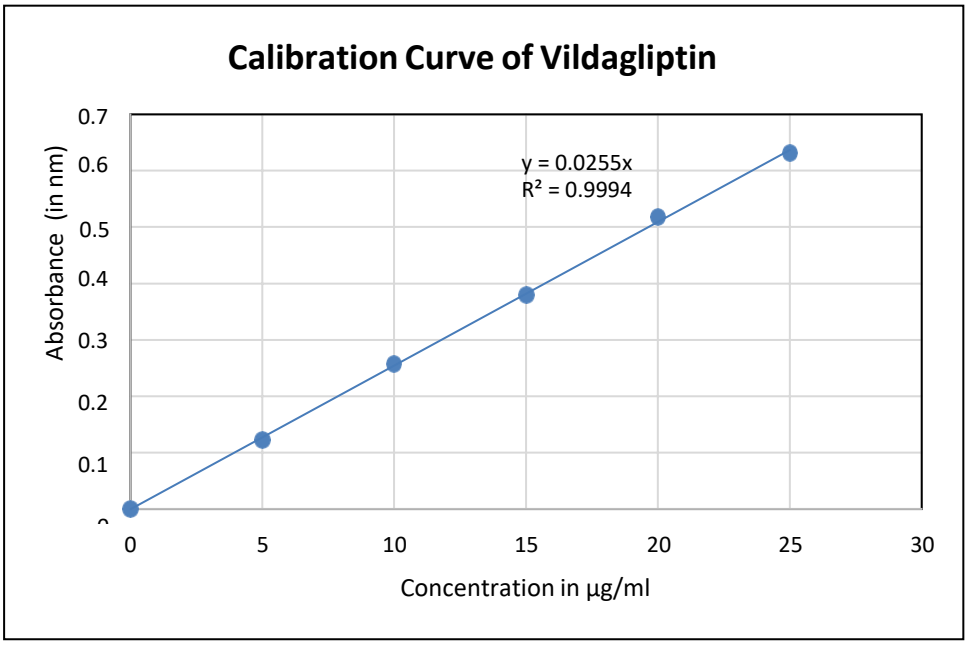
The absorbance of the prepared stock solutions was measured at 227 nm in an UV spectrophotometer. Plot a graph between concentration (in µg/ml) vs absorbance (in nm) on X-axis and Y-axis respectively.

Table.No.5. Calibration curve of Vildagliptin

S.no.	Concentration(in µg/ml)	Absorbance (in nm)
1.	0	0.000

2.	5	0.123
3.	10	0.258
4.	15	0.380
5.	20	0.519
6.	25	0.631
R^2	0.994	

Figure.No.: 2: Calibration curve of Vildagliptin



Formulation development:

Different batches of Vildagliptin sustained release tablets (F1 to F9) were prepared with varying concentrations of different formulation ingredients according to Table. Pass the all material in 80 meshes. Mix well API, polymer, Lactose then add binder, Blend well to form a coherent mass and dried in oven. And pass the granules in 18 meshes. The granules were lubricated with Magnesium stearate and compressed in proton mini press 10 station tablet punching machine. The amount required for formulation is given for following Table.

Table No.6: Formula for SR Tablet formulation

Ingredients	F1 mg	F2 mg	F3 mg	F4 mg	F5 mg	F6 mg	F7 mg	F8 mg	F9 mg
Vildagliptin	100	100	100	100	100	100	100	100	100
Guar Gum	50	100	150	-	-	-	50	50	100
Xanthan Gum	-	-	-	50	100	150	50	100	50
Lactose	148	98	48	148	98	48	98	48	48
PVK 30	3%	3%	3%	3%	3%	3%	3%	3%	3%
Magnesium Sterate	2	2	2	2	2	2	2	2	2
Total	**300**	**300**	**300**	**300**	**300**	**300**	**300**	**300**	**300**

EVALUATION

Pre-compression parameters for core & press coated tablets:

Angle of repose:

Take a small quantity of powder (5 gm) in a cone shaped funnel and fix it to a holder at an appropriate height say 6 cm above the surface. Place a graph sheet below it. The sample was passed slowly through the funnel. The height of the powder heap was formed. Then measure the circumference of the heap by drawing with the pencil on the graph sheet. The radius of the heap was measured. The angle of repose is calculated by using the following formula. This is repeated five times for accurate results.

$$\text{Ø} = \text{Tan}^{-1}\ h/r$$

Where,h = height of file

R= radius of the base of the pileØ = angle of repose

Bulk density and Tapped density:

Weigh a small quantity of the powder (w) was carefully poured into the graduated cylinder and the volume (v_0) was measured. Then the graduated cylinder was closed with lid, set into the density determination apparatus (Bulk density apparatus) set for 500 taps and after that, the volume (vf) was measured and continued operation till the two consecutive readings were equal.

The bulk density and tapped density were calculated using thefollowing formulas.

$$\text{Bulk Density} = W/V_0 \qquad \text{Tapped Density} = W/V_f$$

Where, V_0= Initial volume,V_f = final volume

.

Compressibility index and Hausner ratio:

The compressibility index and hausner ratio are calculated by measuring the values for bulk density (P_{bulk}) and tapped density (P_{tapped})as follows:

$$\text{Compressibility index} = P_{tapped} - P_{bulk}/P_{tapped} \times 100 \qquad \text{Hausner ratio} = P_{tapped} / P_{bulk}$$

Evaluation of Formulated Tablets of Vildagliptin

All the formulated sustained release tablets were evaluated for following official and unofficial parameters.

Weight Variation

Twenty tablets were randomly selected from each batch and individually weighed. The average weight and standard deviation of twenty tablets was calculated. The batch passes the test for weight variation test if not more than two of the individual tablet weight deviates from the average weight by more than the percentage shown in a nonedeviate by more than twice the percentage shown.

$$\% \text{ deviation} = \frac{\text{tablet weight-average weight}}{\text{Tablet weight}} \times 100$$

Observation:

The average weight and standard deviation of the tablets of eachbatch were given.

Weight variations Specification

Table.No.7.Weight variations Specification

Average weight of tablets(X mg)	Percentage deviation
130 or less	±10
130 to 324	±7.5
More than 324	±5

Dimensions

Control of physical dimension of the tablets thickness is essential for consumer acceptance and to maintain tablet to tablet uniformity. The dimensional specifications were measured using digital Vernier calipers. The thickness of tablets is mostly related to the tablet hardness can be used as initial control parameter.

Six tablets were randomly selected from each batch and their thickness was measured by using Digital Vernier caliper.

Hardness

It is determined to get perfect compactness during shipping, coating, and packaging and to get proper shape and design. Hardness was measured by using hardness tester. (Pfizer hardness tester) for each batch six tablets were tested. The force required to break the tablet is recorded by the unit is Kg/cm^2.

Observation:

The measured hardness of tablets of each batch was range from 6-16Kg/cm^2.

Friability

Twenty tablets were weighed and placed in the Roche friabilator and apparatus was rotated at 25 rpm for every 4 minutes. After revolution the tablets were dedusted and weighed again. The percentage friability was measured using the formula,

$$\%F = \{1-(Wt/W)\} \times 100$$

Where, %F=friability in percentage

W=initial weight of tablets after revolution

Observation:

All the formulated batches were found under acceptable limit ofnot more than 1% as specified in IP.

Drug Content:

Crush 20 tablets and weigh equivalent to 20 mg Vildagliptin and dissolved in 0.1N Hcl and make up the volume to 100 ml. From that, withdraw 10 ml and diluted to 100 ml with 0.1 N Hcl. Read the absorbance at 232 nm in UV spectrophotometer.

