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

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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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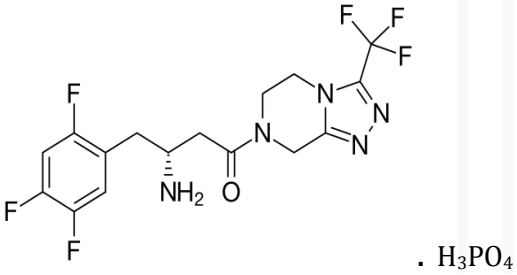
INTRODUCTION: [1-6]

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 1: Drug Profile[4, 5-6]

Sr. No.	Parameters	Description
1	Category	Antidiabetic drug of the dipeptidyl peptidase-4 (DPP-4) inhibitor class
2	Structure	 . H_3PO_4
3	Chemical Formula	$C_{16}H_{18}F_6N_5O_5P$
4	IUPAC Name	(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
5	Molecular Weight	505.31 gm/mol
6	Characteristic	White to Off white, crystalline, Non hygroscopic powder
7	Solubility	Soluble in Methanol, water and slightly soluble in ethanol
8	CDSCO Approval	03-07-2010

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 3: Reported methods of Sitagliptin phosphate [7-43]

Sr. No.	Drug	Method	Description	Ref. No.
1	Sitagliptin in bulk and pharmaceutical formulation	UV Spectrophotometric Method	**Detection wavelength:** 267 nm **Solvent:** 0.1 N HCl **Linearity range:** 20-100% **Correlation coefficient:** 0.998 **%Recovery :** 96-99%	7
2	Sitagliptin in pharmaceutical preparations	UV Spectrophotometric method	**Detection wavelength:** 430 nm **Concentration range:** 5-25 µg/ml **Apparent molar absorptivity:** $1.067x10^4$ $Lmol^{-1}cm^{-1}$ **Correlation coefficient:** 0.9998	8

			%RSD: 1.13 % **Limit of detection:** 1.947 µg/ ml **Limit of quantification:**5.90µg/ ml	
3	Sitagliptin in bulk and in Formulation	First order derivative UV-Spectrophotometric method	**The λmax of sitagliptin in methanol and water:** 267 nm **Maximum amplitude of the trough:** 275 nm **Linearity range:** 10-60 µg/ml **Correlation coefficient:** 0.9998 **% Amount of drug:** 99.19 % **% Recovery:** 98.54%– 99.98%	9
4	Sitagliptin Phosphate in bulk and pharmaceutical formulations	UV Spectrophotometric Method	**Maximum absorption :** 400nm **Linearity range:** 2-10µg/ml **Solvent :** Methanol **Limit of detection (LOD):** 0.139µg/ml **Limit of quantitation (LOQ):** 0.422µg/ml **Average %Recovery:** 98.72 - 108.2%	10
5	Sitagliptin in Human Plasma	RP-HPLC Method	**Detection wavelength:** 267 nm **Stationary Phase**: Intersil C18 column (150 mm × 4.6 mm, 5µm) **Mobile phase:** Acetonitrile: Methanol: Buffer (2:3:5 v/v)(pH 4.0 by O-phosphoric acid) **Flow rate:** 1.0 mL/min **Linearity range:** 25-125µg/mL	11
6	Sitagliptin in Human Plasma	LC-MS Method (Liquid Chromatography Tandem Mass Spectrometry method using Liquid–Liquid Extraction)	**Linearity range:** 0.1 – 250 ng/mL **Lower limit of quantitation (LLOQ):**0.1 ng/mL **Multiple reaction monitoring (MRM) transition :** **m/z** (Sitagliptin) **:** 408 – 235 **m/z (** Internal standard) : 310 –148 **Run time** of 2.0 min for each sample	12
7	Sitagliptin in Human Plasma	LC–MS/MS method using protein precipitation and tandem mass spectrometry	**Stationary Phase:** Waters Atlantis Hilic Silica column (2.1 mm × 50 mm, 3 µm) **Mobile Phase:** ACN/H_2O (80/20, v/v) containing 10 mM NH_4Ac (pH 4.7). **Multiple reaction monitoring transition :** *m/z* 408 → 235 for sitagliptin and *m/z* 412 → 239 for IS. **Lower limit of quantitation** :1 ng/mL **Linearity range**: 1–1000 ng/mL	13
8	Sitagliptin Phosphate in API and Its Unit Dosage Forms	Extractive Method by Spectrophotometry	Methods are based on complexation of the drug with BromoThymol Blue (BTB Method A) & Bromo Cresol Green (BCG-Method B) **Extraction Solvent:** Chloroform **Absorbance maxima :Method A:** 412 nm **Method B:** 419 nm **Linearity range :** **Method A:**25-125 µg/ml **Method B:** 10-50 µg/ml	14

