Review Article

Review On Analytical Method for Determination of Sitagliptin Phosphate in Bulk and In Different Dosage Forms

Nusratbanu K. Shaikh*, Darshil B. Shah, Dilip G. Maheshwari

ABSTRACT

Dipeptidyl peptidase-4 inhibitors (DPP-4s), also called as gliptins, are a relatively new class of drugs to treat type 2 diabetes. Sitagliptin phosphate competitively inhibit dipeptidyl peptidase-4 (DPP-4). This enzyme breakdown the incretins GLP-1, gastrointestinal hormones released in response to a meal. By preventing GLP-1 inactivation, they are able to increase the secretion of insulin and suppress the release of glucagon by the alpha cells of pancreas. This leads blood glucose level to normal. It also opens new gateways for a personalized medicine in patients with Type 2 diabetes and it also offers various merits when compared to other glucose-lowering agents. Despite they have been commercialized since a few years only, available data obtained in randomized controlled trials are of better quality compared to those available with classical glucose-lowering agents, especially in elderly people who have suffering from renal impairment or at high cardiovascular risk and patients at higher risk of hypoglycemia. But, their remaining uncertainties and controversies that should be resolved by further ongoing large prospective controlled trials and increasing clinical experience combined with a careful post-marketing surveillance. The clinical and pharmaceutical analysis of these drugs requires effective analytical procedures for quality control and pharmacodynamic and pharmacokinetic studies as well as stability study. There are many analytical methods reported so far in the literature for the determination of Sitagliptin phosphate in Biological samples and pharmaceutical formulations. This article narrates different chromatographic (HPLC, HPTLC, UPLC, LC) & different spectrophotometric method (UV) for Sitagliptin single drug as well as combination with other drug.

Key-words: Sitagliptin phosphate, Spectrophotometry, HPLC,UV

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INTRODUCTION: [1-6]

SITAGLIPTIN PHOSPHATE:
Sitagliptin phosphate marketed as the phosphate salt under the trade name (Januvia) is an oral antihyperglycemic (antidiabetic drug) of the dipeptidyl peptidase-4 (DPP-4) inhibitor class. It was developed, and is marketed, by Merck & Co. This enzyme-inhibiting drug is used either alone or in combination with other oral antihyperglycemic agents (such as metformin or a thiazolidinedione) for treatment of diabetes mellitus type 2. Their mechanism of action is to improve insulin secretion from the Beta-cells of the pancreas as a result of an increase in blood sugar and simultaneously decrease glucagon output from the alpha-cells of the pancreas, which in turn decreased hepatic glucose output.

<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>Parameters</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Category</td>
<td>Antidiabetic drug of the dipeptidyl peptidase-4 (DPP-4) inhibitor class</td>
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<tr>
<td>2</td>
<td>Structure</td>
<td><img src="image_url" alt="Chemical Structure" /></td>
</tr>
<tr>
<td>3</td>
<td>Chemical Formula</td>
<td>C_{16}H_{18}F_{6}N_{5}O_{5}P</td>
</tr>
<tr>
<td>4</td>
<td>IUPAC Name</td>
<td>(2R)-4-OXO-4-[3-(trifluoromethyl)-5,6-dihydro[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl]-1-(2,4,5-trifluorophenyl)butan-2-amine</td>
</tr>
<tr>
<td>5</td>
<td>Molecular Weight</td>
<td>505.31 gm/mol</td>
</tr>
<tr>
<td>6</td>
<td>Characteristic</td>
<td>White to Off white, crystalline, Non hygroscopic powder</td>
</tr>
<tr>
<td>7</td>
<td>Solubility</td>
<td>Soluble in Methanol, water and slightly soluble in ethanol</td>
</tr>
<tr>
<td>8</td>
<td>CDSCO Approval</td>
<td>03-07-2010</td>
</tr>
</tbody>
</table>

OFFICIAL METHODS FOR ESTIMATION OF SITAGLIPTIN PHOSPHATE
Sitagliptin phosphate drug is not official in any of the Pharmacopoeia.

