ScienSage

Journal of Advanced Scientific Research

Available online through http://www.sciensage.info

ISSN
0976-9595
Research Article

FORMULATION DEVELOPMENT AND EVALUATION OF SUSTAIN RELEASE NANOPARTICULATE TABLET OF VILDAGLIPTIN

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ABSTRACT

Vildagliptin belongs to a class of orally active anti-diabetic drug which inhibits dipeptidyl peptidase-4 (DPP-4) and to raise the emission of insulin in the β-cells, thereby decreasing blood glucose level. Current study aims to raise the dissolution rate of a water-soluble drug, Vildagliptin by the formulation of the nanoparticles. Antisolvent precipitation technique is used to manufacture Vildagliptin nanoparticles with markedly improved dissolution rate. Due to short half life, Vildagliptin is formulating into sustained release dosage form by incorporating nanoparticle system. In order to maintain the desired blood levels for an extended period of time, better drug utilization, minimum drug accumulation on chronic dosing, improved efficiency in the treatment, more uniform blood concentration, reduction in fluctuation in drug level and hence more uniform pharmacological response a sustain release formulation of Vildagliptin were designed. Vildagliptin nanoparticulate sustained release tablets was formulated using hydrophilic polymers like HPMC (K15M) and Sodium Alginate in a ratio 1:0.75 by using wet granulation method. Dissolution study done by using USP type-II dissolution apparatus gave good results with combination of HPMC K15M and Sodium Alginate. Zero order, first order, Higuchi's equation, and Korsemeyer's equation shows release of the drug from the formulation. The tablet formulated by using nanoparticles shows considerable increase in dissolution characteristics and bioavailability up to 98.8% which is higher than marketed formulation.

Keywords: Bioavailability, Nanoparticles, Antisolvent precipitation method, Span 80, HPMC K15, Sodium Alginate.

1. INTRODUCTION

Bioavaibility is used to achieve the optimal concentration of drug which reaches in systemic circulation and is the most important factor. When a drug has a poor bioavaibility, it shows slow dissolution rate, poor stability and solubility of drug and extensive first pass metabolism. Over the past thirty years, because the expense and complication concerned in new entities have hyperbolic with concomitant recognition of the medical aid benefits of controlled drug delivery, bigger attention has been centered on development of sustained or controlled drug delivery system [1]. Increased effectiveness of the drug at the targeted site of action and reduced frequency of dosing or providing uniform drug delivery is goal of the formulation [2]. The drug delivery systems (ideal) require two things; first is single dose, the treatment span is either weeks or days, as among infection, and second for the life time of the patient, as in hypertension or diabetes. Bioavailability refers to the extent and rate at which the active moiety (drug or metabolite) enters systemic circulation, thereby accessing the site of action [3].

Oral sustained release products give benefit over conventional dosage forms which can optimize biopharmaceutics and pharmacokinetic property of drug when it is incorporated in Nanoparticulate system. Pharmacokinetic property includes bioavaibility of drug. It includes drug delivery system which achieves drug release over an elongated period of time, which is not time dependent [4]. Formulation of sustained dosage form commonly use polymer matrix which is hydrophilic in nature. Recently, nanoparticles production have been reported and modified to improve the dissolution rate of drugs for pharmaceutical applications which leads to substantial enhancement in bioavailability [5]. Nanoparticle engineering enables poorly soluble drugs to be formulated as particles alone, or with a combination of pharmaceutical excipients, increase in the surface area and related dissolution rate by decreasing the particle size from a micron to a nanometer [6].

Vildagliptin belongs to a new class of oral anti-diabetic drugs and is a selective and reversible inhibitor of Dipeptidyl peptidase 4 (DPP-4); the enzyme which inactivates the incretin hormones, glucagon-like peptide-1 (GLP-1), and glucose-dependent insulinotropic polypeptide (GIP) hormones, which significantly contribute to the maintenance of glucose homeostasis.

Fig. 1: Chemical Structure of Vildagliptin

Anti diabetic drug Vildagliptin suffer from several drawbacks, mainly a short biological half-life; about 90min, and a very high pre-systemic metabolism although they have efficient activity. Due to these drawbacks, the fast acting drugs are resulting either in shorter duration of action or fluctuation in plasma levels. To improve the pharmacokinetic properties of such drug candidates for not only preserving the fast action but also to increase the *Tmax* and thus extending elimination half life, a sustained release tablet is developed [7, 8].

The negative aspect of half life indicates the use of high doses or repeated dosing of conventional oral anti-diabetic formulations, which leads to severe side effects including hypoglycemia, diarrhea or constipation, headache, edema, arthralgia, paresthesias, weight gain, hypersensitivity like photosensitivity, purpura, and transient leucopenia. To minimize the side effects of oral anti-diabetic agents and number of doses, it is necessary to formulate the dosage form in a manner such that it sustain the release of active ingredient at the specific site in GI tract and is responsible for maximum absorption [8].

A sustained release nanoparticle of Vildagliptin was designed to maintain constant levels of a drug in the patient's blood stream by releasing the drug over an extended period. This mechanism enhances the therapeutic effectiveness of the drug and reduces the required number of doses. The prepared nanoparticles have smaller particle size, high drug loading efficiency and ability to bypass the acidic pH of the stomach and inhibit the degradation of GLP-1. An additional advantage of this sustained release formulation adds economic value by enhancing the patient compliance, controlled drug input that prevents super and sub therapeutic plasma concentration, enabling targeting of drugs to the site of action, enabling a drug's release at the time when pharmacological action is needed and increasing comfort to the patient and improving health-related quality of life [8].

