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A REVIEW ON SUSTAINED RELEASE TABLET OF VILDAGLIPTIN AS ANTIDIABETIC DRUG

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ABSTRACT: The present review article's main goal is to enlighten readers about Vildagliptin, a new oral anti-hyperglycemic drug that inhibits the dipeptidyl peptidase-4 inhibitor (DPP-4) and increases the release of insulin from Langerhans beta cells, lowering blood sugar levels. Vildagliptin is a medication with a short half-life (1.32-2.43 hours), making it a good candidate for the manufacture of sustained release tablets to extend the therapeutic effect. By applying the direct compression method and varying the ratios of polymers and excipients, sustained release tablets will be created. The mass, tapped, angle of repose, Carr's index, and Hausner's ratios of the powder will assess. The hardness, thickness, friability, weight fluctuation, drug content, and in vitro release of the produced tablets will assess. Utilizing 0.1N HCL as the dissolution medium, a dissolution research should be conducted using a USP type-II dissolution apparatus. The formulation's drug release methods include zero order, first order, the Higuchi model, and the Korsmeyer-Peppas model.

KEYWORDS: Vildagliptin, Sustained Release Tablet, Direct Compression, Dissolution Study, Kinetics Study

1. INTRODUCTION

Prolonged release Oral delivery methods are created to produce long-lasting therapeutic effects after the discharge of a single dose. Therapeutic substances must be administered periodically with conventional drugs. Better patient compliance and increased clinical efficacy are both correlated with the goal to maintain a blood level of a medicine that is almost constant or uniform.

Diabetes is a set of metabolic diseases in which a person has excessive blood sugar levels due to either insufficient insulin production by the body or ineffective insulin action by cells.

It is a significant global cause of death and disability. There are currently 171 million diabetics globally, and by 2030, that number is expected to increase to at least 366 million.

VILDAGLIPTIN:

Vildagliptin's use in the European Union was authorized in November 2007, and the authorization was renewed in 2008.

Vildagliptin is an oral, powerful, and selective DPP-4 inhibitor that improves type II diabetes glucose management by promoting pancreatic alpha and beta Islets of Langerhans.

The inactivation of GLP-1 by DPP-4 is inhibited by the DPP-4, allowing GLP-1 to enhance insulin production in beta cells. Degradation of GIP and GLP-1 is a function of DPP-4 in blood glucose.

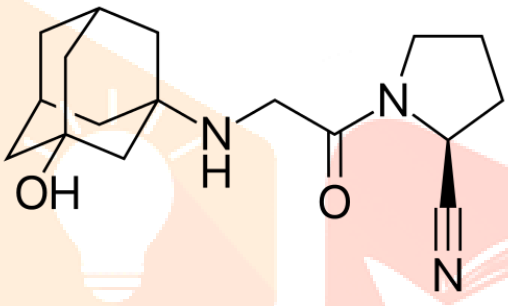
II. DRUG PROFILE

Drug name: Vildagliptin

Molecular weight: 303.3 g/mol

Molecular formula: C17H25N3O2

Molecular structure:



Chemical name: (2S)-1- [2- [(3-Hydroxy -1-admantyl)amino]acetyl]pyrrolidine-2-carbonitrile

Physicochemical properties:

Appearance: White crystalline solid

pKa:9.03

Solubility: Soluble in distilled water, Ethanol, DMSO

Melting point:149-155

Pharmacokinetic profile:

Class: DPP-4 inhibitor

Half-life: 1.32-2.43 hours

Therapeutic use: - DPP-4 Inhibitor used to lowers the blood glucose level in type II diabetes.

MATERIALS AND METHODS:

Materials like HPMC = [(K15 M, K4M), Microcrystalline cellulose, magnesium stearate, PVP, Dicalcium phosphate, sodium alginate.

METHOD OF PREPARATION: -

Table no.1 techniques used In Sustained Released Tablet

Techniques	**Procedure**
Dry granulation	Dry granulation uses mechanical compression (slugs) or compaction (roller compaction) to facilitate the agglomeration of dry powder particles.
Wet granulation	Wet granulation uses granulation liquid (binder/solvent) to facilitate the agglomeration by formation of wet mass by adhesion.
Direct compression	Direct compression process consists of three steps: raw material, blending, tableting, and coating.

