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COMPARATIVE STUDIES OF SITAGLIPTIN GENERIC PRODUCT VS BRAND

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ABSTRACT

Sitagliptin phosphate is a widely used dipeptidyl peptidase-4 (DPP-4) inhibitor employed in the treatment of type 2 diabetes mellitus. The development of an effective dosage form requires appropriate analytical characterization and pharmaceutical evaluation. Various studies have investigated the formulation, analytical determination, and in-vitro performance of Sitagliptin tablets, including immediate-release and enteric-coated formulations, as well as different assay techniques. Analytical investigations have demonstrated that Sitagliptin can be accurately quantified using UV–visible spectrophotometry. The drug exhibits good linearity within the concentration range of 2–10 µg/mL when analyzed as a 2,4-DNP complex with measurement at 400 nm, indicating that the method is reliable for routine quality control and assay purposes.

Method development studies have also established an optimized dissolution testing procedure using USP Apparatus II containing 900 mL of pH 6.8 phosphate buffer at a rotation speed of 50 rpm. This condition provided consistent and reproducible drug-release profiles, which were further validated using HPLC analysis, confirming the suitability of the dissolution method for Sitagliptin tablets.

Formulation research has focused on the preparation of immediate-release tablets incorporating super disintegrants such as croscarmellose sodium and sodium starch glycolate.

The prepared tablets complied with pharmacopeial limits for weight variation, thickness, hardness, friability, and disintegration time. The optimized formulations demonstrated rapid drug release, exceeding 99%. In addition, drug content uniformity and dissolution analysis were supported by UV spectrophotometric evaluation at 267 nm. The developed formulations satisfied the required pharmacopeial quality specifications and exhibited stability under ICH-recommended storage conditions.

KEYWORDS: Sitagliptin phosphate, evaluation, *In-vitro* studies, generic vs rand.

INTRODUCTION

According to the FDA, a generic drug product is defined as a medication that is comparable to a branded drug in terms of dosage form, strength, route of administration, quality, performance characteristics, and intended therapeutic use. Generic drugs are essentially copies of branded medicines whose patent protection has expired, allowing other manufacturers to produce and distribute the drug without exclusive rights. Despite regulatory assurance of equivalence, some patients still believe that generic medicines are less effective than branded drugs [1]. Initially, patients may hesitate to use generic medicines; however, due to their lower cost, they often improve treatment adherence. For bioequivalence approval, the confidence interval of the pharmacokinetic parameters of generic drugs must fall within the accepted range of 80% to 125% when compared with the reference product [2].

Sitagliptin phosphate is a widely prescribed medication for the treatment of type 2 diabetes mellitus and belongs to the class of dipeptidyl peptidase-4 (DPP-4) inhibitors. This drug enhances incretin hormone activity, which leads to improved insulin secretion and reduced glucagon release. Since Sitagliptin is available in both branded and generic forms, it is essential to evaluate their quality, analytical properties, and performance characteristics to confirm therapeutic equivalence. A generic formulation must possess the same dosage form, strength, safety, quality, and therapeutic indications as the branded product. However, differences in excipients and manufacturing processes may influence tablet characteristics such as hardness, friability, disintegration time, and drug-release behavior [3].

Analytical methods play a significant role in evaluating and comparing branded and generic Sitagliptin tablets. Among these methods, UV–visible spectrophotometry has been reported as a simple, accurate, and precise technique for the quantification of Sitagliptin. The

drug exhibits linear absorbance within the concentration range of 2–10 µg/mL when analyzed as a 2,4-dinitrophenylhydrazine (2,4-DNP) complex measured at 400 nm. This analytical approach ensures reliable assay determination for both branded and generic formulations [4].

Dissolution testing is another important parameter used to establish bioequivalence between brand and generic tablets. Standard dissolution conditions using USP Apparatus II (paddle method) with 900 mL of pH 6.8 phosphate buffer at a rotational speed of 50 rpm have been reported as effective for evaluating the in-vitro drug-release profile of Sitagliptin tablets. A validated dissolution method ensures that both branded and generic formulations release the drug at comparable rates and extents [5].