2. MATERIAL AND METHOD

2.1. Material

Vildagliptin was obtained as gift sample from Chemicea Pharmaceuticals Pvt Ltd. Pune. Polymers like HPMC K15M, Sodium Alginate and PVP, Binding agent used was Magnesium stearate and disintegrating agent like Microcrystalline Cellulose, Aerosil, Methanol, Ethanol, Acetone and Span 80 were procured from Thermosil fine chem. Pune.

2.2. Methods

2.2.1. Antisolvent method

Vildagliptin nanoparticles were prepared by the precipitation technique which is also called Anti solvent precipitation method. Accurately weighed 100mg of Vildagliptin was dissolved in 3ml of Methanol (VLMSN1), Ethanol (VLESN2) and Acetone (VLASN3); prepared by separately at room temperature. This was poured into 10ml water containing surfactants Span 80, quantity up to 1 percent (0.3mg) maintained at a temperature of 50°C and subsequently stirred at agitation speed of 250 revolutions per minute (rpm) on magnetic stirrer for 1 hour to allow the volatile solvent to evaporate. Addition of organic solvents was done by means of syringe drop by drop positioned with the needle directly into surfactant containing water [9].

2.2.2. Sonication method

The nanoparticles were prepared by emulsion-solvent evaporation method. Typically, a solution of 100mg of Vildagliptin in ethanol (VLSN) was mixed with 10mL of aqueous solution. This mixture was homogenized for 10min by vortex and then sonicated using a micro tip probe Sonicator set at 55Wof energy output (SONICATOR MM 1010) during 1min to produce the oil-in-water emulsion. The organic phase was evaporated during 20min using a rotative evaporator under partial vacuum. The nanoparticles were recovered by ultracentrifugation (21,000 rpm, 25 min, Hitachi) [9].

2.3. Preformulation and Evaluation of Pure Drug Vildagliptin and Nanoparticles

2.3.1. Determination of Solubility

Solubility study was carried out for Pure drug and Vildagliptin nanoparticulate formulation in distilled water [10, 11].

2.3.2. Particle Size Analysis

The prepared nanoparticle's size was analyzed by using Malvern size analyzer. In this analytical method, the samples were dispersed in water and placed in a sample cell (Disposable sizing cuvette). The cuvette were then placed in analyzer and the measurement position (mm) was set. The analyzer analyzes average particle size of samples (diameter in nanometric range) [12].

2.3.3. XRD Studies

The XRD studies were done for analyzing structural nature of Vildagliptin. The samples were placed in sample cell and spread evenly. The sample cell was placed in X-ray Diffractometer (BRUKER ECO D8). The samples were scanned over the frequency range of 10-90 [12].

2.3.4. Estimation of Drug Content

A known amount of nanoparticles i.e. 100.3mg equal to 100mg of Vildagliptin were crushed into fine powder in a mortar and pestle and 100ml of pH 1.2 buffer was added and kept for 24 hrs. The solution was stirred for 15min. and filtrate was analyzed by UV double beam spectrophotometer (Lab India UV-3000+) at a wavelength of 245nm [12].

2.3.4.1. Preparation of stock solution

Stock solution (100µg/ml) of Vildagliptin was prepared in pH 1.2 buffers. This solution was suitably diluted with pH 1.2 buffers to obtain a concentration of 10µg/ml. The resultant solution was scanned in the range of 200-400 nm using UV double beam spectrophotometer (Lab India UV-3000+).

2.3.4.2. Standard calibration of Vildagliptin in pH 1.2 buffers

A 100mg of Vildagliptin was accurately weighed and dissolved in 100ml of pH 1.2 buffers to obtain a concentration of 1000µg/ml. From the above, 10ml was withdrawn and diluted to 100ml to obtain a concentration of 100µg/ml. From this stock solution aliquots of 0.2, 0.4, 0.6, 0.8, 1.0 and 1.2ml were diluted in 10 ml volumetric flask with phosphate buffer to give concentrations in the range of 2-12µg/ml, respectively and absorbance was measured at 245nm by UV double beam spectrophotometer (Lab India UV-3000+) [13].

2.3.5. Scanning Electron Microscopy

The surface morphology and basic composition of the nanoparticles were investigated using SEM. The nanoparticles were spread evenly on the sample holder with the help of a carbon tape and sputter-coated with platinum, by means of an ion coater machine for 120s before observation under SEM (S-4200; Hitachi, Tokyo, Japan). After obtaining SEM images, the elemental composition of nanoparticles was investigated using an EDX detector connected to the SEM machine [13].

2.3.6. FTIR Studies

The IR spectrum of pure Vildagliptin and optimized nanoparticulate formulation was determined by using FTIR KBR pellet method. It was scanned over the Frequency range of 4000-400 cm^{-1} [14, 15].

2.3.7. Differential Scanning Calorimetry (DSC)

DSC scans were recorded by using Differential scanning calorimeter. Samples weighing 5mg were sealed in aluminum pans and heated to 200°C at rate 10°C/min. The equipment was calibrated using indium. Samples were heated from 40 to 200°C. If required, it was cooled to -10°C and then heating was continued to 200°C [16].