REPORTED METHODS OF SITAGLIPTIN PHOSPHATE (SINGLE COMPONENT)

<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>Drug Description</th>
<th>Method</th>
<th>Detection wavelength</th>
<th>Ref. No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Sitagliptin in bulk and pharmaceutical formulation</td>
<td>UV Spectrophotometric Method</td>
<td>267 nm</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Solvent: 0.1 N HCl</td>
<td>Linearity range: 20-100%</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Correlation coefficient: 0.998</td>
<td>%Recovery : 96-99%</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Sitagliptin in pharmaceutical preparations</td>
<td>UV Spectrophotometric method</td>
<td>430 nm</td>
<td>8</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Concentration range: 5-25 µg/ml</td>
<td>Apparent molar absorptivity: 1.067x10³ Lmol⁻¹cm⁻¹</td>
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<tr>
<td></td>
<td></td>
<td>Correlation coefficient: 0.9998</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Method</td>
<td>Description</td>
<td>Parameters</td>
<td></td>
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<tr>
<td>----------------------------------------------------------------------</td>
<td>----------------------------------------------------------------------------------------------------------</td>
<td>---------------------------------------------------------------------------------------------</td>
<td></td>
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</tr>
<tr>
<td>3 Sitagliptin in bulk and in Formulation</td>
<td>First order derivative UV-Spectrophotometric method</td>
<td>The $\lambda_{\text{max}}$ of sitagliptin in methanol and water: 267 nm</td>
<td></td>
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</tr>
<tr>
<td></td>
<td></td>
<td>Maximum amplitude of the trough: 275 nm</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Linearity range: 10-60 $\mu$g/ml</td>
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<tr>
<td></td>
<td></td>
<td>Correlation coefficient: 0.9998</td>
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<tr>
<td></td>
<td></td>
<td>% Amount of drug: 99.19 %</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>% Recovery: 98.54% – 99.98%</td>
<td></td>
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</tr>
<tr>
<td>4 Sitagliptin Phosphate in bulk and pharmaceutical formulations</td>
<td>UV Spectrophotometric Method</td>
<td>Maximum absorption: 400 nm</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Linearity range: 2-10 $\mu$g/ml</td>
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<td></td>
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<td>Solvent: Methanol</td>
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<td></td>
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<td>Limit of detection (LOD): 0.139 $\mu$g/ml</td>
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<td></td>
<td></td>
<td>Limit of quantitation (LOQ): 0.422 $\mu$g/ml</td>
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<td></td>
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<td>Average % Recovery: 98.72 - 108.2%</td>
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<tr>
<td>5 Sitagliptin in Human Plasma</td>
<td>RP-HPLC Method</td>
<td>Detection wavelength: 267 nm</td>
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<tr>
<td></td>
<td></td>
<td>Stationary Phase: Intersil C18 column (150 mm x 4.6 mm, 5 $\mu$m)</td>
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<td></td>
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<td>Mobile phase: Acetonitrile: Methanol: Buffer (2:3:5 v/v)(pH 4.0 by 0-phosphoric acid)</td>
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<td></td>
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<td>Flow rate: 1.0 mL/min</td>
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<td></td>
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<td>Linearity range: 25-125 $\mu$g/mL</td>
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<tr>
<td>6 Sitagliptin in Human Plasma</td>
<td>LC-MS Method (Liquid Chromatography Tandem Mass Spectrometry method using Liquid–Liquid Extraction)</td>
<td>Linearity range: 0.1 – 250 ng/mL</td>
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<td></td>
<td></td>
<td>Lower limit of quantitation (LLOQ): 0.1 ng/mL</td>
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<tr>
