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Formulation and Evaluation of Sitagliptin Phosphate Tablet

Snehal Balasaheb Shinde[1] ,Pratik B. Bhanage [2],Megha T. Salve[3]

Department of pharmacy, Shivajirao Pawar College of Pharmacy, Pachegaon

ABSTRACT:

This study aimed to develop and evaluate Sitagliptin tablets, an oral antidiabetic medication, using various excipients and formulation techniques. The tablets were formulated using wet granulation or direct compression methods and evaluated for physical properties, such as hardness, thickness, weight variation, and dissolution. The optimized formulation showed satisfactory results, meeting the required standards for tablet quality and drug release. The study demonstrated the feasibility of developing Sitagliptin tablets with improved bioavailability and efficacy for the treatment of type 2 diabetes mellitus.

Keyword : Sitagliptin phosphate, Anti-diabetic drug, Floating Drug Delivery System, Gastro intestinal tract (GRT), Gastroretentive Drug Delivery System,

Introduction Of Disease:

Diabetes : Diabetes, which medical professionals often refer to as diabetes mellitus, is a group of metabolic diseases characterized by elevated blood sugar (glucose), either due to inadequate insulin production, improper insulin use by the body's cells, or both. Patients with elevated blood glucose levels typically experience polyuria, or frequent urination, as well as increasing levels of hunger (polyphagia) and thirst (polydipsia).

Three types of diabetes exist:

1) **Diabetes type 1**
   Insulin is not delivered by the body. Some may refer to this type of diabetes as early-onset diabetes, adolescent diabetes, or insulin-subordinate diabetes. Type 1 diabetes typically develops in people before the age of 40, usually during their high school o" early adult years. Compared to type 2 diabetes, type 1 diabetes is far less common. Type 1 diabetes accounts for about 10% of all diabetes cases.
2) **Diabetes type 2**
   The body either doesn't produce enough insulin to function properly or the body's cells don't react to (insulin blockage). Type 2 diabetes accounts for about 90% of all cases of diabetes worldwide.
3) **Diabetes during pregnancy**
   This type affects women during pregnancy. Some women have blood glucose levels that are abnormally high. And their bodies can't manufacture enough insulin to carry the majority of the glucose into their cells, causing glucose levels to rise logically. Gestational diabetes is diagnosed in the midst of pregnancy.[1]

Introduction Of Drug :

The US FDA approved sitagliptin phosphate, also known as 1,2,4-triazolo[4,3-a]pyrazine,7-[(3R)-3-amino-1-oxo-4-(2,4,5-trifluorophenyl)butyl]-5,6,7,8-tetrahydro-3-(trifluoromethyl),phosphate (Fig. 1), in October 2006 as the first of a new class of drugs that inhibit the proteplytic activity of dipeptidyl peptidase-4 (DPP-4). The molecular weight of 523.32 g/mole indicates that sitagliptin is classified as a Class III (high solubility, low permeability)/borderline Class I (high solubility, high permeability) by the Biopharmaceutics classification system (BCS).[2]
Sitagliptin enhances the release of insulin when blood sugar rises, such as after a meal, by prolonging the activity of proteins. Sitagliptin has an absolute bioavailability of roughly 87% and is quickly absorbed when taken orally. The pharmacokinetics of sitagliptin are unaffected by the co-administration of a highfat meal. It can be administered either by itself or in conjunction with other medications that lower blood sugar levels. Sitaglipti n has an elimination halflife of 12.4 hourDesigning an optimal formulation with a suitable dissolve rate in a short amount of time and with the fewest possible trials is a crucial concern in the development of tablet dosage forms. Using a polynomial equation, Response surface methodology (RSM) or response surface designs are the statistical experiment designs most frequently employed in optimization trials.[3]

Owing to its ease of use, patient compliance, and formulation flexibility, oral drug delivery is by far the most preferred method of drug delivery. Frequent dose administrations are necessary for patients receiving treatment with traditional oral formulations that contain medications with shorter half-lives, which affects patient compliance.[4, 5] Maintaining the medication release can help get around this. The true challenge in developing oral controlled release forms is to extend the duration of the drug's distribution as well as the dosage form's existence in the stomach or upper gastrointestinal tract (GIT) until the entire medication is released for the intended amount of time.[6,7]

Tablets benefits and drawbacks as dosage forms

Since tablets are currently the most often utilized dosage form, using them has a number of benefits. But it's equally critical to draw attention to t he drawbacks of using them.