9	Sitagliptin Phosphate in Formulation and Spiked Human Urine	Spectrofluorimetric Method	**Fluorescence wavelength:** 297 nm **Linearity range :** 0.6-10 µg mL−1 **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%.	15
10	Sitagliptin phosphate in Pharmaceutical Formulation	A Selective Sensor Potentiometric Method	**Linear responses**: 1×10−5 to 1×10−2 M with slope of 40.9 mV/decade **Stock solution:** (1×10-1 M) **Working solutions:** (1×10-7 to 1×10-2 M) **Slope :** 40.9 (mV/ decade) **Intercept :** 260.9 (mV) **LOD :** 2.0×10-6 (M) **Response Time :**30 (Sec.) **Working pH Range :** 4-7	16
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:** 5.0x10-6–1.0x10-2molL-1 (MAA) 1.0x10-5 – 1.0x10-2 mol L-1(2-VP) **Slopes :** 52.7– 40.5 mV decade-1 **Linear range (mol L-1) :** MIP/MAA:5.0x10-6 MIP/MAA+TPB : 5.0x10-6 MIP/2-VP – : 1.0x10-5 MIP/2-VP+TPB-:2.5x10-6	17
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%.	18
REPORTED METHODS OF SITAGLIPTIN PHOSPHATE (WITH COMBINATION)				
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%	19
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_{18} column(100 mm, 4.6 mm, 5 µm)	20

			Linearity range: Sitagliptin : 50-150% Metformin : 50-150% **Flow rate:** 1.0ml/min **Limit of Detection:** Sitagliptin: 0.07 µg/ml Metformin HCl: 0.08 µg/ml **Limit of Quantification:** Sitagliptin: 2.3 µg/ml Metformin HCl: 2.6 µg/ml	
15	Metformin Hydrochloride and Sitagliptin Phosphate in a Formulation	RP-HPLC Method	**Detection wavelength:** 266nm **Mobile Phase:** Methanol: Potassium di-hydrogen phosphate buffer (70:30 v/v) **Stationary Phase:** Hibar-240, Li-chrosphere-100 C18 ODS (250 × 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) (70:30v/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	Sitagliptinphospha te 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

	tablets		**Stationary Phase:** UPLC BEH C_8 column (100 x 2.1 mm i.d, 1.7 µm) **Flow rate:** 0.2 ml/min **Limit of Detection:** Sitagliptin: 0.2 µg/ml Metformin HCl: 0.06 µg/ml **Limit of Quantification:** Sitagliptin: 0.7 µg/ml Metformin HCl: 0.2 µg/ml	
19	Sitagliptin Phosphate and Metformin Hydrochloride	UPLC Method	**Detection wavelength:** 220 nm **Mobile Phase:** Isocratic elution (methanol 20%), pH (3.5) **Stationary Phase:** Symmetry C_{18}column (100 mm × 2.1 mm, 2.2 µm) **Linearity range :** Sitagliptin : 2-12 µg ml^{-1} Metformin : 5-35 µg ml^{-1}	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

			Mean recovery: Metformin: 92% Sitagliptin: 104.5%	
23	Sitagliptin and Metformin in Pharmaceutical Preparations	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	29
24	Sitagliptin in Binary Mixture with Metformin and Ternary Mixture with Metformin and Sitagliptin Alkaline Degradation Product	Spectroflourometric and Spectrophotometric Methods	**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}	30
25	Metformin and Three Gliptins in Pharmaceutical Formulations	RP-HPLC Method & Application to Stability Studies	**Stationary Phase**: Fast monolithic column **Mobile phase:** Mixture of Sodium dihydrogen phosphate, Sodium dedosyl 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	31