<td></td>
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<td>Multiple reaction monitoring (MRM) transition: m/z (Sitagliptin): 408 – 235</td>
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<tr>
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<td>m/z (Internal standard): 310 – 148</td>
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<td></td>
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<td>Run time of 2.0 min for each sample</td>
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<tr>
<td>7 Sitagliptin in Human Plasma</td>
<td>LC–MS/MS method using protein precipitation and tandem mass spectrometry</td>
<td>Stationary Phase: Waters Atlantis Hilic Silica column (2.1 mm x 50 mm, 3 $\mu$m)</td>
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<tr>
<td></td>
<td></td>
<td>Mobile Phase: ACN/H$_2$O (80/20, v/v) containing 10 mM NH$_4$Ac (pH 4.7).</td>
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<tr>
<td></td>
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<td>Multiple reaction monitoring transition: m/z 408 → 235 for sitagliptin and m/z 412 → 239 for IS.</td>
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<td></td>
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<td>Lower limit of quantitation: 1 ng/mL</td>
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<tr>
<td></td>
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<td>Linearity range: 1–1000 ng/mL</td>
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<tr>
<td>8 Sitagliptin Phosphate in API and Its Unit Dosage Forms</td>
<td>Extractive Method by Spectrophotometry</td>
<td>Methods are based on complexation of the drug with BromoThymol Blue (BTB Method A) &amp; Bromo Cresol Green (BCG-Method B)</td>
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<td></td>
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<td>Extraction Solvent: Chloroform</td>
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<td>Absorbance maxima: Method A: 412 nm</td>
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<td>Method B: 419 nm</td>
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<td></td>
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<td>Linearity range: Method A: 25-125 $\mu$g/ml</td>
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<td></td>
<td></td>
<td>Method B: 10-50 $\mu$g/ml</td>
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<tr>
<td>Page</td>
<td>Method Description</td>
<td>Method Details</td>
<td>Remarks</td>
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<td>------</td>
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</tr>
</tbody>
</table>
| 9    | Sitagliptin Phosphate in Formulation and Spiked Human Urine | Spectrofluorimetric Method | **Fluorescence wavelength:** 297 nm  
**Linearity range:** 0.6-10 µg mL<sup>-1</sup>  
**Limit of detection:** 78.782 ng/ml  
**Limit of quantification:** 238.735 ng/ml  
**%Amount of sitagliptin phosphate in tablet formulation:** 93.34-102.67% |
| 10   | Sitagliptin phosphate in Pharmaceutical Formulation | A Selective Sensor Potentiometric Method | **Linear responses:** 1×10<sup>-5</sup> to 1×10<sup>-2</sup> M with slope of 40.9 mV/decade  
**Stock solution:** (1×10<sup>-1</sup> M)  
**Working solutions:** (1×10<sup>-7</sup> to 1×10<sup>-2</sup> M)  
**Slope** : 40.9 (mV/decade)  
**Intercept** : 260.9 (mV)  
**LOD** : 2.0×10<sup>-6</sup> (M)  
**Response Time** :30 (Sec.)  
**Working pH Range** : 4-7 |
| 11   | Sitagliptin in Biological Fluids | MIP (Molecularly imprinted polymers) Based Biomimetic Sensors for Potentiometric Transduction Method - Flow injection analysis (FIA) | **In acidic solution:** pH 5  
**Sensors exhibit Concentration ranges:** 5.0×10<sup>-6</sup>–1.0×10<sup>-2</sup> mol L<sup>-1</sup> (MAA)  
1.0×10<sup>-5</sup> – 1.0×10<sup>-2</sup> mol L<sup>-1</sup> (2-VP)  
**Slopes** : 52.7–40.5 mV decade<sup>-1</sup>  
**Linear range (mol L<sup>-1</sup>)** :  
MIP/MAA: 5.0×10<sup>-6</sup>  
MIP/MAA+TPB: 5.0×10<sup>-6</sup>  
MIP/2-VP - : 1.0×10<sup>-5</sup>  
MIP/2-VP+TPB-: 2.5×10<sup>-6</sup> |
| 12   | Sitagliptin Phosphate for Coated Tablets | Dissolution Method Based on In Vivo Data for Improving Medium Sensitivity | **pH**: 6.8 phosphate buffer  
**Dissolution medium**: 900 mL  
**Temperature**: 37 ± 1 °C  
**Apparatus**: paddle  
**Rotation speed**: 50 rpm.  
**Linearity range**: 10.0–70.0 µg/mL  
**Accuracy mean recovery**: 98.51% |