Benefits :

1.Encourage absorption there and produce local outcomes (e.g., ulcerative colitis). I am capable. Other oral dosage forms might make this difficult to accomplish.

2.Multiple therapeutic agents can be included in tablets, even if there is a chemical or physical incompatibility between the activators. Additionally, the composition and design of the tablets can efficiently control the release of each therapeutic component

3.In general tablet are low cost dosage form.

Drawbacks :

1.Because tableting necessitates a number of unit activities, there is a greater chance of product loss at every stage of production.

2.Physiological factors influence how well medicinal drugs are absorbed from tablets. For instance. Rate of gastric emptying.

3.Some medicinal compounds have poor compressive qualities, which might lead to issues during future formulation and tablet manufacturing.

4.Giving pills to particular groups. For instance. Dysphagia can cause issues in both young people and the elderly. The effervescent tablet dosage form can be used to get around these issues.[8]

Material :

Sitagliptin Phosphate, Cross povidone , lactose, Magnesium stearate **,** Polyethylene glycol, .

Methods :

Pre-compression Parameter

Angle of repose, bulk density, taped density, compressibility index, Hausner's ratio, and Carr's index are some of the pre-compression parameters that were examined.

Bulk Density –

Bulk Density: The bulk density, or Db, of a powder is the ratio of its bulk volume to its entire mass.After pouring the weighted powder into a measuring cylinder, the volume was noted. It is given in G/CC and is given by Db=Mass powder/Volume.

Tapped Density –

Tapped Density – It is the proportion of the powder's total mass to its tapped volume It is given by Dt = M/Vt and represented in G/CC. where M is the powder's mass V t: The powder's taped volume

Angle of repose –

The precisely measured amounts of granules were transferred into a funnel. The funnel's height was changed so that the tip of the funnel barely brushed the granules' peak. Free flow of the granules onto the surface was permitted. The formula was used to determine the powder cone's angle of repose and estimate its diameter. Tan (θ) = h/r where h and r are the powder cone's height and radius, respectively.

Carr's Index and Hausner's Ratio -

The Carr's index (I) and Hausner's ratio are metrics used to quantify the flowability and tendency of granules to be compressed. The following formula was used to calculate Hausner's ratio and Carr's index.(Dt – Db)100/Dt = C.I where Dt is the powder taped density (Db).

Table 1. Formulation Table For Sitagliptin Tablet

Sr. No.	Ingredients	F1	F2	F3	F4	F5
1.	Sitagliptin Phosphate	5	5	5	5	5
2.	Crospovidone	20	23	22	24	21
3.	Polyethylene glycol	20	25	24	23	19
4.	Lactose	32	27	28	26	31
5.	Magnesium stearate	23	20	21	22	24

Preparation of Sitagliptin Tablet by Direct Compression Method :

Each component was weighed using the formula in Table 1 after being passed through sieves independently. After being weighed, the materials were combined for fifteen minutes in a polythene bag. The powder is compressed once it has been well mixed. A number of pre-compression parameters, including bulk volume, tapped volume, bulk density, tapped density, and angle of repose, were assessed for the powder. Following compression, their appearance, diameter, weight, thickness, hardness, and friability, as well as their uniform dispersion, weight fluctuation, content uniformity, were assessed. Additionally, stability tests and an in vitro dissolution profile were conducted.

Post Compression Parameter

Evaluation Of Sitagliptin Phosphate Tablet :

1.Shape of the tablets:

Every prepared tablet was visually inspected. The tablets were judged to have good forms.

2.Friability Test:

The tablets are placed in a rotating drum (friabilator). The drum rotates at a specified speed, usually 25 rpm, for a set duration, typically 100 rotations.

The tablets are subjected to tumbling action within the drum, causing abrasion and potential weight loss.

3.Hardness:

A Monsanto hardness tester was used to measure the mean hardness values for each formulation.

