ISSN: 0976-3031

*Available Online at http://www.recentscientific.com*

*International Journal of Recent Scientific Research*
*Vol. 7, Issue, 10, pp. 13515-13524, October, 2016*

**International Journal of Recent Scientific Research**

**Review Article**

# REVIEW ON ANALYTICAL METHOD FOR DETERMINATION OF GLIMEPIRIDE IN BULK AND IN DIFFERENT DOSAGE FORMS

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**ARTICLE INFO**

***Article History:***
Received 15th July, 2016
Received in revised form 25th August, 2016
Accepted 23rd September, 2016
Published online 28th October, 2016

***Key Words:***
Glimepiride, Spectrophotometric Method, HPLC,UV

**ABSTRACT**

Glimepiride is medium-to-long-acting sulfonylurea antidiabetic drug. It is classified as either the first third-generation sulfonylurea, or as second-generation. It acts as an insulin secretagogue. It lowers blood sugar by stimulating the release of insulin by pancreatic beta cells and by inducing increased activity of intracellular insulin receptors. Their mechanism of action is Glimepiride binds to ATP-sensitive potassium channel receptors on the pancreatic cell surface, reducing potassium conductance and causing depolarization of the membrane. Membrane depolarization stimulates calcium ion influx through voltage-sensitive calcium channels. This increase in intracellular calcium ion concentration induces the secretion of insulin. 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 to suffer from a 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 the drug 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 Glimepiride in Biological samples and pharmaceutical formulations. This article narrates different chromatographic (HPLC, HPTLC, UPLC, LC) & different spectrophotometric method (UV) for Glimepiride single drug as well as combination with another drug.



## INTRODUCTION

### *Glimepiride*

Glimepiride is medium-to-long-acting sulfonylurea antidiabetic drug. It is classified as either the first third-generation sulfonylurea, or as second-generation. It acts as an insulin secretagogue. It lowers blood sugar by stimulating the release of insulin by pancreatic beta cells and by inducing increased activity of intracellular insulin receptors.

**Table 1** Drug Profile [1-6]

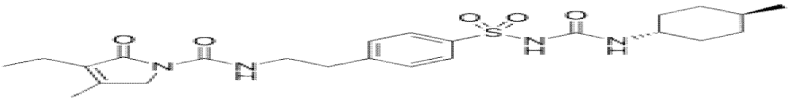
| Sr. No. | Parameters | Description |
|---|---|---|
| 1 | Category | Antihyperglycemic agent (antidiabetic drug) of Sulfonyl urea class |
| 2 | Structure |  |
| 3 | Chemical Formula | $C_{24}H_{34}N_4O_5S$ |
| 4 | IUPAC Name | 3-ethyl-4-methyl-N-{2-[4-({[(4-methylcyclohexyl)carbamoyl]amino}sulfonyl)phenyl]ethyl}-2-oxo-2,5-dihydro-1H-pyrrole-1-carboxam ide |
| 5 | Molecular Weight | 490.617 gm/mol |
| 6 | Characteristic | White to Off white, crystalline compound |
| 7 | Solubility | Soluble in Water and Methanol, Slightly soluble in Methylene chloride, Very Slightly soluble in DMF |
| 8 | CDSCO Approval | 22-07-1999 |

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**Table 2** Official Methods for Estimation of Glimepiride: [5]
Glimepiride is official in Indian pharmacopoeia (IP 2014).

| Sr. No | Drug | Method | Description | Ref. No |
|---|---|---|---|---|
| 1 | Glimepiride in tablet dosage form (IP 2014) | Liquid Chromatography Method | **Detection wavelength:** 228nm<br>**Mobile Phase:**<br>**S**olution of 0.5g in 500mlwater (pH 2.1orthophosphoric acid)<br>Monophasic Sodium phosphate: Acetonitrile (50:50%v/v)<br>**Stationary Phase:**<br>Inertsil ODS $C_{18}$ column (12.5 cm×4mm,4µm)<br>**Flow rate:**1.0 ml/min | 5 |