INGREDIENTS USED IN SUSTAINED RELEASE TABLE: -

Table no. 2 List of Ingredients

HPMC K4m	Polymer
HPMC K 15 M	Polymer
HPMC K 100	Polymer
Carbopol 934	Synthetic Polymer, Absorb Water, Binder
Xanthum Gum	Polymer, Stabilizing Agent
Microcrystalline Cellulose	Anti-Cacking
Mannitol	Diuretic
Dicalcium Phosphate	Buffering, Stabilizer
Talc	Glidant
Magnesium Stearate	Lubricant
Eudragit	Polymer, Taste Masking, Prevent Drug Release in Saliva. Permeable Polymer
Ethyl Cellulose	Binder, Flavouring, Fixative, Filler
SCMC	Flocculating Agent, Thickening Agent, Water Retaining
Polyvinyl Pyrrolidone	Binder
Aerosil	Stabilizer And Additive
Methocel K4mcr	Thickner, Binder

EVALUATION OF PRE-COMPRESSION

1)Bulk density: -

Bulk density is formulated by adding a mass of powder to a cylinder. The density is formulated as mass.

bulk density was calculated by formula,

$$\text{Bulk Density} = \frac{\text{Total mass of powder}}{\text{volume of powder}}$$

2)Tapped density: -

Weigh the powdered transfer to in a 10 ml mechanically tapping cylinder. It is calculated by the formula,

$$\text{tapped density} = \frac{\text{Wt. of powder}}{\text{tapped volume}}$$

3) Angle of repose: -

To measure the friction or resistance to flow between solid particles, one must measure the angle of repose of the powder. This test is carried out using the fixed height funnel method, and we measure the base and overall height of the cone the powder forms as it exits the funnel. It is calculable using a formula,

angle of repose = $\tan \Theta = h/r$

Whereas, Θ is angle of repose, his height of cone and r is radius of cone.

Table -3. Limits of angle of repose

Flowability	**Angle of repose**
Excellent Flow	25-30
Good Flow	31-35
Fair	36-40
Passable	41-45
Poor Flow	46-55
Very Poor Flow	56-66
Approx. No Flow	≥ 66

4) Carr's index and Hausner's ratio: -

These two tests are performed to demonstrate the powder's compressibility. wherein we must add powder to a 100 ml measuring container and a 100 tap. After giving the measuring cylinder 100 taps, measure the untapped and tapped volumes. Since the values of the bulk density and the tapped density are close, the carr's index is low. However, because there is less friction between larger particles, a larger Carr's index finally results.

Formula for calculation: -

1) Carr's index:- $\frac{\text{Tapped density - bulk density}}{\text{Tapped density}} \times 100$

2) Hausner's ratio: Tapped density/Bulk density

Table. Limits of Carr's index & Hausner's ratio Air

Limits	Car's index	Hausner's ratio
Excellent	0-10	1.1-1.11
Good	10-15	1.12-1.18
Fair	16-20	1.19-1.25
Passable	21-25	1.26-1.34
Poor	26-31	1.35-1.45

EVALUATION OF TABLET:-

- **Physical appearance :-**

a) Colour:
b) Odour
c) Taste
d) Texture:

1) Hardness:-

The ability of the tablet to bear mechanical force when handled is reflected in its hardness. Using a hardness tester, such as the Monsanto hardness tester, six tablets from each batch can be crushed and their known weight recorded in kg/Cm^2 to determine the hardness of the tablets.

2) Friability: -

The capacity of a tablet to survive abrasion during handling, packaging, and transportation is known as friability. The Roche friabilator was used to determine the tablets' friability. First, 20 tablets must be correctly weighed and then placed in a plastic chamber spinning at 25 rpm for 4 minutes. After that time, the friabilator must be stopped, and the 20 pills must then be reweighed. Next, the % friability was determined using,

%F = (loss in weight /initial weight) x100

% Friability of tablets less than 1%are considered acceptable.