### REPORTED METHODS OF SITAGLIPTIN PHOSPHATE (WITH COMBINATION)

<table>
<thead>
<tr>
<th>Page</th>
<th>Method Description</th>
<th>Method Details</th>
<th>Remarks</th>
</tr>
</thead>
</table>
| 13   | Sitagliptin and Metformin in bulk and tablet dosage form | UV Spectrophotometric Method | **Detection wavelength:**  
Sitagliptin: 266nm  
Metformin HCl: 232nm  
**Solvent**: Distilled water  
**Linearity**:  
Sitagliptin: 25-225µg/ml  
Metformin HCl: 2-12 µg/ml  
**%Recovery** :  
Sitagliptin: 99.64%  
Metformin HCl: 98.98% |
| 14   | Sitagliptin and Metformin in bulk and tablet dosage form | RP-HPLC Method | **Detection wavelength**: 215nm  
**Mobile Phase**: Potassium dihydrogen orthophosphate(pH-8.5) : Methanol (50:50v/v)  
**Stationary Phase**: Hypersil BDS C<sub>18</sub> column(100 mm, 4.6 mm, 5 µm) |
| 15 | **Metformin Hydrochloride and Sitagliptin Phosphate in a Formulation** | **RP-HPLC Method** | **Detection wavelength:** 266nm  
**Mobile Phase:** Methanol: Potassium dihydrogen phosphate buffer (70:30 v/v)  
**Stationary Phase:** Hibar-240, Li-Chrosphere-100 C18 ODS (250 x 4.6 mm, 5 µm) column  
**Linearity range:**  
Sitagliptin Phosphate: 10-50 µg/mL  
Metformin HCl: 20-100 µg/mL  
**Flow rate:** 1.0ml/min  
**Retention times:**  
Sitagliptin Phosphate: 6.1 min  
Metformin HCl: 4.9 min  
**Limit of Detection:**  
Sitagliptin Phosphate: 0.016 µg/ml  
Metformin HCl: 0.14 µg/ml  
**Limit of Quantification:**  
Sitagliptin Phosphate: 0.048 µg/ml  
Metformin HCl: 0.42 µg/ml | 21 |
|---|---|---|---|
| 16 | **Sitagliptin phosphate monohydrate and Metformin hydrochloride in tablets** | **Stability indicating RP-HPLC method** | **Detection wavelength:** 245nm  
**Mobile Phase:** Acetonitrile : Ammonium acetate buffer (pH - 4.5) (70:30 v/v)  
**Stationary Phase:** Supelco column(25cm, 4.6mm, 5 µm)  
**Linearity range:**  
Sitagliptin: 10-50 µg/ml  
Metformin: 1-5 µg/ml  
**Flow rate:** 0.8ml/min  
**%Recovery :**  
Sitagliptin: 99%  
Metformin HCl: 100.6% | 22 |
| 17 | **Metformin & Sitagliptin in bulk and pharmaceutical dosage form** | **Stability-Indicating RP-HPLC Method** | **Detection wavelength:** 205nm using a photodiode array detector  
**Mobile Phase:**  
OPA buffer: Acetonitrile (80:20 v/v)  
**Stationary Phase:** Agilent CN(250mm x 4.6mm, 5µm) column  
**Linearity range:**  
Metformin: 25-750 µg/ml  
Sitagliptin: 3-75 µg/ml  
**Flow rate:** 1.0 ml/min | 23 |
| 18 | **Sitagliptin phosphate monohydrate and Metformin hydrochloride in UPLC Method** | **Detection wavelength:** 210nm  
**Mobile Phase:** 10mM Potassium dihydrogen phosphate : 2mM Hexane 1 sulfonic acid sodium salt : Acetonitrile | 24 |
| 19 | Sitagliptin Phosphate and Metformin Hydrochloride | UPLC Method | Detection wavelength: 220 nm  
Mobile Phase: Isocratic elution (methanol 20%), pH (3.5)  
Stationary Phase: Symmetry C₁₈ column (100 mm × 2.1 mm, 2.2 μm)  
Linearity range:  
Sitagliptin: 2-12 μg/ml  
Metformin: 0.2-35 μg/ml | 25 |
| 20 | Metformin Hydrochloride and Sitagliptin Phosphate in Tablet Dosage Form | HPTLC Method | Stationary Phase: Silica gel 60 F254 plates  
Mobile phase: Butanol : Water : Glacial acetic acid (6 : 2 : 2, v/v/v)  