**Table 3** Reported Methods of Glimepiride (Single Component) [6-47]

| Sr. No | Drug | Method | Description | Ref No |
|---|---|---|---|---|
| 1 | Glimepiride in pharmaceutical dosage form | UV Spectro-Photometric Method | **Detection wavelength :** 249 nm<br>**Linearity range**: 5-30 µg/ml<br>**Correlation coefficient:** 0.999732<br>**Precision:** 0.159437<br>**Limit of Detection:** 0.4 µg/ml<br>**Limit of Quantification:** 1.2 µg/ml | 6 |
| 2 | Glimepiride in tablet dosage form | RP-HPLC Method | **Detection wavelength:** 210 nm<br>**Mobile Phase:**<br>Acetonitrile : 0.05M monophasic potassium phosphate (pH 6.0)(40:60) (v/v).<br>**Stationary Phase:**<br>Hypersil $C_{18}$ column (15x3.9mm)<br>**Retention time:** 7.8 min<br>**Flow rate**: 1.5 ml/min<br>**Recoveries** : 99-101% | 7 |
| 3 | Glimepiride in tablet formulation | Stability indicating RP-HPLC Method | **Detection wavelength:** 228nm<br>**Mobile Phase:**<br>potassium phosphate buffer (pH 6.5; 27.5 mmol/L)-methanol (34 + 66, v/v)<br>**Stationary Phase:**<br>C18 column (250 x 4.6 mm, 5.0 pm)<br>**Flow rate:** 1 ml/min<br>**Retention time:** 9 min<br>**linearity** 2 to 40 mg/L<br>**LOD** : 0.315 mg/L<br>**LOQ** : 1.050 mg/L | 8 |
| 4 | Glimepiride in supersaturatable self-nanoemulsifying (SNE) formulation | RP-HPLC Method | **Detection wavelength:** 228nm<br>**Mobile Phase:** potassium dihydrogen phosphate buffer(pH-4): Acetonitrile (50:50 v/v)<br>**Stationary Phase:**<br>Kromasil C18 column (150 x 4.6 mm; 5µ)<br>**Retention time:** 0.9152 min<br>**Flow rate:** 1.0ml/min | 9 |
| 5 | Glimepiride in Self-nanoemulsifying powder (SNEP) formulation | RP-HPLC method and its dissolution study | **Detection wavelength:**228 nm using PDA detector.<br>**Mobile Phase:** Acetonitrile: 0.2 M phosphate buffer (pH-7.4) 40:60 n*v/v*<br>**Stationary Phase:**<br>octadesyl silane (ODS) column (250x4.6mm, 5µm in particle size)<br>**Flow rate:** 1.0ml/min | 10 |
| 6 | Glimepiride in tablets | UV-derivative spectrophotometric method | **Linearity range:**<br>Glimepiride : 0.2-2 µg/ml<br>**Limit of Detection:** Glimepiride : 0.38 µg/ml<br>**Limit of Quantification:** Glimepiride: 1.17 µg/ml<br>**Detection wavelength:** Using a wavelength interval of 8 nm in the range of 220-300 nm.<br>**Solvent :** $5\times10^{-3}$ mol $L^{-1}$ NaOH<br>**Linearity range :** 2 to 40 mg $L^{-1}$ | 11 |
| 7 | **Glimepiride In Pure And Tablet Dosage Forms** | Direct spectrophotometric method **Through Ion-Pair Complex Formation Using Bromocresol Green** | Formed complex was measured at $l_{max}$ : 416 nm<br>**Concentration range :** 0.981-9.812 µg/ml<br>**Correlation coefficient$R^2$ :** 0.9992<br>**Limit of detection (LOD) :** 0.088 µg/ml<br>**Limit of quantification (LOQ) :** 0.29 µg/ml<br>**Robustness :** 98.9 to 102.4%<br>**Assay of marketed formulations :** 97.8 to 102.4% | 12 |