2.3.8. In-vitro Release Studies

In-vitro dissolution studies of all formulations were carried out using 900ml of buffer solution of pH 1.2 at 37±0.5°C as the dissolution medium in a Type II apparatus (LABINDIA, DISSO 2000) at a stirring speed of 100rpm. Accurately weighed 100.3mg Vildagliptin nanoparticles containing 100mg of Vildagliptin were sprinkled directly to surface of the dissolution medium. Five milliliter sample solution of dissolution medium were withdrawn at the time interval of 10, 20, 30, 40, 50 and 60min (For rapid initial burst release and drug adsorption on the large surface of polymeric nanoparticles) and immediately replaced with an equal volume of the dissolution medium (maintained at 37±0.5°C) in order to maintain constant volume of dissolution medium. The withdrawn samples were filtered and analyzed for drug content at 245nm and cumulative percentage of drug dissolved was calculated. The amount of drug removed in each sample was compensated in the calculations. The data analysis was

carried out by using software PCP Disso version V3 powered by Peatix [12, 13].

2.4. Method of Preparation Vildagliptin Sustained Release Nanoparticle Tablet

In the present investigation Vildagliptin sustained release nanoparticulate tablets were prepared by Wet granulation method according to formula given in table 1. The Vildagliptin tablets were prepared by employing different synthetic polymers such as Hydroxy Propyl Methyl Cellulose K15M, Sodium alginate and Microcrystalline cellulose. The polymers and drug Vildagliptin were mixed and passed through the #40 meshes. Binder solution (PVP) was then added and again passed through the #20 mesh. After that it was allowed for drying at 50°C-55°C by using tray dryer for 6 to 7 hrs till desired LOD is achieved. Dried granules were passed through #16 mesh sieve and loaded in a double cone blender. Magnesium stearate, and Aerosil was passed through #40 meshes and it was added to the contents of double cone blender and mixed for 10min. Blended material was loaded in a hopper and compressed the powder into tablets by using compression machine [16, 17].

Table 1: Formulation of Vildagliptin Sustained Release Nanoparticulate tablet

Batch	F1	F2	F3	F4	F5	F6
Drug loaded Nanoparticles Equivalent to 100mg of Drug (mg)	100.3	100.3	100.3	100.3	100.3	100.3
HPMC K15M (mg)	55	70	-	-	30	40
Sodium Alginate (mg)	-	-	55	70	25	30
MCC (mg)	127.5	112.5	127.5	112.5	127.5	112.5
PVP (mg)	12.5	12.5	12.5	12.5	12.5	12.5
Magnesium Stearate (mg)	3	3	3	3	3	3
Aerosil (mg)	2	2	2	2	2	2
Total Weight (mg)	300.3	300.3	300.3	300.3	300.3	300.3

2.5. Evaluation of Vildagliptin Sustained Release Nanoparticulate Tablets

2.5.1. Precompression Evaluation

Mixed powder were evaluated for various properties like bulk density, tapped density, compressibility index, Hausner ratio, flow properties (angle of repose) by using standard procedures [18, 19].

2.5.2. Post Compression Evaluation

Formulated tablet were evaluated for Hardness, Thickness, Weight variation, Friability and Drug Content [18, 19].

2.5.3. In-vitro dissolution studies

The *in vitro* dissolution study was carried out using dissolution test apparatus USP Apparatus II (paddle) type at 50 rpm in 900 ml simulated gastric fluid (pH 1.2) for first 2 hrs followed by simulated intestinal fluid (pH 7.4) from 2-24 hrs. Aliquots of 5 ml were withdrawn every one-hour continued till 24 hrs and an equivalent amount of fresh dissolution fluid equilibrated at the same temperature was replaced. Aliquots withdrawn were diluted suitably, filtered and analyzed at 245nm spectrophotometrically [17]. The data analysis was carried out by using software PCP Disso version V3 powered by Peatix.

2.5.4. Curve fitting analysis (Kinetics of drug Release)

The results of *in vitro* release data obtained for optimized formula was fitted in four popular models of data treatments as follows [12, 20, 21]

- Zero-order kinetic model (percentage drug release verses time).
- First-order kinetic model (log percentage drug remaining verses time).
- Higuchi's equation (percentage drug release verses square root time).
- Korsemeyer's equation (log percentage drug release verses log time).

3. RESULTS

3.1. Preformulation Studies

3.1.1. Determination of λ Max

UV- Spectra of pure Vildagliptin was obtained from UV- Spectrophotometer and the absorption maximum was found to be 232 nm.

3.1.2. Development of Calibration Curve

The absorption maximum for Vildagliptin was found to be 232 nm in 0.1N HCl. The concentrations in range of 5µg/ml to 25µg/ml respectively, Regression

Coefficient R2 Values of Vildagliptin was found to be in 0.1N HCl is R2 = 0.999.

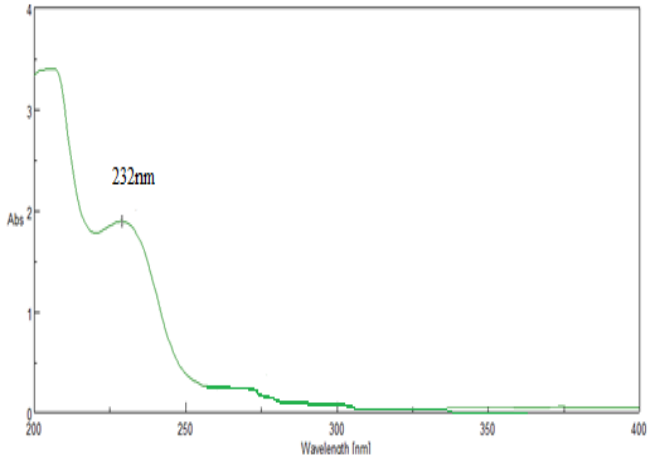

Fig. 2: UV spectrum of Vildagliptin

Table 2: Standard Calibration Curve of Vildagliptin

Sr. No	Concentration (µg/ml)	Absorbance (λmax =232nm)
1	0	0
2.	5	0.098
3.	10	0.203
4.	15	0.306
5.	20	0.399
6.	25	0.501

3.1.3. Melting Point

Melting point of Vildagliptin was found to be 153°C using capillary tube method.