Detection wavelength: 227 nm  
Rf value:  
Metformin hydrochloride: 0.35 ± 0.01  
Sitagliptin phosphate: 0.75 ± 0.01  
Limits of Detection:  
Metformin hydrochloride: 13.05 ng/μL  
Sitagliptin phosphate: 2.65 ng/μL  
Limits of Quantitation:  
Metformin hydrochloride: 39.56 ng/μL  
Sitagliptin phosphate: 8.03 ng/μL | 26 |
| 21 | Sitagliptin and Metformin Hydrochloride in Bulk Drug and Formulation | HPTLC Method | Stationary Phase: TLC plates precoated with silica gel 60F254  
Mobile phase: Methanol: Ammonia: Glacial acetic acid (9.4:0.4:0.2 v/v/v)  
Detection and TLC scanner wavelength: 214 nm  
Concentration range:  
Sitagliptin: 100–1100 ng band-1  
Metformin hydrochloride: 1000–11000 ng band-1  
Limits of Detection:  
Sitagliptin: 7.08 ng band-1  
Metformin hydrochloride: 19.31 ng band-1  
Limits of Quantitation:  
Sitagliptin: 21.82 ng band-1  
Metformin hydrochloride: 58.51 ng band-1 | 27 |
| 22 | Metformin and Sitagliptin in Human Plasma | LC-MS-MS Method and Its Application in a Bioequivalence Study | Solvent: Acetonitrile  
Stationary Phase: SCX column  
Linearity range:  
Metformin: 10–2,206 ng/mL  
Sitagliptin: 3-800.5ng/mL | 28 |
<table>
<thead>
<tr>
<th>23</th>
<th>Sitagliptin and Metformin in Pharmaceutical Preparations</th>
<th>Mean recovery: Metformin: 92% Sitagliptin: 104.5%</th>
</tr>
</thead>
</table>
|    | Capillary Zone Electrophoresis and its Application to Human Plasma Analysis | Detection wavelength: 203 nm  
Stationary Phase: Separation in fused silica capillary (50.0 cm total length and 43.0 cm effective length, 49 μm i.d.)  
Mobile phase: Buffer containing 60 mM phosphate buffer at pH 4.0  
Temperature of the capillary cartridge: 25°C  
Internal standard (IS): Phenformin  
Linearity ranges:  
Sitagliptin: 10–100 μg/mL  
Metformin: 50–500 μg/mL  
Limits of detection: Sitagliptin: 0.49 μg/mL  
Metformin: 2.11 μg/mL  
Limits of quantification:  
Sitagliptin: 1.48 μg/mL  
Metformin: 6.39 μg/mL |
| 24 | Sitagliptin in Binary Mixture with Metformin and Ternary Mixture with Metformin and Sitagliptin Alkaline Degradation Product | The zero order spectrophotometric method for STG: 50–300 μg mL⁻¹  
The first derivative spectrophotometric method  
For MET: 2–12 μg mL⁻¹  
For STG: 50–300 μg mL⁻¹  
Peak amplitude: 246.5 nm and 275 nm  
For MET: 2–12 μg mL⁻¹  
Peak amplitudes: 232 nm and 239 nm  
The Fluorimetric method: 0.25–110 μg mL⁻¹ |
| 25 | Metformin and Three Gliptins in Pharmaceutical Formulations | Stationary Phase: Fast monolithic column  
Mobile phase: Mixture of Sodium dihydrogen phosphate, Sodium deoxy sulphate and Acetonitrile  
Detection wavelength:  
Metformin, Vildagliptin & Sitagliptin: 208 nm  
Metformin & Linagliptin: 228 nm  
Flow rate: 2.5 mL/min  
Linearity range:  
Metformin: 10–100 μg/mL and 50–400 μg/mL  
Vildagliptin & Sitagliptin: 1–10 μg/mL  
Linagliptin: 0.25–2.0 μg/mL  
Retention time:  
Metformin: 0.78 and 0.76 min  
Vildagliptin: 1.18 min  
Sitagliptin: 3.83 min  
Linagliptin: 2.65 min  
LOD (μg/mL): Metformin: 0.01 and 0.09  
Vildagliptin: 0.03  
Sitagliptin: 0.02  
Linagliptin: 0.02  
LOQ (μg/mL): Metformin: 0.04 and 0.29