Dissolution study:

Requirements:
Medium: 0.1N Hcl & 6.8 Phosphate BufferVolume: 900 ml
Apparatus: USP II (paddle)RPM: 50
Time: upto 2 hrs in 0.1 N Hcl and 6.8 pH Phosphate buffer after 2 hours
Temperature: 37^0 c $\pm$ 0.5^0c
Λmax: 232 & 227 nm
Perform the test on six tablets one tablet in each dissolution vessel containing 900 ml of 0.1 N Hcl & 6.8 pH Phosphate buffer maintained at 37^0c $\pm$ 0.5^0c. at specific time withdrawn required amount of sample and replace same amount of 0.1N Hcl & 6.8 pH Phosphate buffer (maintain sink condition), then absorbance was taken and calculate percentage release.

$$\% \text{ purity} = \frac{\text{absorbance} * 900 * \text{dilution}}{\text{Slope} * 1000} * 100 * \text{label claim}$$

Kinetics of drug release

The in vitro dissolution profile of all batches were fitted to Zero order,
first order, Higuchi model and Koresmeyer-Peppas model to ascertain the kinetic modeling of drug release. Correlation coefficient (R^2) values were calculated for linear curves obtained by the regression analysis of the above plot.

- **Zero-order kinetic model** – Cumulative % drug released Vstime.
- **First-order kinetic model** – log cumulative % drugremaining Vs time.
- **Higuchi model** - Cumulative % drug released Vs square rootof time.
- **Korsmeyer-Peppas model** - log cumulative % drug releasedVs log time.

Stability Studies:

In any rational drug design or evaluation of dosage forms for drugs, the stability of the active component must be a major criterion in determining their acceptance or rejection. Stability of a drug can be defined as the time from the date of manufacture and the packaging of the formulation, until its chemical or biological activity is not less than a predetermined level of labelled potency and its physical characteristics have not changed appreciably or deleteriously.

Objective of the Study:

The purpose of stability testing is to provide evidence on how the quality of a drug substance or drug product varies with time under the influence of a variety of environmental factors such as temperature, humidity and light, enabling recommended storage conditions, re-test periods and shelf-lives.

The International Conference on Harmonization (ICH) Guidelines titled “Stability Testing of New Drug Substance and Products” (QIA) describes the stability test requirements for drug registration applications in the European Union, Japan and the United States of America. ICH specifies the length of study and storage conditions.

Accelerated Testing: 40^0C ± 2^0C/75 % RH ± 5 % RH for 6 Months.

Method: Stability studies were carried out at 40^0C / 75 % RH for 3 months for the selected formulation. This formulation was selected because of its reproducibility of the *In-vitro* drug release of the drug from the extended release tablets. The formulation was charged for stability at conditions 40^0C / 75 % RH which are usually conditions for the Real time and Accelerated stability study. The formulation was tested for parameters like appearance, assay, uniformity of weight, *In-vitro* drug release.

Table.No.:8. Stability Testing

Formulation	Stability Condition	Testing Frequency	Tested For
Selected Formulation	Accelerated 40^0C / 75 % RH	1st month3rd month	Appearance, Assay, Uniformity of weight, *In-vitro* drug release

RESULTS AND DISCUSSION

Preformulation Studies: Organoleptic properties:

The tests were performed as per the procedure. The results weretabulated below.

Table.No.9. organoleptic properties

Test	Specifications/limits	Observations
Colour	White crystalline solid	White crystalline solid
odour	Odourless	Odourless

The result complies as per specifications.

Physical properties:

Angle of repose: It was determined as per procedure. The results were tabulatedbelow.

Table.No.10. Flow properties

Material	Angle of repose
Vildagliptin	29.08^0

The results show that the drug having good flow.

Bulk density and tapped density:

It was determined as per procedure. The results were tabulated below.

Table.No.11. Bulk density and Tapped density

Material	Bulk density(gm/ml)	Tapped density(gm/ml)
Vildagliptin	0.32	0.41

Powder compressibility: It was determined as per procedure. The results were tabulated below.

Table.No.:12. Powder compressibility

Material	Compressibility index	Hausner's ratio

Vildagliptin	17.18	1.21

Melting point: It was determined as per procedure. The results were tabulated below.

Table.No.:13. Melting point

Material	Melting point range	Result
Vildagliptin	150^0c	Complies

The result indicates that the Vildagliptin drug was pure one.

Solution PropertiesSolubility: It was determined as per procedure. The results were tabulated below.

Table.No.14. Solubility

Material	Test	Specification	observation
Vildagliptin	Solubility	soluble in organic solventssuch as ethanol, DMSO, and dimethyl formamide (DMF)	Complies

The result complies as per specification.

Loss on Drying:

Loss on drying was determined and the results are illustrated.

Table.No.15. Loss on drying

Drug	Specification	Observation
Vildagliptin	Less than 4%	0.9%

The Loss on Drying for the drugs is within limits.

Melting point of drug:

The melting point of Active ingredient was determined by capillarymethod.

Table.No.:16. Melting Point

Drug	Specification	Observation
Vildagliptin	173^0C	172.5^0C

The overall objective of preformulation studies is to generate useful information to the formulator in developing stable and bioavailabledosage forms that can be mass produced.

Physical Drug-excipient Compatibility studies:

The successful formulation of a stable and effective solid dosage form depends on the careful selection of the excipients that are added in the formulation. The drug and excipients must be compatible with one another to produce a product that is stable, Efficacious

and easy to administer and safe. The physical compatibility evaluation was performed in visual basis. The study implies that the drug, polymer and other excipients were physically compatible with each other as there was no change of physical description.

Drug and Drug – excipient Compatibility studies:

The samples that were charged in 45^0C/75% RH stability chambers were analyzed by IR spectroscopy after 30 days. The graphs of the samples were given below:

Table.No.:17. Compatibility Studies of Vildagliptin with Excipients

SL.O	Excipients	Drug/ Excipients Ratio	Physical Description Initial	35^0C ± 2^0C / 60% ± 5% RH		
				1 Week	2 Week	3 Week
1	Vildagliptin	-	White crystalline powder	*	*	*
2	Drug+ GuarGum	1:1	White crystalline powder	*	*	*
3	Drug + XanthanGum	1:1	White crystalline powder	*	*	*
4	Drug + GuarGum + Xanthan Gum + Lacose + PVK 30 + MagnesiumSterate	1:1	White crystalline powder	*	*	*