			Vildagliptin: 0.097 Sitagliptin : 0.064 Linagliptin: 0.067	
26	Sitagliptin and Pioglitazone in combination of drugs	UV Spectrophoto-metric Method	**Detection wavelength:** Sitagliptin: 267nm Pioglitazone HCl: 269nm **Solvent:** Double Distilled water,0.1N HCl, Methanol **Linearity :**Sitagliptin : 20-120µg/ml Pioglitazone HCl: 2.5-25 µg/ml **%Recovery :** Sitagliptin:101.3±0.88% Pioglitazone HCl: 94.5±3.47%	32
27	Sitagliptin and Pioglitazone in pharmaceutical dosage form	RP-HPLC Method	**Detection wavelength:** Sitagliptin: 267nm Pioglitazone HCl: 225nm **Mobile Phase:** Acetonitrile: potassium dihydrogen phosphate buffer (pH - 3) (30:70v/v) **Stationary Phase:** C_{18} column {250 mm, 4.6 mm, 5 µm} **Linearity range :** Sitagliptin : 20-60µg/ml Pioglitazone HCl: 6-14 µg/ml **Flow rate:** 1.0ml/min	33
28	Gliclazide And Sitagliptin Phosphate Monohydrate In Bulk And Pharmaceutical Dosage Form	UV Spectrophotome tric Method	**Solvent:** Methanol **Detection wavelength:** Gliclazide: 226 nm Sitagliptin Phosphate Monohydrate : 267 nm **Linearity range:** Gliclazide: 7-27 µg/ml Sitagliptin Phosphate Monohydrate : 20-100 µg/ml	34
29	Gliclazide And Sitagliptin Phosphate Monohydrate In Bulk And Tablet Dosage Form	RP-HPLC Method	**Stationary phase :** Phenomenex Luna (C18) A 100RP Column (250mm x 4.6mm x 5µm) **Injection volume :** 20µl **Mobile phase:** Water: Acetonitrile (40:60 v/v) **Flow rate :** 1.0ml/min **Retention time:** Gliclazide: 3.268 Sitagliptin Phosphate Monohydrate : 2.260 min **Detection wavelength:** 253nm **Linearity range:** Gliclazide: 5-25 µg/ml Sitagliptin Phosphate Monohydrate : 20-100 µg/ml **Percentage Assay :** Gliclazide: 100.01 Sitagliptin Phosphate Monohydrate : 99.3 **Limit of detection:** Gliclazide: 0.4364 µg/ml Sitagliptin Phosphate Monohydrate : 0.6 µg/ml **Limit of quantification:** Gliclazide: 1.3232 µg/ml Sitagliptin Phosphate Monohydrate : 1.9 µg/ml	35