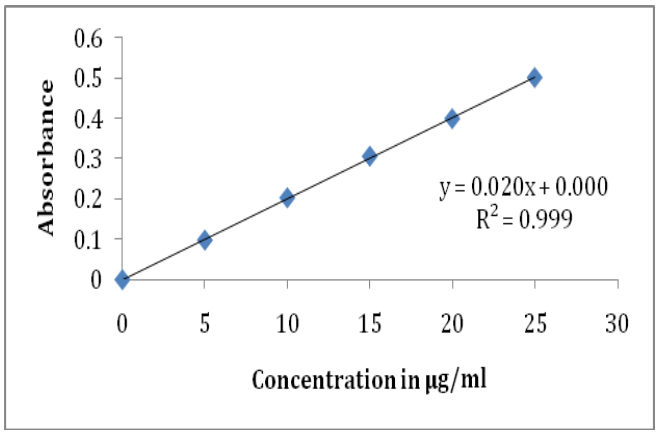

Fig. 3: Standard calibration curve of Vildagliptin

3.1.4. FTIR Studies of Pure Drug Vildagliptin

FTIR of pure Vildagliptin showed characteristic sharp peaks at 3422.88cm^{-1}due to N-H stretching vibrations, 2978.98cm^{-1}corresponding to C-H stretching, 1804.42 cm^{-1}due to carbonyl group vibrations and 1261.71cm^{-1} corresponding to C-H (aliphatic) stretching vibrations. The peaks observed in the FTIR spectra of pure drug were found to be matching with reported values for Vildagliptin, thus confirming identity and purity of drug.

Table 3: Interpretation of FTIR spectra

Wave Number (cm^{-1})	Interpretation
3345.14	N-H stretching vibrations
2978.98	Methyl Symmetrical Stretching
1804.42	Aromatic ketone C=O stretching
1261.71	C-H stretching [aliphatic]

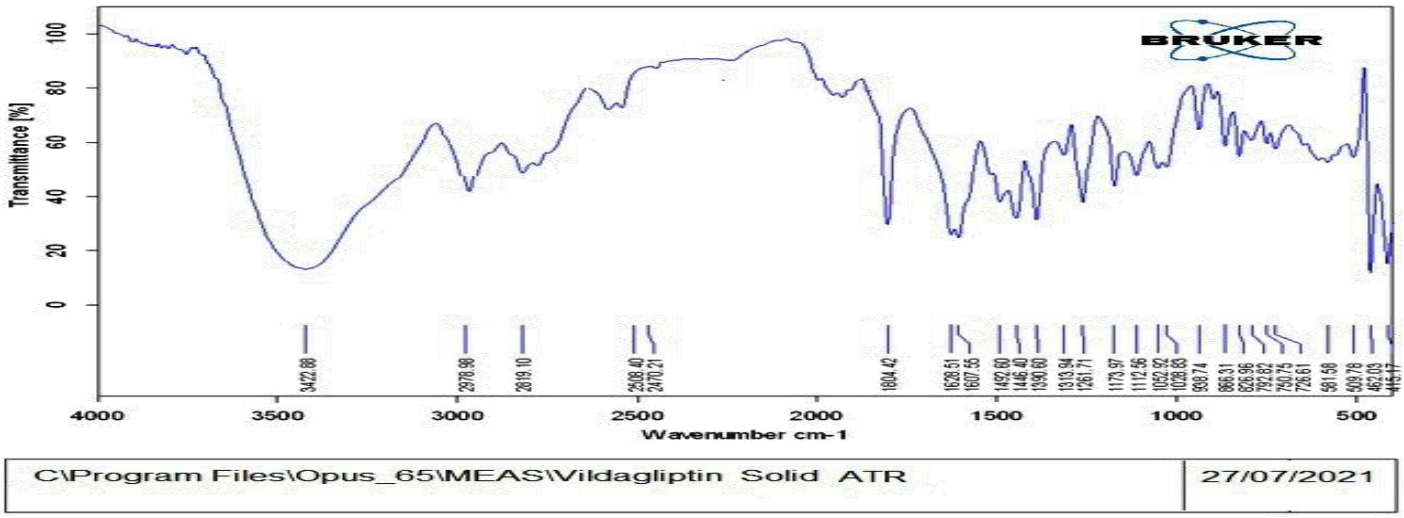

Fig. 4: FTIR Graph of Pure Vildagliptin

3.1.5. DSC

The DSC thermogram of pure drug is shown in the Fig. 5. The curve showed melting of drug at 153.8°C and endothermic peak at 155.17°C. The values are corresponding to the melting point of pure drug and thus confirmed the identity and purity of the drug.