*** indicates no incompatibility.**

Figure No.3: Infra-red spectra of pure Vildagliptin

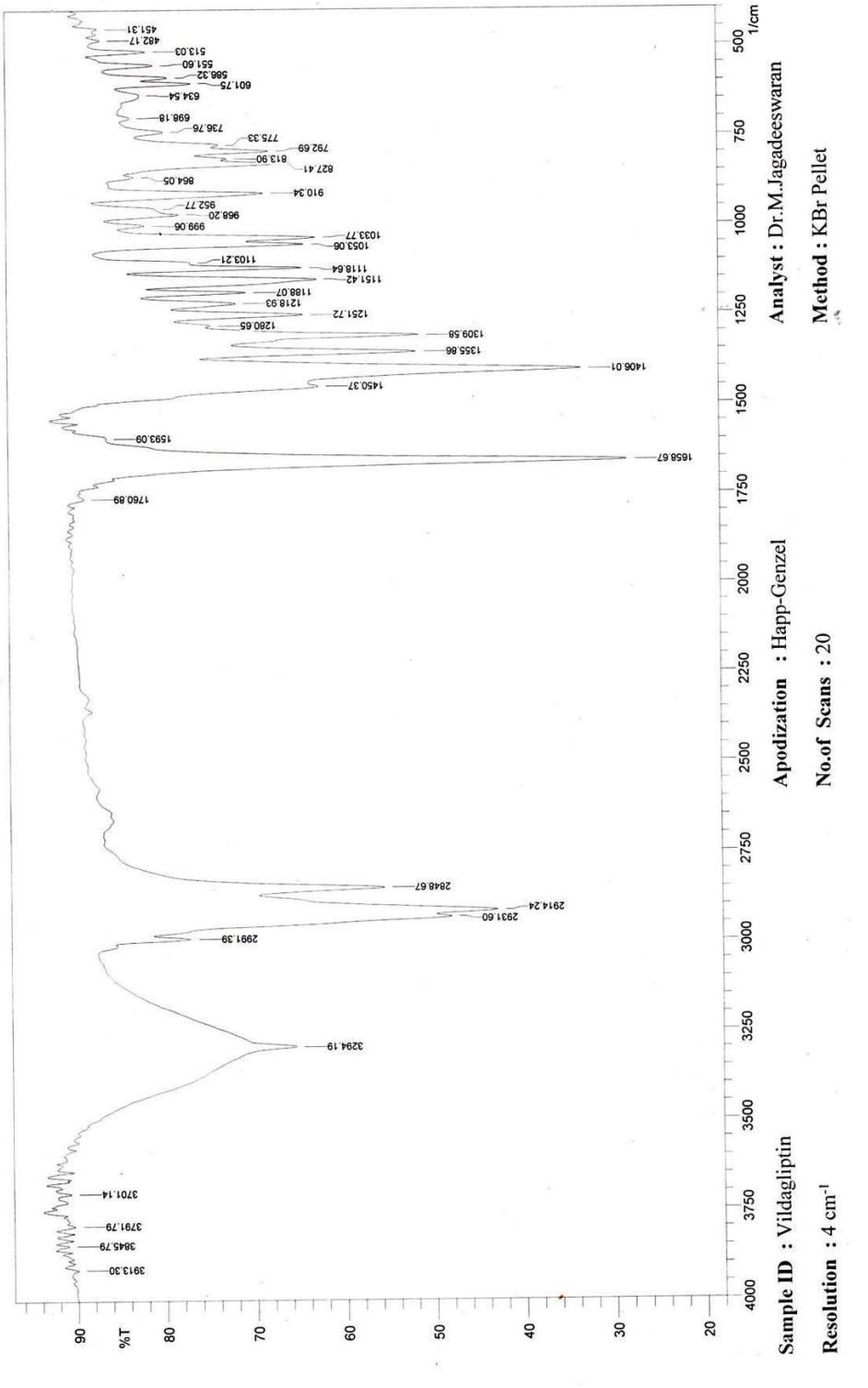


Table.No.18. Characteristic peaks of pure drug Vildagliptin

S.No	Type of bond	Type of vibration	Actual frequency (cm^{-1})	Observed frequency (cm^{-1})
1	amide peaks	Stretching	1662	1658.67
2	urea carbonylstretching (urea N-H stretching)	Stretching	1618.4	1593.09,
3	SO2	Stretching	1158 and 1341.5	1151.42, 1309.58
4	C-H	Stretching	2900.7	2914.24
5	OH	Stretching	3292	3294.19
6	C-N	Stretching	2841	2848.67

The procured API sample comply with the characteristics ofreference standard reported in literature, confirming their identity.