30	Simvastatin and Sitagliptin in combined dosage form	RP-HPLC Method	**Detection wavelength:** 266nm PDA detector **Mobile Phase:** Methanol : Water (25:75, v/v) **Stationary Phase:** Agilent C8 column{250 x 4.6mm, 5 µm} **Linearity range:** Sitagliptin : 20-120 µg/ml Simvastatin : 10-50 µg/ml **Flow rate:** 1 ml/min **Retention time:** Sitagliptin : 3.227min Simvastatin : 15.760 min	36
31	Sitagliptin Phosphate And Simvastatin In Bulk And Tablet Dosage Form	RP-HPLC Method	**Detection wavelength:** 250nm **Mobile Phase:** Acetonitrile, Methanol and 10 mM Phosphate buffer (65:25:10 % v/v/v) pH 4 adjusted with orthophosphoric acid **Stationary Phase:** aHi-Q Sil C18(250 mm × 4.6 mm, 5 µm Particle size) column **Linearity range:** Sitagliptin : 20-120 µg/ml Simvastatin : 10-50 µg/ml **Flow rate:** 1.2 ml/min **Retention time:** Sitagliptin : 2.2 min Simvastatin : 6.8 min **Linearity range:** Sitagliptin : 100-600 µg/ml Simvastatin : 20-120 µg/ml	37
32	Simvastatin and Sitagliptin in tablet dosage form	Stability indicating RP-HPLC Method	**Detection wavelength:** 252 nm **Mobile Phase:** 0.05M phosphate buffer (pH 4±0.02 adjusted with o-phosphoric acid): Acetonitrile (70:30 v/v) **Stationary Phase:** BDS Hypersil C18, (250mm × 4.6mm × 5µm) column. **Linearity range:** Sitagliptin : 20-120 µg/ml Simvastatin : 10-50 µg/ml **Flow rate:** 1.0 ml/min **Total run time :** 10 minutes **Linearity range:** Sitagliptin : 7.5-52.5 µg/ ml Simvastatin : 3.5-10.5 µg/ ml **Amount of drugs present in the formulation (Juvisync):** Sitagliptin : 99.81 ± 0.73 Simvastatin : 99.97 ± 0.61	38
33	Simvastatin and Sitagliptinin Tablets	Stability indicating RP-HPLC Method	**Detection wavelength:** 253nm PDA detector **Mobile Phase:** Methanol : Water (70:30, v/v) **Stationary Phase:** Qualisil BDS C8 column{250x 4.6mm, 5 µm} **Linearity range:** Sitagliptin : 20-150 µg/ml Simvastatin : 8-60 µg/ml **Flow rate:** 1 ml/min **Retention time:** Sitagliptin : 4.3min	39

			Simvastatin : 30.4 min	
34	Sitagliptin And Simvastatin In Pharmaceutical Formulation	HPTLC Method	**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	40
35	Sitagliptin andVildagliptin in bulk and dosage form	UV spectroscopy (based on charge transfer complexes)	**Detection wavelength:** 461nm Sitagliptin: 461nm (with DDQ) 837nm (with TCNQ) 555nm (with p-chloranil) Vildagliptin: 486nm (with DDQ) 838nm(with TCNQ) 555nm(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: 50-300µg/ml (with DDQ) 20-120µg/ml (with TCNQ) 100-900µg/ml (with p-chloranil) Vildagliptin: 50-300µg/ml (with DDQ) 10-85µg/ml (with TCNQ) 50-350µg/ml (with p-chloranil)	41
36	Sitagliptin, Metformin and Atorvastatin in Pure form and in Pharmaceutical Formulation	RP-HPLC Method	**Detection wavelength:** 254nm **Mobile Phase:** Mix buffer: Methanol (30:70 v/v) **Stationary Phase:** HyperSil GOL (150mm x 4.6mm, 5µm)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	42

			Atorvastatin : 4.837 min Quetiapine (IS): 6.000 min **Limit of Detection:** Sitagliptin: 0.82 µg/ml Metformin : 0.4 µg/ml Atorvastatin : 0.09 µg/ml **Limit of Quantification:** Sitagliptin: 2.46 µg/ml Metformin : 1.2 µg/ml Atorvastatin : 0.27 µg/ml	
37	Metformin, Pioglitazone, Sitagliptin, Repaglinide, Glibenclamide and Gliclazide	Liquid Chromatographic-c Method & Application for Counterfeit Drug Analysis	**Detection wavelength:** 220 nm **Mobile Phase:** Acetonitrile (solution A) and buffer (solution B); the latter was composed of 0.05 M MKP and 0.01M SOS, pH adjusted to 3.55 by 85% ortho-phosphoric acid **Stationary Phase:** Kromasil 100-C18 (30 × 0.4 cm, 10 µm) **Flow rate:** 0.85 ml/min **Injection volume:** 20 µl. **Run time for each injection :** 20 minutes. **Retention time :** Metformin:2.24 Sitagliptin: 3.13 Pioglitazone: 6.3 Gliclazide: 7.41 Glibenclamide: 8.41 Repaglinide : 14.32	43

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.

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