Formulation studies indicate that many generic Sitagliptin tablets incorporate superdisintegrants such as croscarmellose sodium and sodium starch glycolate to achieve disintegration and dissolution behavior similar to that of the branded product. Evaluation parameters including weight variation, thickness, hardness, friability, disintegration time, drug content, and dissolution have generally been reported within pharmacopeial limits for optimized generic formulations. These findings demonstrate that properly developed generic products can achieve both physical and functional equivalence with branded Sitagliptin tablets [6].

In certain modified or extended-release formulations, such as enteric-coated Sitagliptin tablets, coating polymers like Eudragit L-100 are employed to enable drug release in the intestinal environment. Such formulation strategies highlight the importance of design considerations in achieving performance characteristics comparable to, or sometimes better than, those of the branded formulations [7].

Therefore, a comprehensive comparison between branded and generic Sitagliptin tablets requires detailed evaluation through analytical assays, dissolution studies, and assessment of tablet quality parameters. The available literature indicates that well-formulated generic Sitagliptin tablets can demonstrate comparable quality and performance to branded products when assessed using standardized analytical methods and pharmacopeial guidelines [8].

Sitagliptin ((2R)-4-oxo-4-[3-(trifluoromethyl)-5,6-dihydrotriazolo[4,3-a] pyrazin-7(8H)-yl]-1-(2,4,5-trifluorophenyl) butan-2-amine) is an orally administered

antihyperglycemic agent used to control blood glucose levels in patients with type 2 diabetes mellitus. It belongs to the class of dipeptidyl peptidase-4 (DPP-4) inhibitors. After food intake, incretin hormones such as glucagon-like peptide-1 (GLP-1) are released. These hormones help regulate glucose homeostasis by stimulating insulin secretion and suppressing the release of glucagon from the pancreas, thereby reducing hepatic glucose production. Sitagliptin inhibits the DPP-4 enzyme responsible for the degradation of incretin hormones, particularly GLP-1 and glucose-dependent insulinotropic polypeptide (GIP). By preventing their breakdown, Sitagliptin increases the circulating levels and activity of these hormones, which ultimately leads to improved glycemic control and reduced blood glucose levels. Linagliptin, another DPP-4 inhibitor, received FDA approval in May 2011 [9].

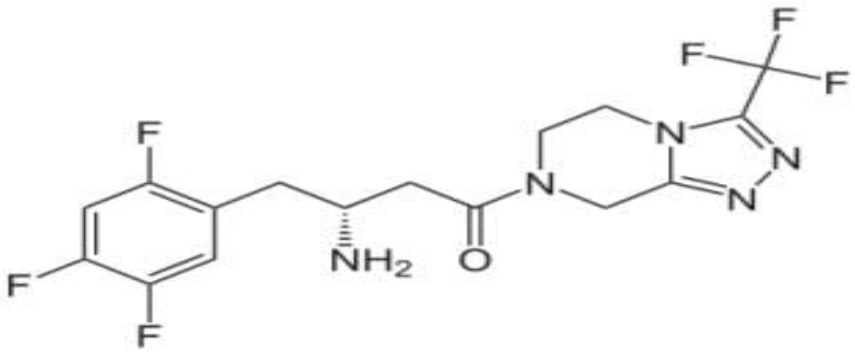

FIGURE 1: CHEMICAL STRUCTURE OF SITAGLIPTIN

MATERIALS AND METHODS

Shimadzu 1800 double beam UV/Vis spectrophotometer, digital balance (Citizen Co. Mumbai, India), and micropipette (The Modern scientific industries, Meerut, India) were used in this study. Sitagliptin API was obtained from Honour Lab Limited. All other chemical used were of analytical reagent grade. Freshly prepared distilled water was used in the study[10].

METHODOLOGY

Sitagliptin Tablet 50mg of both generic and branded drug was subjected for quality control test as per Indian Pharmacopoeia 2018 [10].