3) Weight variation: -

Weight variation is used to make sure that each pill has the right amount of medication. This approach involves weighing each tablet individually using an analytical balance, calculating the average tablet weight, and then averaging the individual tablet weights. It is determined using the formula,

$$\%\text{Weight variation} = \frac{(\text{average wt.} - \text{individual wt.})}{\text{Average wt.}} \times 100$$

Average weight of tablets	Deviation (%) (IP)
Less than 80 mg	±10 %
More than 80 mg or less than 250 mg	±7.5 %
250 mg or more	±5 %

4) Uniformity of content: -

Five tablets are precisely pulverized and weighed. A 100 ml volumetric flask was filled with powder that was correctly weighed to equal 50 mg of vildagliptin. The volumetric flask first received some pH 7.4 phosphate buffer, which was added, and the flask was shaken for 10 minutes before the mixture was sonicated. Phosphate buffer was then used to increase the volume to 100 ml, and 0.45 m membrane filter paper was used to filter the result. The filtrate was appropriately diluted with pH 7.4 phosphate buffer before being spectrophotometrically tested for drug concentration at 202 nm against a blank (pH 7.4 phosphate buffer) solution.

5) In vitro study: -

Vildagliptin sustained release tablets will produced, and in vitro drug release tests will perform using USP type II equipment at 37°C and 50 rpm. 900 cc of pH 6.8 phosphate buffer and 0.1 N HCl were employed as the dissolution mediums. The first two hours of the matrix tablet release rates were done in HCl solution (pH 1.2), while the following two hours were spent in phosphate buffer (pH 6.8). The samples were removed from the dissolving media at predetermined intervals and replaced with new media with the appropriate Ph. By means of a UV-Visible Spectrophotometer, the samples were examined. With the aid of suitable calibration curves created from reference standards, the levels of drugs present in the samples were computed. A % release versus time curve was used to plot the drug release at the designated times.

KINETICS STUDY: -

The Higuchi model, the Korsemeyer-Peppas model, the zero order and first order models, as well as the dissolution view of the major acceptable preparation, are provided to help determine the best model.

1. Cumulative drug release percentage against time (zero order kinetic models)

2.Log the cumulative percent of the medication released over time (first order kinetics model)

3. Cumulative drug release percentage vs square root of time (Higuchi model)

Drug cumulative log c v/o log (Peppas model)

1) Zero order:

A zero-order response occurs in a small number of reactions, where the measurement is adequately equivalent to reactant concentration. The rate of zero order reactions does not significantly differ from the reaction's continuous rate (k), nor does it increase or decrease as the reactants' alternativeness does.

2) First order: -

A first order reaction is one that develops at a rate that is rectilinear with respect to the concentration of a single ingredient.

3) Higuchi model: -

In cases when a small number of sort matrix systems are used in modified release formulations, the moiety dissolves from the matrix. In this higuchi approach, a plot of the cumulative % moiety released v/o square root of time is linear.

4) Krosmeyer peppas model: -

The Krosmeyer peppas model empirically relates the function of time for diffusion-controlled mechanisms. It is provided as follows:

$$Mt/M\infty = ktn$$

Where, Fraction of drug release time = $Mt/M\infty$

Release rate constant = Kt

The release exponent = n

Marketed Preparations:

1. **VILATIN SR 100**
2. **VIDADEB 100 SR**
3. **VIMFAST-100**
4. **GALVUS OD 100**
5. **VILDANA 100 SR**
6. **ZOMELIS SR 100**
7. **VIDAGLIPT 50**
8. **JALRA OD 100**
9. **VILDAX 100 SR**
10. **VILDAMAC OD 100**
11. **DEBIGLIP 100 SR**
12. **VILDARAY SR 100**
13. **VILDAILY-DZ 10/100**
14. **VEDUGLIP-50**
15. **VILDAGLIPT-M 1000**
16. **VIDLER M**
17. **VILATIN SR 100**
18. **VILSURE-100 SR**

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