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|---|---|---|---|---|
| 8 | Glimepiride in human plasma | LC-ESI-MS-MS Method | **Internal standard, IS:** glimepiride d8<br>**Column:** C(18) column<br>**Mobile phase :** acetonitrile-2 mm ammonium formate (88:12, v/v), with the pH adjusted to 3.5 with formic acid<br>**Flow rate:** 0.5 mL/min.<br>**Retention times:** Glimepiride and IS : 0.93 min<br>**Runtime:** 1.6 min per sample.<br>**Linearity range:** 2.0-650.0 ng/mL.<br>**Recovery range:** Glimepiride&IS : 81.91-83.36%.<br>**Assay :** one step liquid-liquid extraction with methanol | 13 |
| 9 | Glimepiride in Rat Serum | RP-HPLC Method | **Internal standard:** Gliclazide<br>**Detection wavelength:** 230nm.<br>**Mobile Phase:** Methanol: 10 mM phosphate buffer (80:20 v/v) pH 3.0 with orthophosphoric acid<br>**Stationary Phase:** C18 column<br>**Retention time:** Glimepiride : 5.5 min<br>Gliclazide : 4.0 min<br>**Flow rate:** 1.0ml/min<br>**Acceptable Linearity range:** 0.5- 500 µg/ml<br>**Separation completion:** less than 10 min. | 14 |
| 10 | **Glimepiride in Rat Plasma** | **RP-HPLC Method And Application to Pharmacokinetic Studies** | **Detection wavelength:** 230nm.<br>**Mobile Phase:**<br>Methanol: Water (85:15 v/v)<br>**Stationary Phase:** C18 column<br>**Retention time:**<br>Glimepiride: 2.5 min<br>**Flow rate:** 1.0ml/min<br>**Acceptable Linearity range:** 100 – 6000 ng/mL | 15 |
| | | **Reported Methods of Glimepiride (With Combination)** | | |
| 11 | Metformin HCl and Glimepiride in bulk and tablet dosage form | Simultaneous UV Spectro-photometric Method | **Detection wavelength:**<br>Metformin: 236 nm<br>Glimepiride: 228 nm<br>**Solvent:** Methanol<br>**Linearity range:** 5-25µg/ml | 16 |
| 12 | Metformin HCl and Glimepiride in combined tablet dosage form | RP-HPLC Method | **Detection wavelength:** 285 nm<br>**Mobile Phase:**<br>Orthophosphoric acid (pH -9.2)<br>Methanol(60:40 v/v)<br>**Stationary Phase:**<br>Water symmetry shielde Rp 18 column(250x4.6mm, 5µm in particle size)<br>**Retention time:**<br>Metformin: 2.344min<br>Glimepiride: 3.725 min<br>**Flow rate:** 1.0ml/min | 17 |
| 13 | Metformin HCl and Glimepiride in Fixed-Dose Combination | Stability-Indicating RP-HPLC Method | **Detection wavelength:** 230nm<br>**Mobile Phase: 1** an aqueous phase (20 mM phosphate buffer, adjusted to pH 3.0) and an organic phase (methanol:acetonitrile;62.5:37.5) in the ratio of 80:20<br>**Stationary Phase:** JASCO Finepak SIL (250 mm × 4.6 mm i.d. 5 µm)<br>**Retention time:**<br>Metformin HCl :2.75 min<br>**Glimepiride**: 5.87 min<br>**Flow rate:** 1 ml/min | 18 |
| 14 | GLIMEPIRIDE and Metformin in Human Plasma | HPLC Method | **Detection wavelength:** 231nm<br>**Mobile Phase:** Methanol: Water (90:10%v/v)<br>**Stationary Phase:** C18 column(250 x 4.6 mm; 5µ)<br>**Retention time:**<br>Glimepiride: 4.286 min<br>Metformin HCl :2.262 min<br>**Flow rate:** 1 ml/min<br>**Linearity:**<br>Glimepiride :0.2-1microg/ml<br>Metformin HCl: 1-5microg/ml<br>**%Recovery :**<br>Glimepiride: 99.98%<br>Metformin HCl: 99.9%<br>**Assay**: % Purity<br>Glimepiride: 98.05<br>Metformin HCl: 99.69 | 19 |