TABLE1: LABELLING CONTENTS OF SITAGLIPTIN TABLET

Tablet Name	Cost of Drug(₹)	Manufacturer	Batch No.	Mfg. Date	Expiry Date
Generic	43.00 (10 Tablets)	Pharmaceuticals & Medical Devices Bureau of India(PMBI)	ST250401	04/2025	03/2027
Brand	102 .00 (10 Tablets)	Sun pharma laboratories Pvt Ltd	GTG1208A	04/2025	03/2027

EVALUATION OF TABLETS

1. THICKNESS

Select 10 tablets at random from the batch.A vernier caliper was used to measure the thickness of the tablet. Place each tablet between the jaws of the instrument.Apply no excessive pressure that may deform the tablet.Record the thickness of each tablet in millimeters (mm).Determine the average thickness of the 10 tablets.Note the individual variations from the mean value.Variation should not exceed ±5% from the average value [10].

2. HARDNESS

Hardness or tablet crushing strength (fc), the force required to break a tablet in a diametric compression was measured using Monsanto or Pfizer hardness tester.Ten tablets were tested for each formulation .It is expressed in kg/cm^2 [10].

3. FRIABILITY

Ten tablets were weighed and placed in the Roche friabilator and the apparatus was allowed to rotate for 100 times. After the revolutions, the tablet were dedusted and weighed again. The percentage friability was measured using the formula,[11]

Friability= Initial weight-Final weightInitial weight ×100

Limit: Less than 1.0%

4. WEIGHT VARIATION

The test for uniformity of weight is performed by weighing individually 20 tablets randomly selected from a tablet batch and determining their individual weights. The individual weights are compared with the average weight [11].

The sample complies with IP standard if no more than 2 tablets are outside the percentage limit and if no tablet differs by more than 2 times the percentage limit. Coated tablets are exempted from these requirements but must confirm to the test for content uniformity [10].

% Deviation= Average weight-individual weightAverage weight ×100

TABLE 2: IP STANDARDS FOR WEIGHT VARIATION TEST

S.No	Average weight of tablet (mg)	Max percentage difference allowed (%)
1	80 or less	10
2	80 – 250	7.5
3	More than 250	5

4.DISINTEGRATION

This was determined at 37°C using Disintegration Testing (DT) apparatus (Indian equipment corpo- ration, India) in simulated gastric fluid until no particle remained on the basket of the system. This test not only evaluates the quality but also the bioavailability and effectiveness of tablets. The disintegration time of Each tablet was determined and the average disintegration time was calculated[12].

5.DISSOLUTION

Apparatus No:1 (Paddle Type)

Dissolution is the process by which a solid substance dissolves in a solvent to form a solution. In pharmaceutical studies, *in-vitro* dissolution testing is used to determine the rate and extent at which a drug substance is released from a dosage form, such as tablets or capsules, into the dissolution medium under controlled conditions. This test measures the percentage of the active drug that goes into solution within a specified time period. According to the United States Pharmacopeia (USP), dissolution testing using Apparatus II (paddle method) is commonly performed by placing the dosage form in a vessel containing a specified volume of dissolution medium, usually 900 mL, maintained at a temperature of 37 ± 0.5 °C. The paddle is rotated at a predetermined speed, typically 50 rpm, unless otherwise specified in the pharmacopeial monograph. The dosage form is placed at the bottom of the vessel to ensure proper contact with the medium. Samples are withdrawn at predetermined time intervals from a position midway between the surface of the dissolution medium and the top of the rotating paddle, maintaining a distance of at least 1 cm from the vessel wall. The collected samples are filtered immediately and analyzed, generally using UV spectrophotometry or high-performance liquid chromatography (HPLC), to determine the percentage of drug released. The obtained results must comply with the dissolution acceptance criteria specified in the relevant Indian Pharmacopoeia (IP) monograph [13].