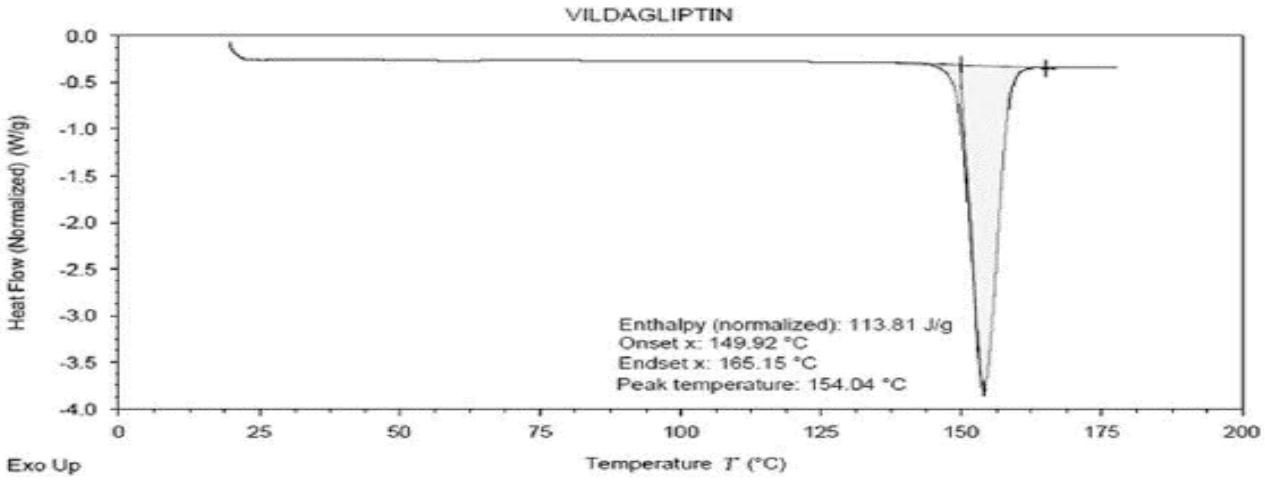

Fig. 5: DCS of Pure Drug Vildagliptin

3.2. Evaluation of Nanoparticles

3.2.1. Solubility of Nanoparticle drug formulations

Solubility of nanoparticle drug formulations in distilled water was found for VLMSN1 (1.77gm/ml), VLESN2 (1.74gm/ml), VLASN3 (1.98gm/ml) and VLSN (1.82gm/ml).

3.2.2. Particle Size Analysis

Particle size of best releasing formulations was analyzed by using Malvern particle size Analyzer the results were as follows: VLMSN1-225.5nm, VLESN2-228.2nm, VLASN3- 213.7nm and VLSN- 141.8nm.

3.2.3. XRD Studies

The nature of Vildagliptin was determined using XRD (BRUKER ECO D8) set up at 30 kV and 40 mA with Cu Kα radians at an angle of 2θ. Powdered NPs were loaded by even spreading on the sample holder (glass slides) following the procedure. The sample holder has positioned appropriately in the XRD machine and analyzed using the inbuilt software.

XRD analysis revealed the presence of four distinct peaks as shown in fig. 6. These peaks are the characteristic of the metallic face-centered cubic phase matching with the database and confirmed the crystalline nature of the Vildagliptin nanoparticles.

The XRD configuration of the Vildagliptin nanoparticles and the diffraction configuration showed four well-resolved diffraction peaks at 2θ angles of 31.10, 42.13, 63.59 and 71.43 corresponding to 111, 200, 220 and 311 respectively.

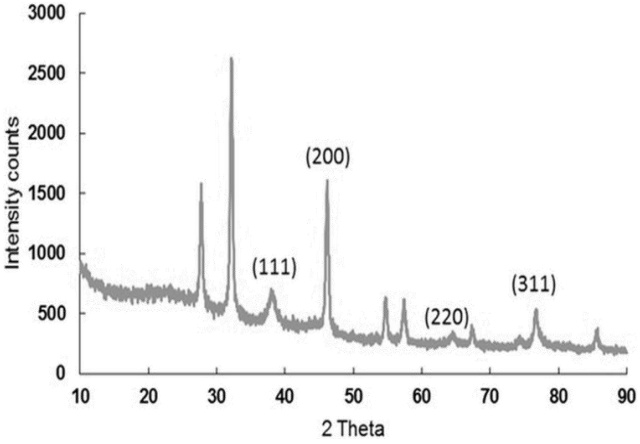

Fig. 6: XRD study of Vildagliptin

3.2.4. Estimation of Drug Content

The drug content in nanoparticle formulations was found as (VLMSN1) 98.2%, (VLESN2) 98.1%, (VLASN3) 98.7% and (VLSN) 98.2%.

3.2.5. Scanning Electron Microscopy

The results of surface morphology revealed that the Vildagliptin nanoparticles were clustered in nature with nearly spherical structures. By means of the EDX analysis, with a detector connected to the SEM machine, the drug element accounted for 41.28% of the total composition.