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| 15 | *Glimepiride And Metformin Hydrochloride* | *Stability Indicating HPTLC Method* | **Detection wavelength:** 228nm<br>**Stationary Phase:** TLC aluminium plates precoated with silica gel 60F254<br>**Mobile Phase:** 0.5% Ammonium Sulfate: Methanol (7.5:2.5 v/v)<br>**RF values :** Glimepiride : 0.73<br>Metformin hydrochloride:0.45<br>**Linearity :** Glimepiride : 600-2100 ng/band<br>Metformin hydrochloride: 200-700 ng/band<br>**Limit of detection :**Glimepiride : 0.05 ng/band<br>Metformin hydrochloride: 0.32 ng/band<br>**Limit of quantification** :Glimepiride : 0.16 ng/band<br>Metformin hydrochloride: 0.96 ng/band | 20 |
| 16 | Glimepiride/Metformin (2/500 mg)Tablets in Healthy Volunteers | Bioequivalence Study | **$C_{max}$ and $AUC_t$ range :** 80-125%.<br>**The GMRs(90% CI) of the glimepiride :**<br>$C_{max}$ : 1.006(0.947-1.069)<br>$AUC_t$ :1.010(0.953-1.071)<br>**For Metformin:** $C_{max}$ :1.019(0.959-1.083) $AUC_t$ :1.035(0.989-1.084) | 21 |
| 17 | Pioglitazone and GLIMEPIRIDE in bulk and combine dosage form | UV Derivative($1^{st}$ order) Spectro-Photometric Method | **Detection wavelength:**<br>Pioglitazone :225 nm<br>Glimepiride: 248 nm<br>**Solvent:** 0.1 N HCl<br>**Linearity range:** Pioglitazone **:**5-30µg/ml<br>Glimepiride : 4-20 µg/ml<br>**Correlation coefficient:** Pioglitazone **:** 0.9912<br>Glimepiride : 0.9964<br>**Limit of Detection:** Pioglitazone **:** 0.0187 µg/ml<br>Glimepiride : 0.132 µg/ml<br>**Limit of Quantification:**Pioglitazone **:** 0.056µg/ml<br>Glimepiride : 0.40µg/ml | 22 |
| 18 | Pioglitazone and Glimepiride in tablet-Dosage form | UV By multiwavelength Spectroscopy | **Detection wavelength:** 280nm and 238nm<br>**Solvent :** 0.1 N NaOH<br>**Linearity range:**<br>Pioglitazone **:**10-50 µg/ml<br>Glimepiride : 1-5 µg/ml<br>**% RSD**: Pioglitazone **:** 0.74<br>Glimepiride : 0.96<br>**% Recovery:** Pioglitazone **:** 101.0<br>Glimepiride : 100.9 | 23 |
| 19 | Pioglitazone and Glimepiride in tablets | RP-HPLC Method | **Detection wavelength:** 225 nm<br>**Mobile Phase:**<br>Phosphate buffer(pH-4.5): Acetonitrile (45:55 v/v)<br>**Stationary Phase:** Inertsil ODS (250x4.6mm, 5µm)<br>**Retention time:**<br>Pioglitazone: 4.6 min<br>Glimepiride: 7.7 min<br>**Flow rate:** 1.0ml/min<br>**Linearity range:**<br>Pioglitazone **:**5-50 µg/ml<br>Glimepiride : 5-25 µg/ml | 24 |
| 20 | Pioglitazone and Glimepiride in pharmaceutical dosage form | RP-HPLC Method | **Detection wavelength:** 230nm<br>**Mobile Phase:** Acetonitrile: $KH_2PO_4$ buffer(pH6) (60:40 v/v)<br>**Stationary Phase:**<br>Phenomenex Luna (150x4.6mm, 5µm in particle size)<br>**Retention time:**<br>Pioglitazone: 4.4min<br>Glimepiride: 2.7 min<br>**Flow rate:** 1.5ml/min<br>**Linearity range:**<br>Pioglitazone **:** 240-360µg/ml<br>Glimepiride :32-48 µg/ml | 25 |
| 21 | Pioglitazone And Glimepiride In Bulk And Pharmaceutical Formulation | RP-HPLC Method | **Detection wavelength:** 248nm (PDA Detector)<br>**Mobile Phase:** 0.1M $CH_3COONH_2$**:**Methanol (60:40v/v)<br>**Stationary Phase:** YMC Pack Pro C18 column (250mm × 4.6mm, 5µm)<br>**Column temperature:** 30 C<br>**Flow rate:** 1.0 ml/min<br>**Linearity range** :<br>Pioglitazone HCl: 54-162 µg/ml<br>GLIMEPIRIDE: 7.2-21.60µg/ml<br>**Correlation coefficient:** 0.999<br>**Limit of detection (LOD):**<br>Pioglitazone HCl: 0.149 µg/ml<br>Glimepiride: 0.0133 µg/ml<br>**Limit of quantification (LOQ)**:<br>Pioglitazone HCl: 0.496 µg/ml<br>Glimepiride: 0.0442 µg/ml | 26 |