In the present study, the dissolution analysis was performed using IP dissolution apparatus type-I. The dissolution medium consisted of 900 mL of phosphate buffer (pH 7.4) maintained at 37 ± 0.5 °C, and the apparatus was operated at a rotational speed of 50 rpm. At specific time intervals (0, 5, 10, and 15 minutes, followed by every 15 minutes thereafter), 5 mL samples were withdrawn and analyzed spectrophotometrically at 267 nm using a Shimadzu-1700 UV–visible spectrophotometer. Each withdrawn sample was immediately replaced with an equal volume of fresh phosphate buffer (pH 6.8) to maintain constant dissolution conditions. The concentration of the drug in the collected samples was determined with the aid of a standard calibration curve prepared using the pure active pharmaceutical ingredient (API). The sample concentration was calculated using the linear regression equation $Y = mX + C$ derived from the standard curve [14].

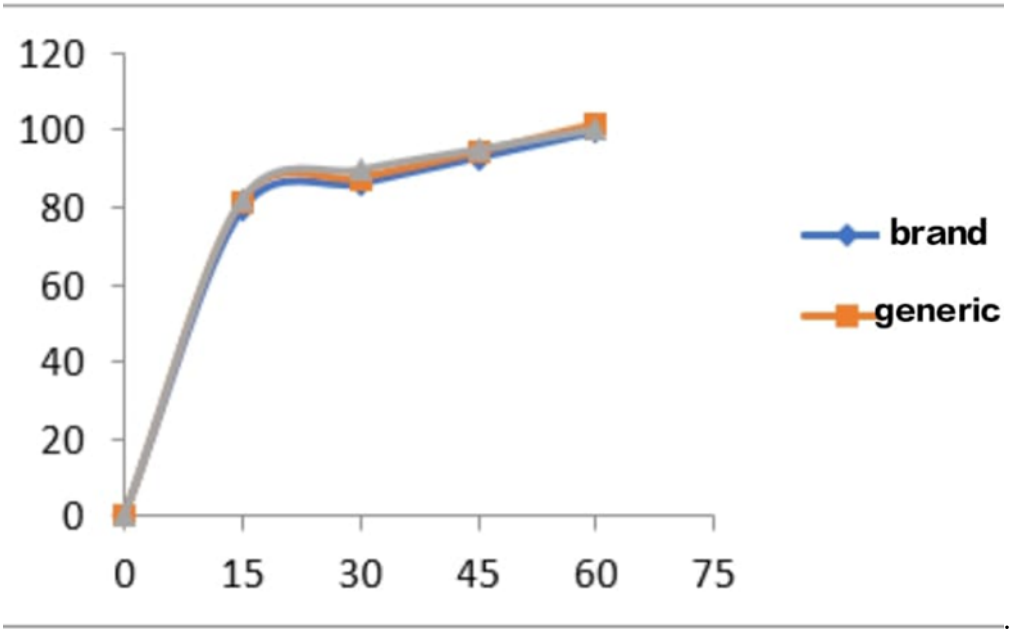

FIGURE 2: DISSOLUTION PROFILE OF GENERIC AND BRAND DRUG OF SITAGLIPTIN

6.ASSAY

Preparation of Stock solution

Sample was prepared by weighing and crushing 10 tablets, transferring amount of drug powder equivalent to 10 mg (100µg/ml) in distilled water solution and placing it in sonicator [14].

Preparation of Working standard solution

The portion of solution 10ml/100ml was filtered and the filtrate was suitably diluted to give concentration of 1µg/ml respectively. Absorbance was taken at 267nm by using UV-visible spectrophotometer. Finally, the potency of different tablets was determined by using the following equation [14].

$$Y=0.007X-0.199$$

Procedure for Calibration curve

The standard stock solution was prepared by dissolving sitagliptin distilled water to

make final concentration of 100 µg/ml. Different aliquots were taken from stock solution and diluted with distilled water separately to prepare series of concentrations from 2,4,6,8,10,12 µg/ml. The λmax was found by UV spectrum of sitagliptin in phosphate buffer (pH7.4), in the range of 200-400 nm and it was found to be 267nm. Absorbance was measured at 267nm against as blank. The calibration curve was prepared by plotting absorbance versus concentration of Sitagliptin [14].