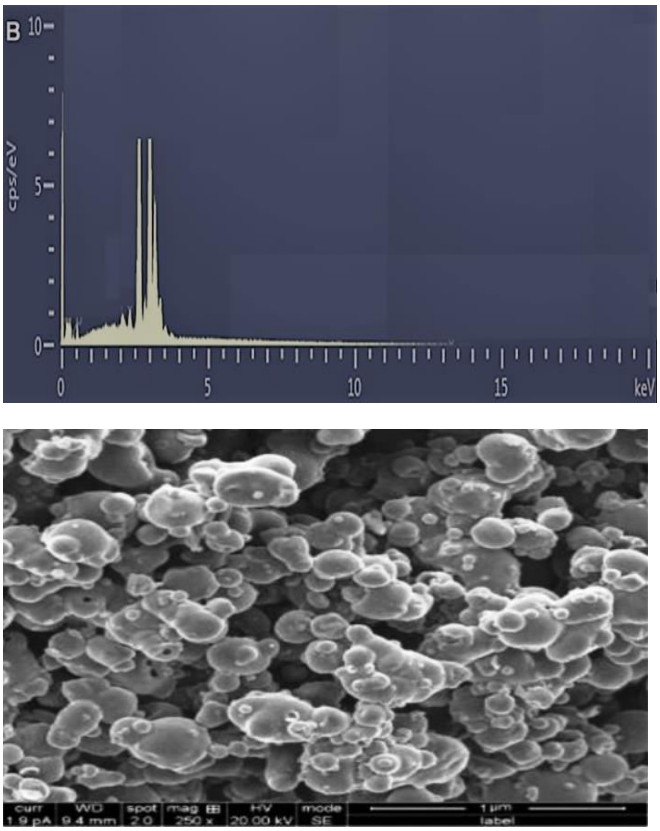

Fig. 7: Scanning Electron Microscopy of Optimized Vildagliptin Nanoparticles

3.2.6. FTIR Studies of optimized Vildagliptin Nanoparticles (VLASN3)

FTIR of Vildagliptin nanoparticles showed characteristic sharp peaks at 3196.43cm^{-1}due to N-H stretching vibrations, 2895.69cm^{-1} corresponding to C-H stretching, 1737.55 cm^{-1}due to carbonyl group vibrations and 1060.66cm^{-1} corresponding to C-H (aliphatic) stretching vibrations. The peaks observed in the FTIR spectra of Vildagliptin nanoparticles were found to be matching with reported values for Vildagliptin, thus confirming identity and purity of drug.

3.3. Evaluation of Vildagliptin Nanoparticulate Sustained Release Tablet

The precompression evaluation parameters determination are necessary for fixing compression parameters like flow speed, compression force. The angle of repose, housner ratio and compressibility index gives the information about flow properties and compressibility properties of the prepared granules. The obtained values of the same shows that the prepared granules of all lots shows good flow behavior and compressibility index which is important for tablet formulation.

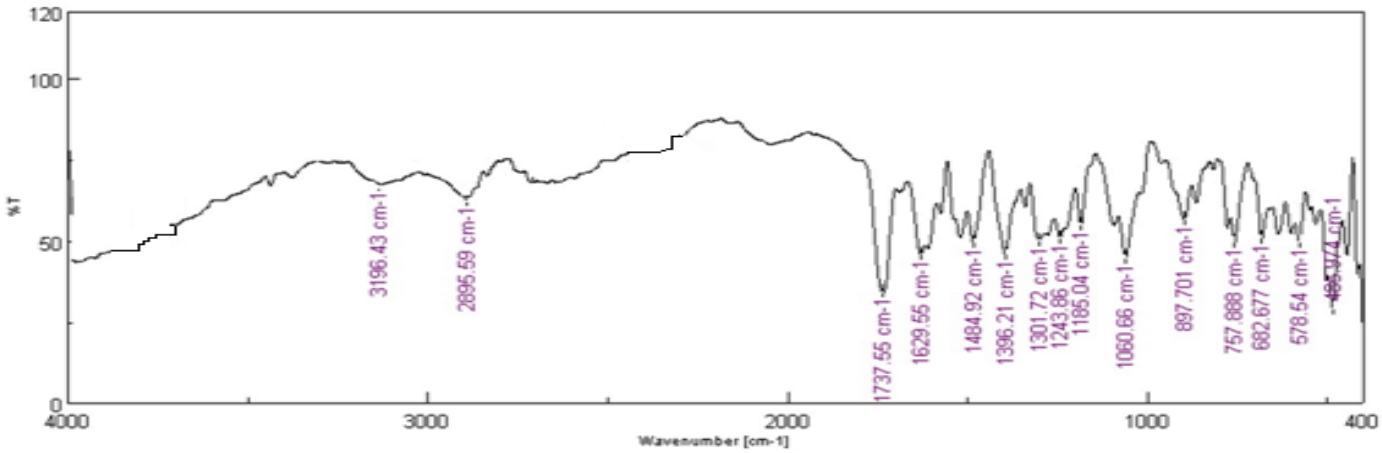

Fig. 8: FTIR Graph of Optimized Nanoparticles

Table 4: Evaluation parameters of characteristics of powder blend

Formulation	Bulk Density (g/ml)	Tapped Density (g/ml)	Hausner Ratio	Angle of Repose (Θ)	Compressibility Index (%)
F1	0.496	0.619	1.251	25.09	20.58
F2	0.557	0.692	1.239	23.76	20.42
F3	0.566	0.688	1.218	23.44	17.78
F4	0.526	0.656	1.269	24.56	22.23
F5	0.536	0.671	1.259	25.07	21.42
F6	0.590	0.746	1.251	26.75	21.73

3.3.1. Post Compression Evaluation

3.3.1.1. Thickness of tablets

All the formulations were evaluated for their thickness using "Vernier calipers" and the results are shown in table 5. The average thickness for all the formulations was found in the range of 3.44-3.46 mm which is within the allowed limit of deviation 5% of the standard value.

3.3.1.2. Hardness

Tablet hardness is one of the critical parameter to evaluate the resistance of tablets to capping, abrasion or breakage under conditions of storage, transportation and handling before its administration. All the sustained release tablet formulations of Vildagliptin were evaluated for their hardness and the results were shown in table 5. Hardness test was performed by "Monsanto hardness tester". All the formulations have an average hardness in between 5.91 to 7.22 kg/cm^2. This ensures good handling characteristics of all formulation batches.

3.3.1.3. Friability

Friability is determined to evaluate the ability of the tablets to withstand abrasion in packing, handling and transporting. Friability of prepared tablets was determined by using "Roche friabilator". The entire Sustained release tablet formulations were evaluated for their percentage friability and the results are shown in table 4. The average percentage friability for all the formulations was found in between 0.26% to 0.46%, which is found within the acceptable limit (i.e. less than 1%).