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<table>
<thead>
<tr>
<th>Page</th>
<th>Methodology</th>
<th>Detection wavelength:</th>
<th>Solvent:</th>
<th>% Recovery:</th>
<th>Linearity range:</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>26</td>
<td><strong>Sitagliptin and Pioglitazone in combination of drugs</strong></td>
<td>Sitagliptin: 267nm</td>
<td>Double Distilled water, 0.1N HCl, Methanol</td>
<td>Sitagliptin: 101.3±0.88%</td>
<td>Sitagliptin: 20-120μg/ml</td>
<td>32</td>
</tr>
<tr>
<td></td>
<td><strong>UV Spectrophotometric Method</strong></td>
<td>Pioglitazone HCl: 269nm</td>
<td></td>
<td>Pioglitazone HCl: 94.5±3.47%</td>
<td>Pioglitazone HCl: 2.5-25 μg/ml</td>
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</tr>
<tr>
<td>27</td>
<td><strong>Sitagliptin and Pioglitazone in pharmaceutical dosage form</strong></td>
<td>Sitagliptin: 267nm</td>
<td></td>
<td></td>
<td>Sitagliptin: 20-60μg/ml</td>
<td>33</td>
</tr>
<tr>
<td></td>
<td><strong>RP-HPLC Method</strong></td>
<td>Pioglitazone HCl: 225nm</td>
<td></td>
<td></td>
<td>Pioglitazone HCl: 6-14 μg/ml</td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Detection wavelength:</strong> Sitagliptin: 267nm</td>
<td>Mobile Phase: Acetonitrile: potassium dihydrogen phosphate buffer (pH - 3) (30:70v/v)</td>
<td></td>
<td>Flow rate: 1.0ml/min</td>
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<tr>
<td></td>
<td>Pioglitazone HCl: 225nm</td>
<td><strong>Stationary Phase:</strong> C&lt;sub&gt;18&lt;/sub&gt; column {250 mm, 4.6 mm, 5 µm}</td>
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<td></td>
<td><strong>Linearity range:</strong> Sitagliptin: 20-60μg/ml</td>
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<td>Pioglitazone HCl: 6-14 μg/ml</td>
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<tr>
<td>28</td>
<td><strong>Gliclazide And Sitagliptin Phosphate Monohydrate In Bulk And Pharmaceutical Dosage Form</strong></td>
<td>Solvent: Methanol</td>
<td></td>
<td></td>
<td>Gliclazide: 5-25 μg/ml</td>
<td>34</td>
</tr>
<tr>
<td></td>
<td><strong>UV Spectrophotometric Method</strong></td>
<td><strong>Detection wavelength:</strong> Gliclazide: 226 nm</td>
<td></td>
<td>Gliclazide: 100.01</td>
<td>Gliclazide: 20-100 μg/ml</td>
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<td></td>
<td></td>
<td><strong>Linearity range:</strong> Sitagliptin Phosphate Monohydrate: 267 nm</td>
<td></td>
<td>Sitagliptin Phosphate Monohydrate: 99.3</td>
<td>Sitagliptin Phosphate Monohydrate: 20-100 μg/ml</td>
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<td></td>
<td></td>
<td><strong>Linearity range:</strong> Gliclazide: 7-27 μg/ml</td>
<td></td>
<td>Limit of detection: Gliclazide: 0.4364 μg/ml</td>
<td>Limit of detection: Gliclazide: 0.6 μg/ml</td>
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</tr>
<tr>
<td>29</td>