TABLE 3: RESULTS OF CALIBRATION CURVE DATA OF SITAGLIPTIN

S.No	Concentration (µg/ml)	Absorbance
1	0	0
2	2	0.181
3	4	0.293
4	6	0.442
5	8	0.591
6	10	0.789
7	12	0.999

TABLE 4: QUALITY CONTROL TEST FOR SITAGLIPTIN

S.No	Tablets Name	Weight Variation (%)	Hardness Test (kg/cm^2)	Friability Test (%)	Thickness Test (mm)	Disintegration Test (min)	Dissolution Test (%)	Assay (%)
	Standard as per I.P	±10 for less than 80mg	4-8	<1	±5	30	Not less than 80	95 - 105
1.	Generic	3.26	5.6	0.39	3.5	9.25	89.6	98.22
2.	Brand	1.54	6.2	0.42	3.3	7.37	96.4	99.17

5. RESULTS AND DISCUSSION

The comparative evaluation of branded and generic Sitagliptin tablets demonstrated that both formulations complied with pharmacopeial requirements for parameters such as weight variation, hardness, thickness, friability, and disintegration time. Generic tablets formulated with super disintegrants including croscarmellose sodium and sodium starch glycolate exhibited rapid disintegration while maintaining satisfactory mechanical strength, comparable to the branded formulation. UV–visible spectrophotometric analysis confirmed the presence and appropriate concentration of the active pharmaceutical ingredient in both products. The analytical method based on the 2,4-DNP complex showed excellent linearity within the concentration range of 2–10 µg/mL ($R^2 \approx 0.999$), indicating its suitability for accurate drug estimation. These findings suggest that generic Sitagliptin tablets can achieve drug-content uniformity and physical characteristics similar to those of the branded product.

Dissolution studies performed using USP Apparatus II with 900 mL of pH 6.8 phosphate buffer at a rotation speed of 50 rpm demonstrated that both branded and generic tablets released a substantial amount of the drug within the specified time period. The comparable in-vitro drug-release profiles indicate similarity in dissolution performance between the two formulations. The validated dissolution method provides a reliable approach for assessing potential bioequivalence between branded and generic Sitagliptin tablets. In addition, investigations on enteric-coated Sitagliptin formulations showed that generic products prepared with Eudragit L-100 exhibited effective resistance to acidic conditions and enabled drug release in the intestinal environment, similar to the branded coated tablets. Stability studies further confirmed that these formulations maintained their quality and integrity under ICH-recommended storage conditions. Overall, the findings demonstrate that properly formulated generic Sitagliptin tablets can achieve comparable quality attributes, dissolution behavior, and potential therapeutic effectiveness to those of branded formulations when evaluated using validated analytical and pharmacopeial methods.

CONCLUSION

The evaluation results of branded and generic Sitagliptin tablets demonstrate that both formulations can achieve comparable pharmaceutical quality when formulated with suitable excipients and assessed using validated analytical methods. UV–visible spectrophotometric analysis, including the 2,4-DNP method, showed excellent linearity within the concentration

range of 2–10 µg/mL, confirming accurate and consistent drug content in both branded and generic products. These results indicate that the formulations comply with pharmacopeial requirements for drug assay. In addition, physical quality parameters such as weight variation, hardness, thickness, friability, and disintegration time were found to be within acceptable limits. Optimized generic formulations containing super disintegrants such as croscarmellose sodium and sodium starch glycolate demonstrated performance characteristics comparable to those of branded Sitagliptin tablets.

Dissolution studies further revealed that both branded and generic formulations exhibited similar drug-release profiles when evaluated using the validated USP Apparatus II method with 900 mL of pH 6.8 phosphate buffer at a rotation speed of 50 rpm, indicating comparable in-vitro drug availability. Studies on enteric-coated Sitagliptin tablets also showed that generic formulations prepared with suitable polymers such as Eudragit L-100 provided adequate protection in acidic conditions and enabled targeted drug release in the intestinal environment, similar to the branded formulations. Stability studies additionally confirmed that these formulations maintained their integrity and quality under ICH-recommended storage conditions. Overall, the findings suggest that properly developed generic Sitagliptin tablets can offer therapeutic performance comparable to branded products, making them reliable, safe, and cost-effective alternatives for the management of diabetes.

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