3.3.1.4. Weight variation test

As the powder material was free-flowing, tablets obtained were uniform in weight due to uniform die fill with acceptable variation as per IP standards. The weight variation for all formulations was found in the range of 291-309mg and results were dissipated in table 5. All the formulated tablets passed weight variation test as the % weight variation was within the Pharmacopoeial limits.

3.3.1.5. Drug content

The percentage of the drug content for formulation F1 to F6 was found to be between 96.4 %w/w and 101.5 %w/w. It complies with official specifications. The results were shown in table 5.

The invitro dissolution study show that there is initial burst released in acidic condition. In first two hrs. approximately upto 25 to 30% drug is released in acidic condition and then slow released of drug from tablet formulation upto 24hrs takes place. The only formulation F6 show highest percentage of drug released i.e. 98.80% in 24 hrs. which is desired for sustain release tablet.

Table 5: Evaluation parameters of Post compression of Vildagliptin Sustained Release Nanoparticulate Tablet

Formulation	Thickness (mm)± SD	Hardness (kg/cm^2) ± SD	Weight Variation (mg) ± SD	Friability %± SD	Drug Content (%)± SD
F1	3.44±0.03	6.92± 0.07	296±0.02	0.39± 0.06	98.6 ± 0.04
F2	3.37±0.06	6.79± 0.04	302±0.05	0.46± 0.04	97.5 ± 0.03
F3	3.46±0.07	6.96± 0.06	291±0.07	0.26± 0.02	101.5 ± 0.06
F4	3.38±0.08	6.25± 0.04	305±0.08	0.31± 0.08	96.40 ± 0.07
F5	3.18±0.09	7.22± 0.06	309±0.03	0.29± 0.10	97.5 ± 0.08
F6	3.46±0.07	5.91± 0.04	302±0.06	0.46± 0.06	99.8 ± 0.06

Data are expressed as Mean ±S.D. (n=3)

3.4. Kinetic Release for Vildagliptin Sustained Release Nanoparticulate tablet Mathematical modeling of drug release profile

Investigation for the drug release from the Vildagliptin sustain release tablets was done by studying the release data with zero order, first order kinetics and Higuchi equation. The release mechanism was understood by fitting the data to Korsmeyer Peppas model.

The linear plot shows that the data obeys zero- order release Kinetics. The zero order released means the elimination per unit time is independent of conc. of drug administered.

The plot of log of % cumulative released against square root of time yields a straight line, indicating that the drug was released by diffusion mechanism.

When the data is plotted as log of % cumulative drug released versus log of time, yields a straight line, which describe the drug release behavior from polymeric systems.

Table 6: *In vitro* drug release data by Dissolution study of Vildagliptin Sustained Release Nano-particulate tablet (F1-F6)

Time (hrs)	F1	F2	F3	F4	F5	F6
0	0	0	0	0	0	0
1	20.14± 2.12	23.45±1.6	16.25±1.19	20.35±1.36	16.90±1.90	13.90±1.25
2	27.96±1.69	29.45±2.12	24.50±0.87	30.78±0.65	23.48 ±1.68	20.68±1.63
3	34.45±1.43	37.16±2.12	30.75±2.65	37.58±2.77	29.78±0.42	26.60±0.20
4	43.76±2.23	43.56±2.12	35.30±2.28	40.07±3.23	35.80±1.50	31.90± 0.25
5	48.33±1.67	49.24±2.34	40.90±4.24	44.58±2.62	40.48±1.63	35.89±1.45
6	53.89±0.78	54.76±2.45	44.60±3.99	50.90±1.84	44.90±1.06	39.40±0.23
7	59.23±2.65	59.36±2.65	49.00±1.88	55.05±2.10	48.75±1.67	43.60±1.64
8	65.23±1.92	65.67±2.89	56.24±1.51	60.15±1.50	52.59±1.27	46.80±1.21
9	71.45±1.78	70.67±1.79	58.3±0.98	65.89±2.13	59.58±2.14	50.09±1.82
10	76.56±1.67	75.98±1.89	67.60±1.66	71.15±2.48	63.69±0.74	54.08±0.30
11	80.89±0.78	79.99±1.63	68.70±2.15	77.38±2.78	66.79±1.48	60.54±0.16
12	84.89±1.45	85.89±2.15	71.18±3.16	84.48±1.68	71.58±1.92	64.58±1.43
16	98.89±0.93	95.56±1.68	81.48±3.58	98.49±1.49	84.52±2.18	77.30±1.68
20	-	-	90.28±1.25		97.90±2.25	84.90±1.96
24	-	-	96.31±1.80			98.80±0.98

Data are expressed as Mean ±S.D. (n=3)

Table 7: Kinetic release of Vildagliptin Sustained Release Nanoparticulate tablet

Formulation Code	KINETIC MODELS (R^2)			
	Zero order R2	First order R2	Higuchi R2	Korsmeyer R2
F1	0.963	0.982	0.972	0.994
F2	0.943	0.935	0.978	0.976
F3	0.929	0.985	0.830	0.996
F4	0.961	0.944	0.978	0.976
F5	0.962	0.983	0.968	0.996
F6	0.963	0.983	0.955	0.997