<td><strong>Gliclazide And Sitagliptin Phosphate Monohydrate In Bulk And Tablet Dosage Form</strong></td>
<td><strong>Stationary phase:</strong> Phenomenex Luna (C18) A 100RP Column (250mm x 4.6mm x 5µm)</td>
<td></td>
<td>Limit of quantification: Gliclazide: 1.3232 μg/ml</td>
<td>Limit of quantification: Gliclazide: 1.9 μg/ml</td>
<td>35</td>
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<tr>
<td></td>
<td><strong>RP-HPLC Method</strong></td>
<td>Injection volume: 20μl</td>
<td></td>
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<td></td>
<td></td>
<td>Mobile phase: Water: Acetonitrile (40:60 v/v)</td>
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<td></td>
<td></td>
<td>Flow rate: 1.0ml/min</td>
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<td></td>
<td></td>
<td><strong>Retention time:</strong> Gliclazide: 3.268</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td><strong>Detection wavelength:</strong> 253nm</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td><strong>Linearity range:</strong> Gliclazide: 5-25 μg/ml</td>
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<td></td>
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<tr>
<td></td>
<td></td>
<td>Sitagliptin Phosphate Monohydrate: 20-100 μg/ml</td>
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<tr>
<td></td>
<td></td>
<td><strong>Percentage Assay:</strong> Gliclazide: 100.01</td>
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<tr>
<td>Page</td>
<td>Method</td>
<td>Detection wavelength</td>
<td>Mobile Phase</td>
<td>Stationary Phase</td>
<td>Linearity range</td>
<td>Flow rate</td>
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<tr>
<td>30</td>
<td>RP-HPLC</td>
<td>266 nm PDA detector</td>
<td>Methanol : Water (25:75, v/v)</td>
<td>Agilent C8 column {250 x 4.6mm, 5 µm}</td>
<td>Sitagliptin : 20-120 µg/ml&lt;br&gt; Simvastatin : 10-50 µg/ml</td>
<td>1 ml/min</td>
</tr>
<tr>
<td>31</td>
<td>RP-HPLC</td>
<td>250 nm</td>
<td>Acetonitrile, Methanol and 10 mM Phosphate buffer (65:25:10 % v/v/v) pH 4 adjusted with orthophosphoric acid</td>
<td>aHi-Q Sil C18 (250 mm × 4.6 mm, 5 µm Particle size) column</td>
<td>Sitagliptin : 20-120 µg/ml&lt;br&gt; Simvastatin : 10-50 µg/ml</td>
<td>1.2 ml/min</td>
</tr>
<tr>
<td>32</td>
<td>RP-HPLC</td>
<td>252 nm</td>
<td>0.05M phosphate buffer (pH 4±0.02 adjusted with o-phosphoric acid): Acetonitrile (70:30 v/v)</td>
<td>BDS Hypersil C18, (250mm × 4.6mm × 5µm) column.</td>
<td>Sitagliptin : 20-120 µg/ml&lt;br&gt; Simvastatin : 10-50 µg/ml</td>
<td>1.0 ml/min</td>
</tr>
<tr>
<td>33</td>
<td>RP-HPLC</td>
<td>253 nm PDA detector</td>
<td>Methanol : Water (70:30, v/v)</td>
<td>Qualisil BDS C8 column {250x 4.6mm, 5 µm}</td>
<td>Sitagliptin : 20-150 µg/ml&lt;br&gt; Simvastatin : 8-60 µg/ml</td>
<td>1 ml/min</td>
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<tr>
<td>Page</td>
<td>Content</td>
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<tr>