Figure No.4: Infra-red spectra of Guar Gum

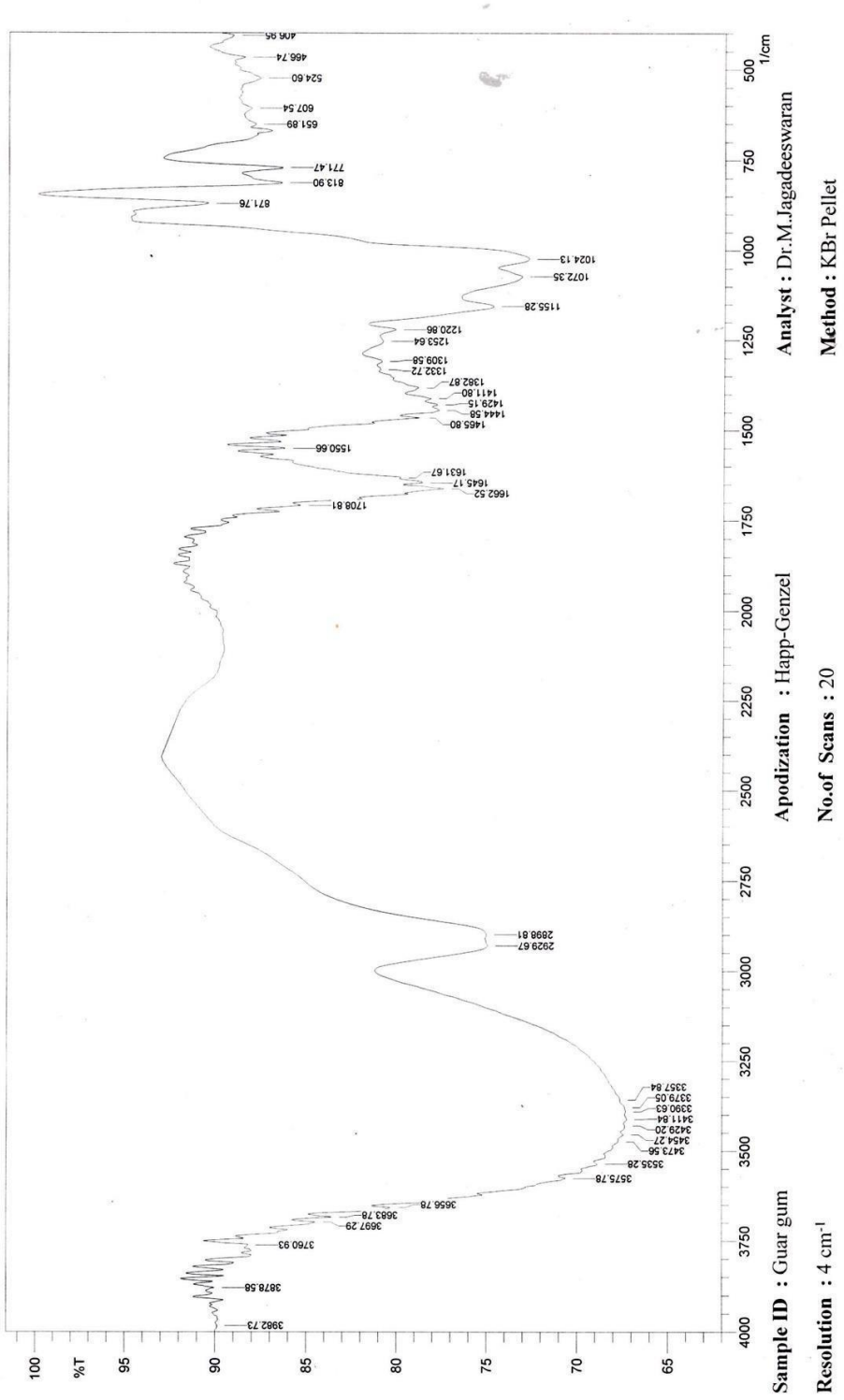


Figure No.5: Infra-red spectra of Xanthan Gum

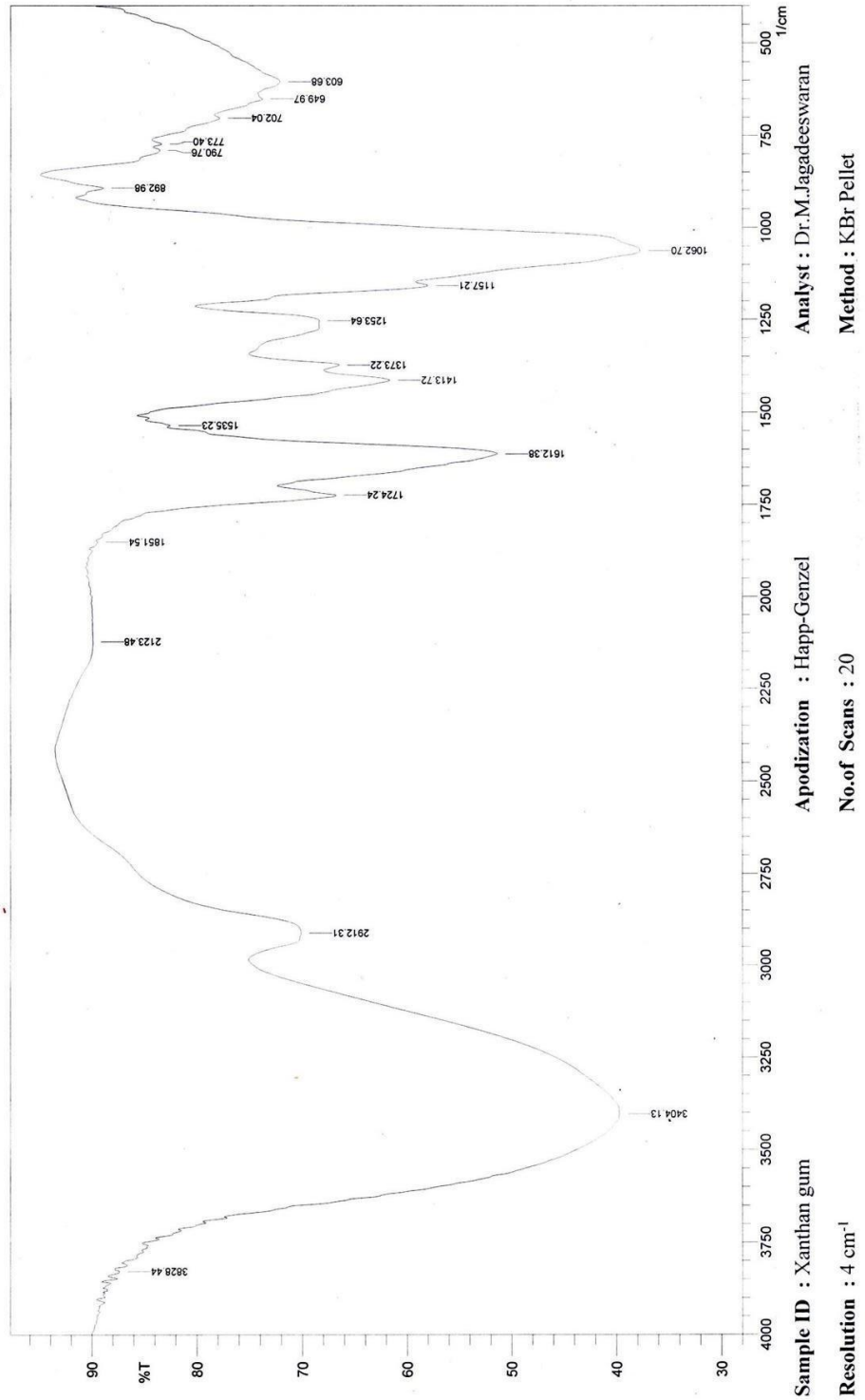


Figure No.:6 Infra-red spectra of Lactose

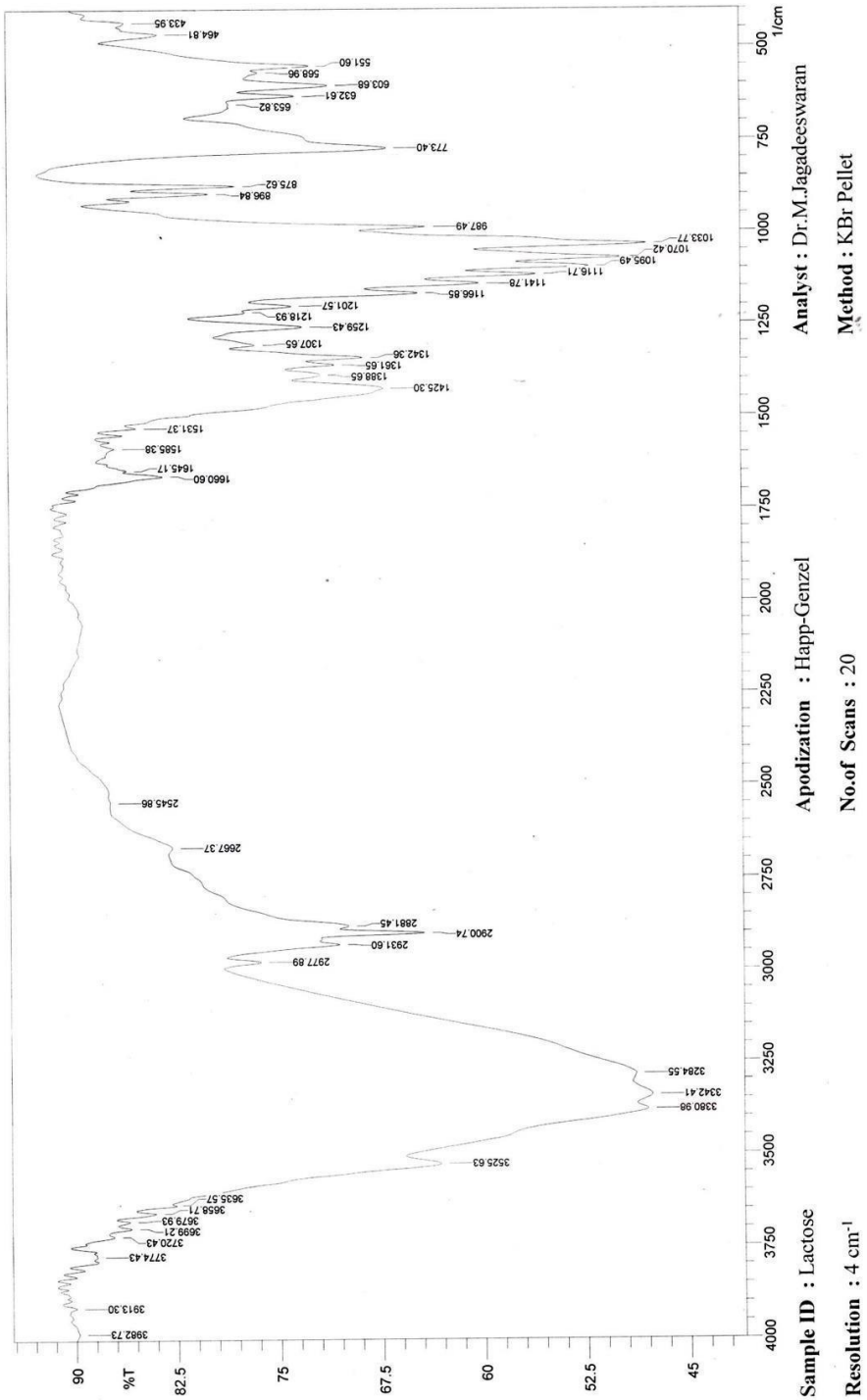


Figure No.7: Infra-red spectra of PVK 30

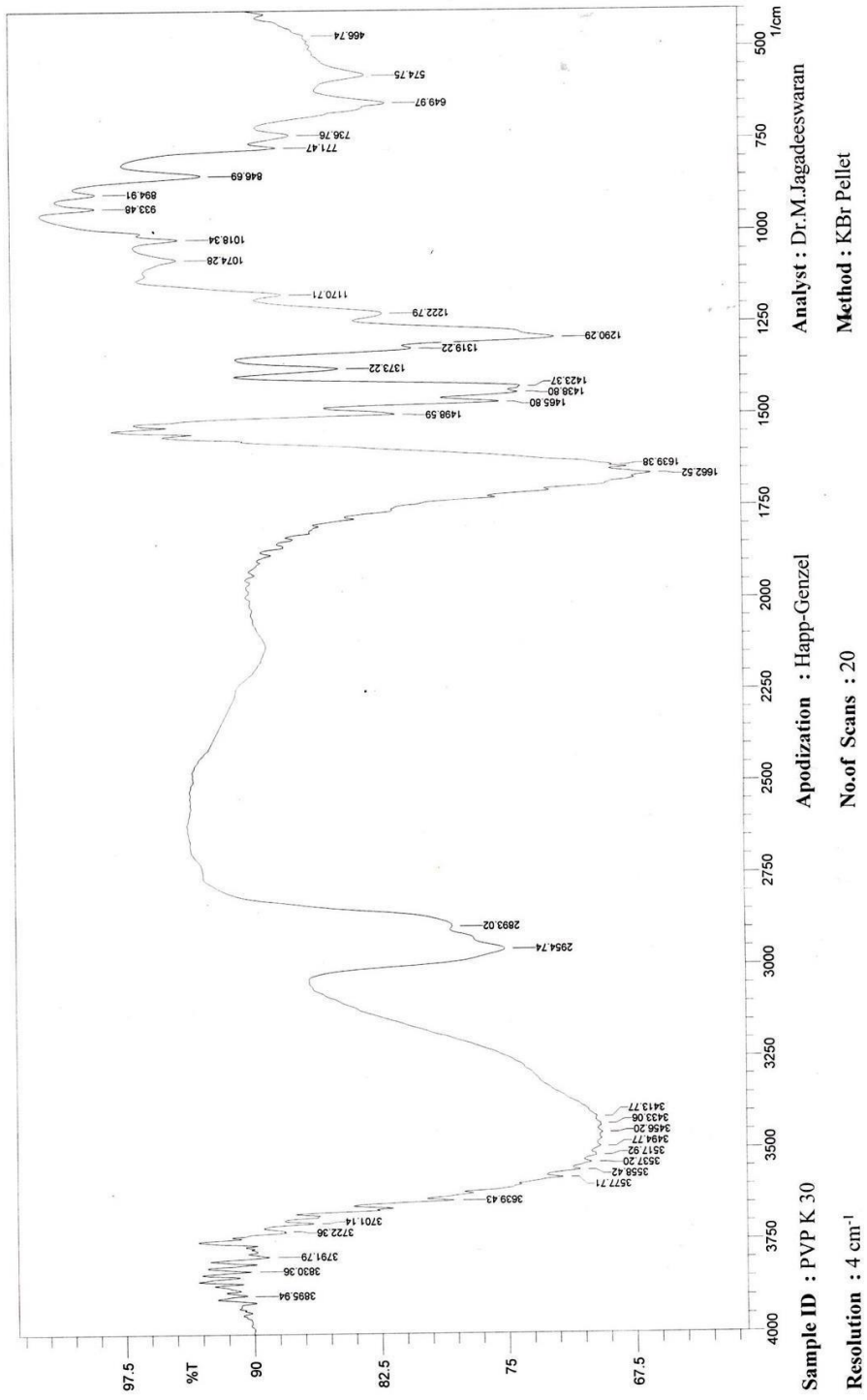


Figure No.8: Infra-red spectra of Magnesium sterate

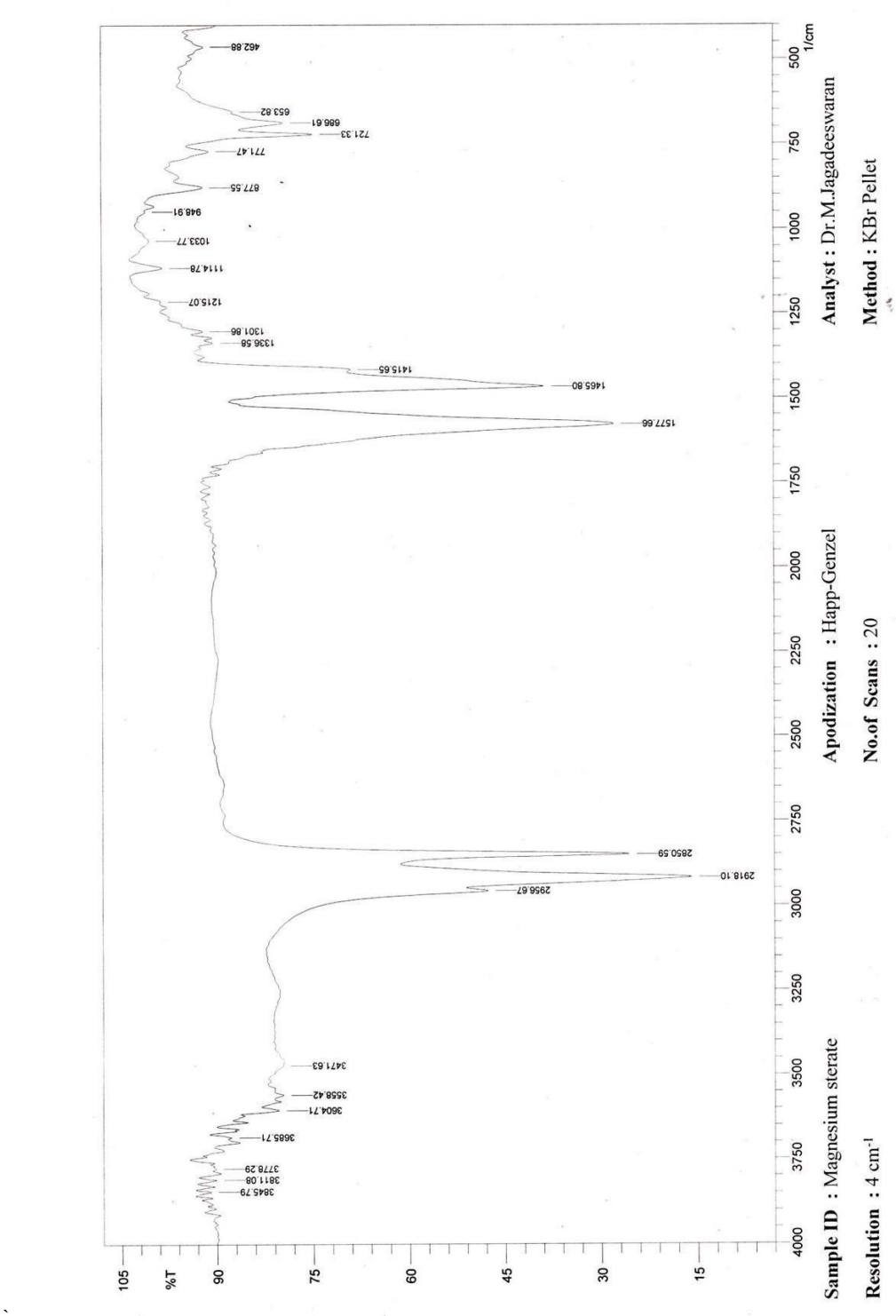


Figure No.9: Infra-red spectra of Vildagliptin + Guar Gum

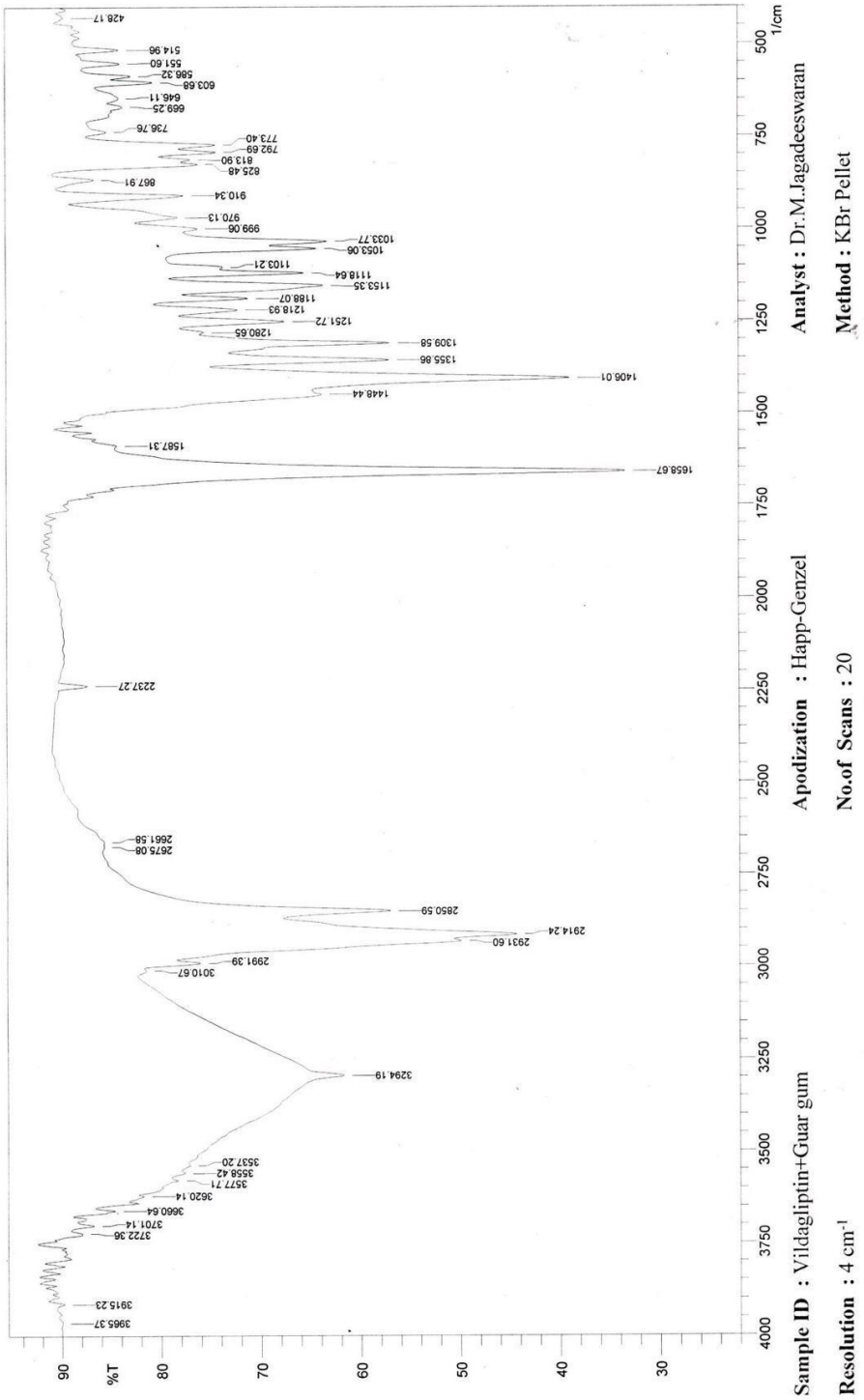


Figure No.10: Infra-red spectra of Vildagliptin + Xanthan Gum

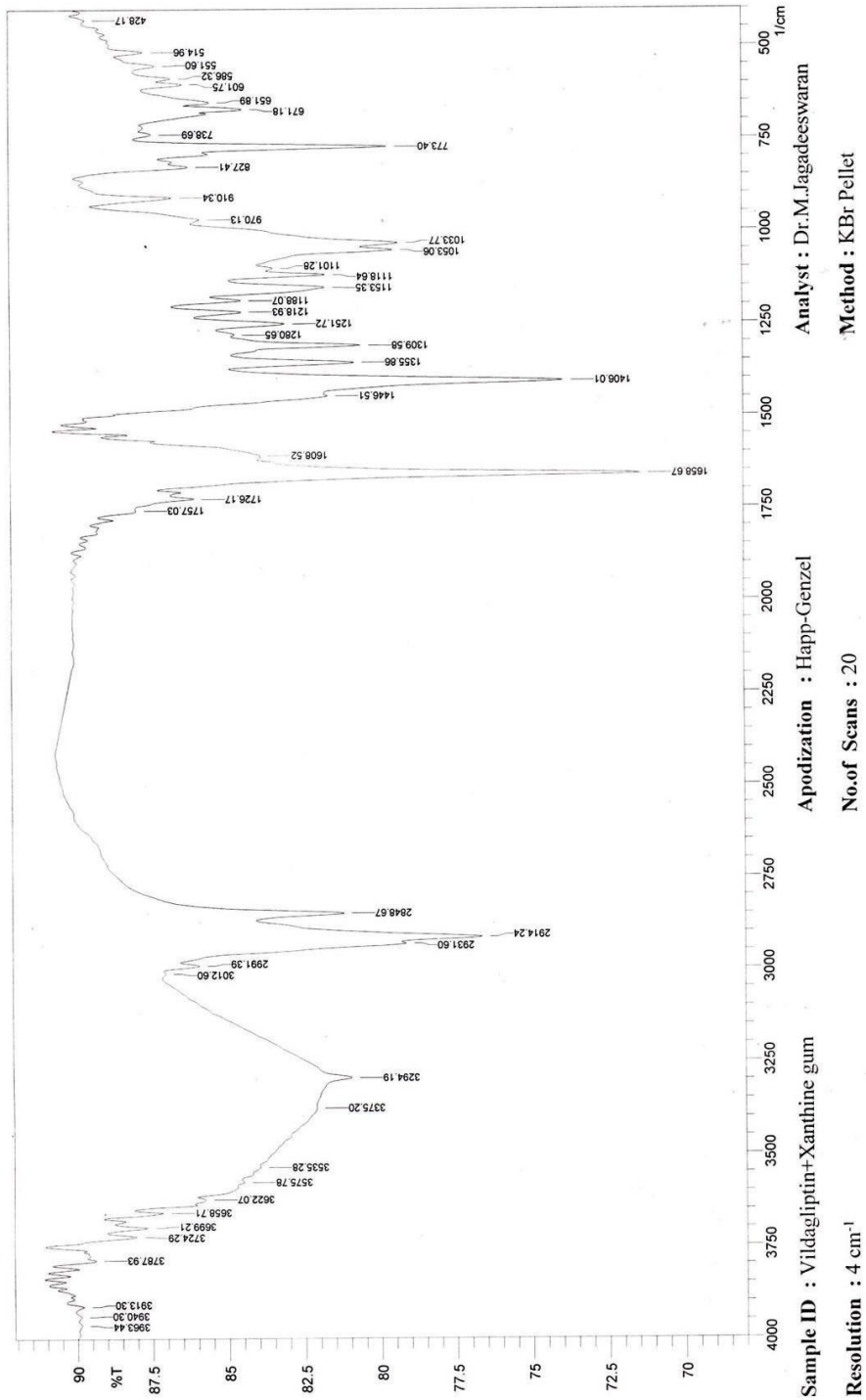
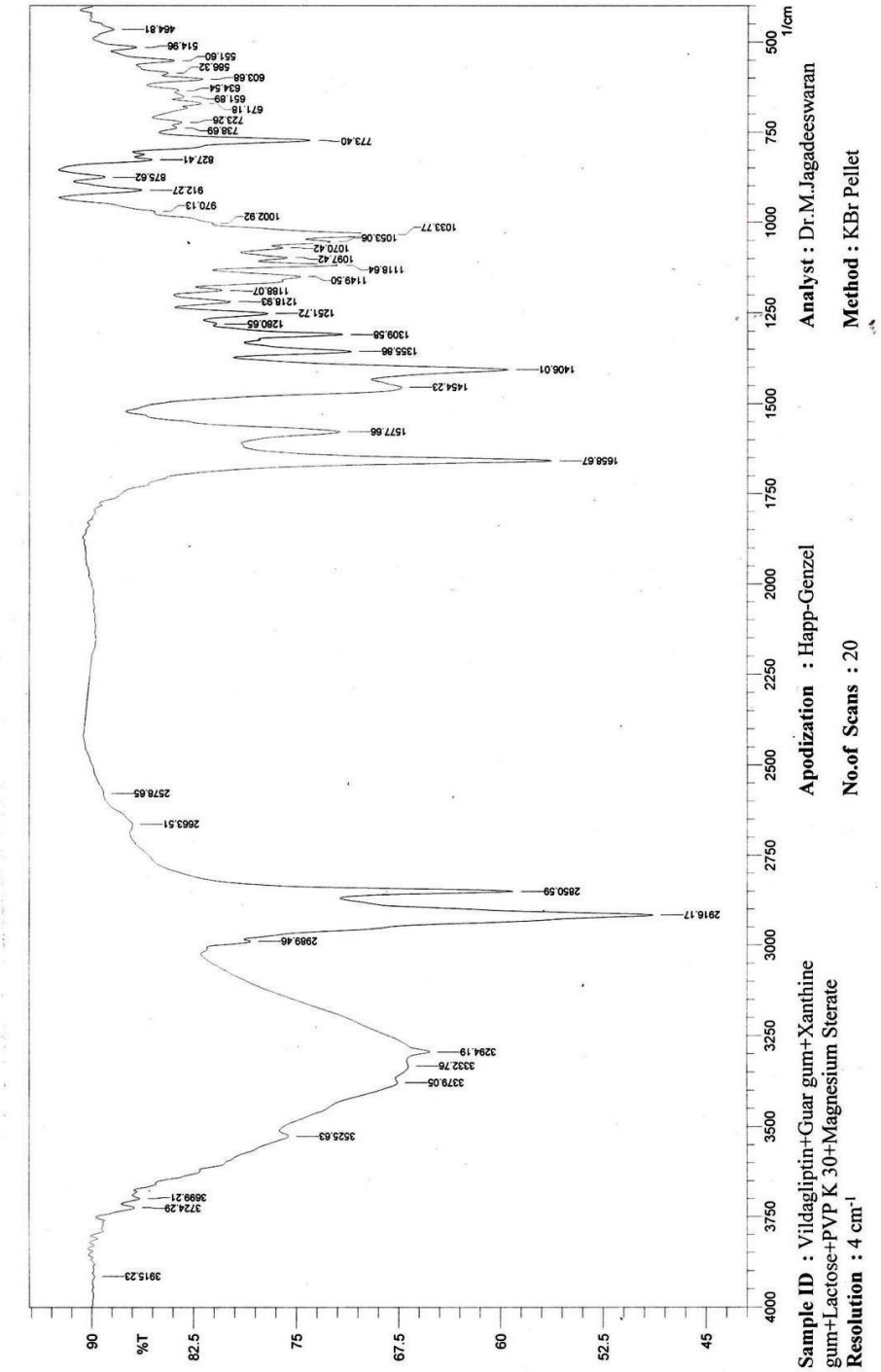


Figure No.11: Infra-red spectra of Vildagliptin + Guar Gum +Xanthan Gum + Lacose + PVK 30 + Magnesium Sterate



Discussion:

From the IR studies and Physical observation it can be concluded that there will be no possible chemical interaction between the excipientsand the drugs. There is no appearance or disappearance of any characteristic peaks. This shows that there is no interaction between the drug and polymer used.

EVALUATION PARAMETERS:

Pre Compression Parameters

Table.No.19. Evaluation parameters of powder blend

Formultion	Angle of repose	Bulk density (gm/cc)	Tapped density (gm/cc)	Compressibility index (%)
F1	$25^{0}5$	0.39	0.43	11.2
F2	$26^{0}9$	0.40	0.44	11.5
F3	$25^{0}6$	0.41	0.45	12.9
F4	$29^{0}5$	0.39	0.43	10.7
F5	$24^{0}4$	0.39	0.42	11.2
F6	$26^{0}5$	0.38	0.42	12.5
F7	$29^{0}6$	0.41	0.45	10.8
F8	$28^{0}1$	0.39	0.43	12.2
F9	$28^{0}2$	0.40	0.44	11.6

- Different ratio of viscosities of xanthan Gum & Guar is known to be beneficial in improving tablet property and release characteristics.
- The pre- compression parameters obtained for all formulations aretableted in the table. The value of angle of repose was found to be in the range of $24^{0}4^{1}$ to $29^{0}5^{1}$. This indicates good flow property of powder blend. Carr's index value ranges between 10.7 to 12.9% indicates that the powder blend have the required flow property for direct compression.

Post Compression Parameters:

a. Weight variation, Thickness & Drug Content

The theoretical Average weights of the various formulated tablets are 250 mg and weight variation of the various formulation are depictedin the Table. The percentage deviation of the weight was within 5% as per monograph.

Table.No.20. Physical Parameters of Vildagliptin Sustained ReleaseTablets

Formulation	Weight variation**	Thickness*	Drug content*
F_1	300.5±0.50	4.95±0.113	101.23±0.05
F_2	300.3±1.3	4.93±0.214	101.53±0.06
F_3	300.2±0.8	4.93±0.063	102.04±0.01
F_4	300.4±0.4	4.96±0.017	103.21±0.04
F_5	300.0±1.0	4.98±0.082	99.71±0.04
F_6	300.1±2.1	4.94±0.129	99.43±0.04
F_7	300.5±1.5	4.93±0.064	101.38±0.01
F_8	300.5±0.5	4.92±0.164	101.23±0.02
F_9	300.5±1.5	4.91±0.144	101.53±0.06

- The weight variation for different formulations was found to be 0.5to 2.1, indicates consistency in each batch. The drug content was found to be 99.43 to 103.21 which meets according to standard Specifications

Table.No.21. Evaluation parameters of formulations

Formulation	Hardness(kg/cm^2)	Friability (%)
F_1	9.2	0.75
F_2	9.3	0.21
F_3	9.2	0.13
F_4	9.4	0.19
F_5	9.4	0.22
F_6	9.5	0.16
F_7	9.5	0.14
F_8	9.3	0.17
F_9	9.4	0.18

- The measured hardness for the tablets for each batch arranged between 9.2 to 9.5 kg/cm^2, this ensures the good handling characteristics of all the batches.
- The % friability was less than 1% in all the formulations ensuring that the tablets were mechanically stable.