4. Weight Variation Test:

Using an electronic balance, 20 tablets of each formulation were weighed in order to examine weight variation. The test was conducted in accordance with the established protocol.

5.Thickness:

1. Instrument Selection:Choose a micrometer or vernier caliper, ensuring it's clean and calibrated.
2. Tablet Placement:Carefully position the tablet between the jaws of the instrument.
3. Pressure Application:Gently move the movable jaw to press the tablet firmly against the fixed jaw, without causing damage, as described by Pharmainform.
4. Reading:Note the reading displayed on the instrument's dial or digital display, says Pharmainform.
5. Repeat and Average:Measure multiple tablets to ensure consistency and calculate the average thickness, according to Pharmainform.

Result and Discussion :

Precompression assessment parameters:

As previously mentioned, the active pharmaceutical ingredients and excipients were prepared for each kind of formulation and assessed for a range of pre-
compression characteristics. The tapped density was determined to be between 0.4and 0.62G/CC, whereas the bulk density was found to be between 0.3 0 and 0.47G/CC. The compressibility and flow ability data showed good flow qualities for all blended formulations, and the Carr's compressibility inde x, which was computed using the two density data mentioned above, was determined to be between 5 and 25% Angle of repose also showed that all powder blends had superior flow characteristics. The range of the angle of repose was 28.02 to 36 A favorable flow characteristic is indicated by an angle of repose less than 30 degrees. All of the powder blends in the current investigation demonstrated good flow properties. The Table displays the findings.

Batch	Bulk Density	Tapped Density	Angel of Repose	Hausner's Ratio	Carr's Index
F1	0.44	0.5	29.74	1.25	20
F2	0.37	0.4	28.02	1.08	25
F3	0.42	0.44	39	1.1	5
F4	0.47	0.62	29.62	1.31	24
F5	0.30	0.33	36	1.1	10

Post Compression Parameter :

Formulation Code	Friability(%)	Hardness Kg/cm2	Weight Variation (mg) n = 20	Thickness (mm) (n=3) Mean±S.D
1	24.89	4.5±0.208	101±0.701	1.8±0.15
2	11.34	4.4±0.22	101±0.805	1.6±0.16
3	7.22	4.1±0.05	104±1.67	1.7±0.10
4	23.18	5±0.3	100.5±1.5	1.8±0.10
5	12.44	4.6±0.1	100±1.30	1.5±0.11

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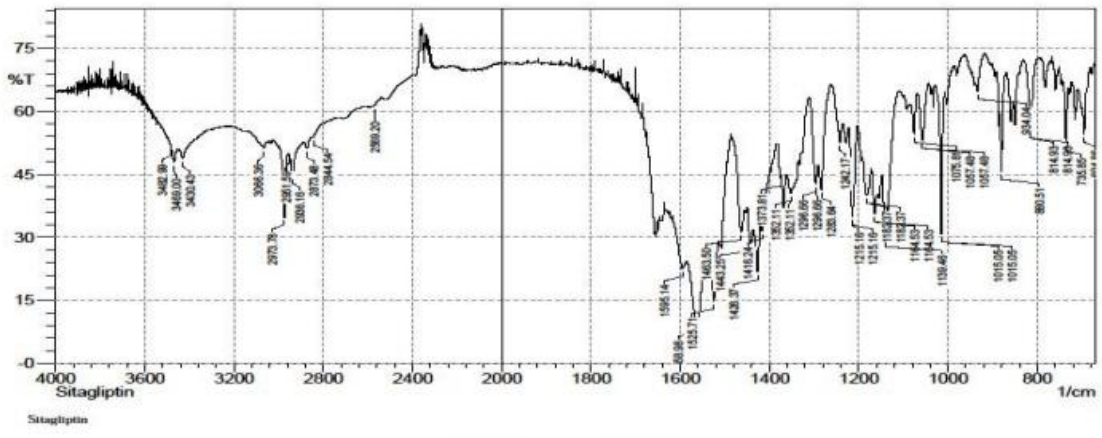

Conclusion:

In conclusion, sitagliptin phosphate can be successfully compressed into tablets, particularly through direct compression techniques, utilizing various excipients and methods to optimize tablet properties like hardness, friability, Bulk density, tapped density.

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