<td>34</td>
<td>Sitagliptin And Simvastatin In Pharmaceutical Formulation</td>
<td>HPTLC Method</td>
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</tr>
</tbody>
</table>
|      | Simvastatin : 30.4 min | **Stationary Phase:** Merck TLC aluminum sheets of silicagel G60 F254 with the thickness of 200 µm.  
**Mobile phase:** Ethyl acetate: Toluene: Methanol (6:2:2 v/v/v)  
**Detection wavelength by densitometry:** 254 nm  
**Rf value:** Sitagliptin: 0.6 ± 0.02  
Simvastatin: 0.3 ± 0.02  
**Concentration range:** Sitagliptin: 2-6 µg/spot  
Simvastatin: 0.2-0.6 µg/spot |
| 35   | Sitagliptin and Vildagliptin in bulk and dosage form | UV spectroscopy (based on charge transfer complexes) |
|      | Detection wavelength: 461 nm  
Sitagliptin: 461 nm (with DDQ)  
837 nm (with TCNQ)  
555 nm (with p-chloranil)  
Vildagliptin: 486 nm (with DDQ)  
838 nm (with TCNQ)  
555 nm (with p-chloranil)  
**Solvent:**  
Sitagliptin: Methanol (with DDQ)  
Methanol (with TCNQ)  
DMF (with p-chloranil)  
Vildagliptin: Acetonitrile (with DDQ)  
Methanol (with TCNQ)  
DMF (with p-chloranil)  
**Linearity:**  
Sitagliptin: 50-300 µg/ml (with DDQ)  
20-120 µg/ml (with TCNQ)  
100-900 µg/ml (with p-chloranil)  
Vildagliptin: 50-300 µg/ml (with DDQ)  
10-85 µg/ml (with TCNQ)  
50-350 µg/ml (with p-chloranil) |
| 36   | Sitagliptin, Metformin and Atorvastatin in Pure form and in Pharmaceutical Formulation | RP-HPLC Method |
|      | Detection wavelength: 254 nm  
**Mobile Phase:** Mix buffer: Methanol (30:70 v/v/v)  
**Stationary Phase:** HyperSil GOL (150 mm x 4.6 mm, 5 µm) column  
**Internal Std.:** Quetiapine  
**Flow rate:** 1.0 ml/min  
**Linearity range:** Sitagliptin: 3.125-100 µg/ml  
Metformin: 0.625-25 µg/ml  
Atorvastatin: 3.125-10 µg/ml  
**Retention time:**  
Sitagliptin: 3.384 min  
Metformin: 2.640 min |
**CONCLUSION:**

This review depicts the reported Spectrophotometric and Chromatographic methods; developed and validated for estimation of Sitagliptin phosphate. According to this review it was concluded that for Sitagliptin phosphate (DPP-IV inhibitor) different Spectroscopic & Chromatographic methods are available for Single component as well as for combination and also it was found that the Mobile phase containing Phosphate buffer, Methanol and Acetonitrile were common for most of the chromatographic method to provide more resolution. It was observed that most common combination of DPP-IV inhibitors were with Metformin. For chromatographic method flow rate is observed in the range of 0.8-1.5 ml/min to get good retention time. For most of the Spectroscopic methods common solvent is Methanol. Hence this all methods found to be simple, accurate, economic, precise, and reproducible in nature.
ACKNOWLEDGEMENT:

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REFERENCE:


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