INVITRO DRUG RELEASE:

Table.No.22. *In vitro* Dissolution profile Vildagliptin SustainedRelease tablets

Time in Hours	F_1	F_2	F_3	F_4	F_5	F_6	F_7	F_8	F_9
0	0	0	0	0	0	0	0	0	0
1	21.56	18.34	16.82	24.16	17.22	15.41	18.24	14.81	16.49
2	37.32	31.97	27.11	33.89	28.91	26.62	27.04	20.69	22.31
3	49.69	44.84	35.76	41.65	36.24	34.28	36.92	29.04	33.08
4	60.14	56.27	48.78	54.22	49.37	48.87	46.47	37.42	44.85
5	74.82	65.75	61.19	68.56	63.92	60.72	59.24	45.92	51.08
6	85.69	76.14	73.64	79.23	74.12	71.29	70.65	51.74	59.22
7	98.24	88.63	80.47	89.22	81.48	78.62	80.11	59.93	66.82
8		99.18	91.24	98.73	90.23	84.23	85.69	64.24	70.96
9			98.93		99.69	91.45	90.67	73.82	78.21
10						98.31	99.22	84.76	89.47
11								92.04	98.26
12								99.67	

In vitro dissolution release profile of various formulations studied. From the results of *in vitro* Dissolution studies of Sustained Release formulations it was observed that the formulation F1 to F9. Formulation F8 having a release profile up to 12 hours was selected for formulation ofSR tablet. It was concluded that the drug release from the combination of Natural polymers, Guar Gum & Xanthan Gum shows the better release rate.

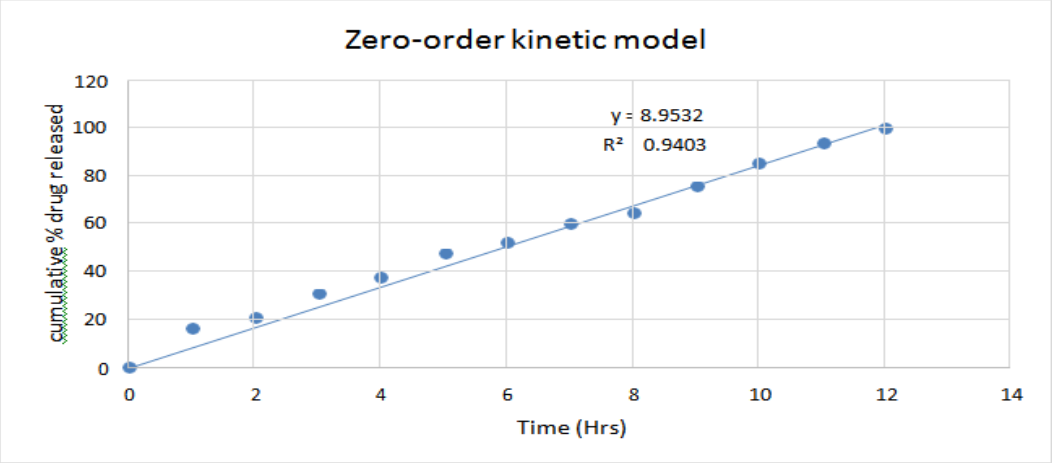


Figure. 12 Zero order kinetic model of F8

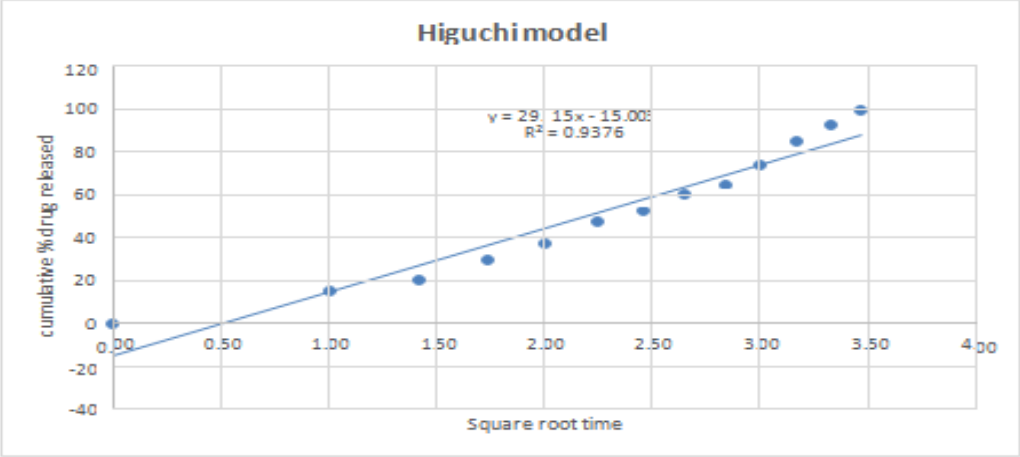


Figure 13:First order kinetic model of F8

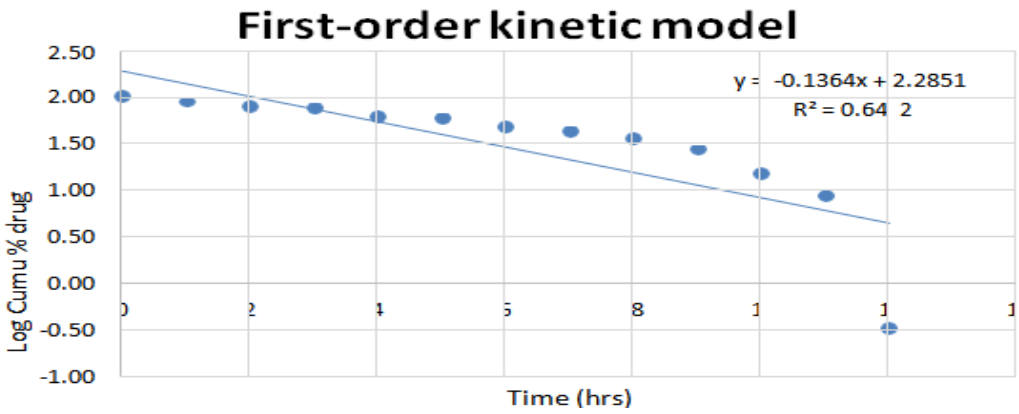


Figure. 14: Higuchi model of F8

Figure. 15: Korsmeyer-Peppas model of F8

STABILITY STUDIES:

Table.No.23. Stability studies of optimized formulation F8

Time (days)	25°C ± 2°C/60% RH ± 5% RH, 30°C ± 2°C/65% RH ± 5% RH, 40°C ± 2°C/75% RH ± 5% RH		
	Hardness(kg/cm²)	Drug content (%)	% Drug release
0	9.4	101.3	99.67
30	9.4	101.3	99.42
60	9.4	101.2	99.35
90	9.4	101.2	99.21

CONCLUSION:

The Present research endeavor is directed towards the development of Once daily sustained release Tablets of vildagliptin 100mg.The different concentration of polymer was used to control the drug release from the dosage form.This sustained release tablet is effective in improving the type II diabetic glucose control. Sustained release System was based on Natural polymer was selected for sustaining the drug release. Different polymers toget the desired release profile over a period for 12 hours. Different batches of sustained release were prepared by direct compression method respectively.All the formulations were evaluated for physical characteristics, pre-compression properties, in vitro dissolution study, kinetic study andstability. Following conclusions have been made from the present study. The physical characteristics of all the blended formulations were satisfactory.The prepared tablets evaluated for Assay, weight variation,thickness and Friability were found to be within the official limits. The *in vitro* dissolution studies were performed for all the SR formulations *In Vitro* Dissolution study of SR formulations F8 showed release profile were satisfactory with respect to drug compared with another 8 formulation.

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