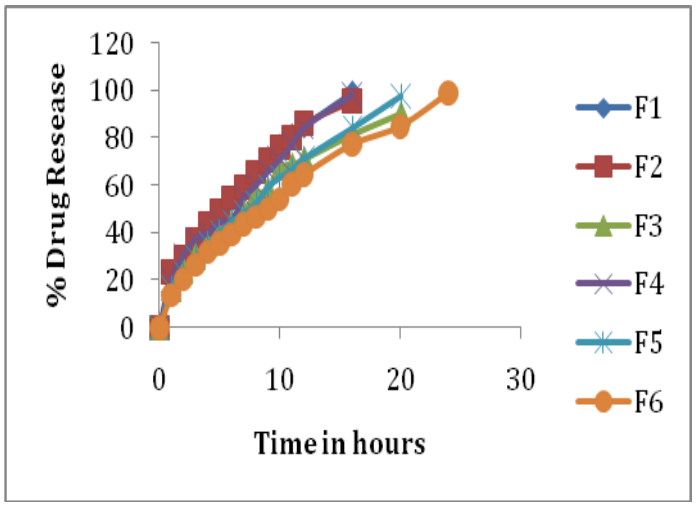

Fig. 9: *In-vitro* drug Release of Vildagliptin Sustained Release Nanoparticulate Tablet (F1-F6)

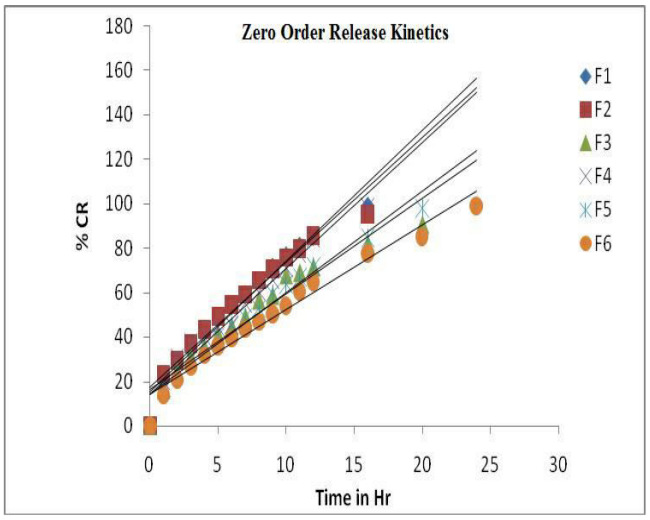

Fig. 10: Zero order Kinetics for Vildagliptin Sustained Release Nanoparticulate tablet

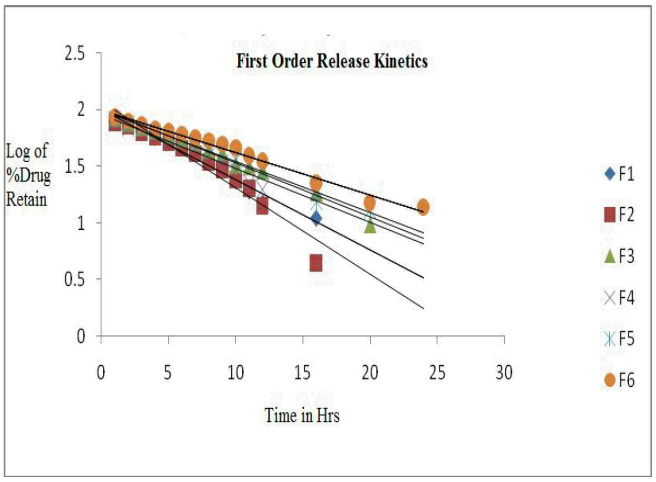

Fig. 11: First orders Kinetics for Vildagliptin Sustained Release Nanoparticulate tablet

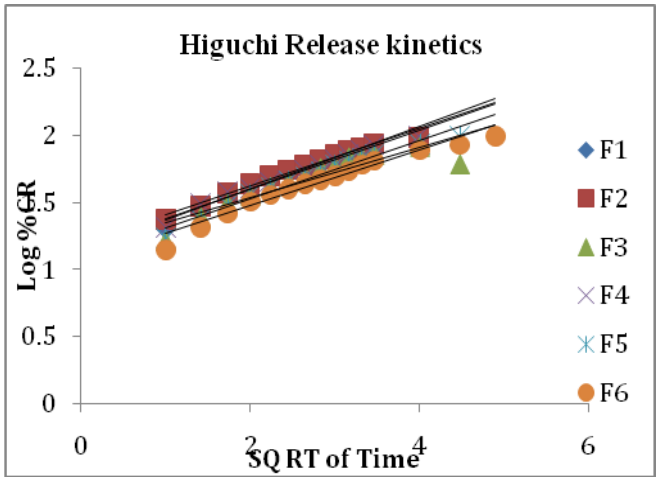

Fig. 12: Higuchi release Kinetics for Vildagliptin Sustained Release Nanoparticulate tablet

4. CONCLUSION

In the present investigation, novel nanoparticulates sustain release formulation of Vildagliptin were developed. The nanoparticles prepared by using Antisolvent method showed better initial burst release and increase the dissolution characteristic and bioavailability of the formulation upto 98.8% which is higher than conventional tablet formulation. The nanoparticulate sustain release tablet prepared by using polymers like HPMC K15M and Sodium Alginate gives the linear drug release upto 24hrs, better drug utilization, reduction in fluctuation in drug level and hence more uniform pharmacological response.

The developed sustain release nanoparticulate tablet of Vildagliptin are found to be safer and more effective which is the need of day in pharmaceutical industry as an alternative drug delivery system for a highly prevalent and chronic disease like type II diabetes mellitus.

5. ACKNOWLEDGMENT

The author is thankful to Dr.V.V.P.F'S College of Pharmacy for providing a facility for conducting a research work.

Conflict of interest

None declared

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