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|---|---|---|---|---|
| 22 | Rosiglitazone and Glimepiride in combined dosage forms and human plasma | RP-HPLC method | **Detection wavelength:** 235 nm using nicardipine as an internal standard.<br>**Mobile Phase:**Acetonitrile: 0.02M Phosphate buffer(pH5) (60:40 v/v)<br>**Stationary Phase:** C18 column (150 x 4.6 mm; 5µ)<br>**Retention time:**<br>Rosiglitazone: 3.7 min<br>Glimepiride: 4.66 min Nicardipine : 6.37 min.<br>**Flow rate:** 1.0ml/min<br>**Linearity range:**<br>Rosiglitazone **:**0.10-25 µg/ml<br>Glimepiride : 0.125-12.5 µg/ml<br>**Limit of Detection:**<br>Rosiglitazone & Glimepiride : 0.04µg/ml<br>**Limit of Quantification:**<br>Rosiglitazone **:** 0.13µg/ml<br>Glimepiride : 0.11µg/ml<br>Simultaneous equations (Vierodt's method | 27 |
| 23 | Ezetimibe And Glimepiride In Bulk Drugs And Marketed Formulation | Stability Indicating UV Spectrophotometric Method | **Solvent:** Methanol<br>**Absorbance maxima λ max:**<br>Glimepiride : 226 nm<br>Ezetimibe : 233 nm<br>**Linearity range:**<br>Glimepiride : 10-30 µg/ml<br>Ezetimibe : 1-3 µg / ml<br>**%Recovery :**<br>Glimepiride : 99.65%<br>Ezetimibe : 100.3%<br>**Limit of detection (LOD) :**<br>Glimepiride : 2.64 µg/ml<br>Ezetimibe : 26.4 µg / ml<br>**Limit of quantification (LOQ) :**<br>Glimepiride : 8 µg/ml<br>Ezetimibe : 80 µg / ml | 28 |
| 24 | Glimepiride Ezetimibe In Bulk And Pharmaceutical Dosage Form | RP-HPLC Method | **Detection wavelength:** 247nm<br>**Mobile Phase:** 0.01N Potassium dihydrogen Ortho phosphate and Acetonitrile (70:30 v/v)<br>**Stationary Phase:** BDS (250mm x 4.6 mm, 5µ) column<br>**Retention time:**<br>Glimepiride : 2.76 min<br>Ezetimibe : 3.65 min<br>**Flow rate:** 1.0 ml/min<br>**Linearity range:**<br>Glimepiride : 2.5-15 µg/ml<br>Ezetimibe : 25-150 µg / ml | 29 |
| 25 | Ezetimibe And Glimepiride In Bulk Drugs And Marketed Formulation | Stability Indicating RP-HPLC Method | **Detection wavelength:** 228nm.<br>**Mobile Phase:**<br>ACN: Phosphate Buffer (70:30) (v/v)<br>**Stationary Phase:** Inertsil C18 (250 x 4.6 mm; 5 µm) column<br>**Retention time:**<br>Ezetimibe : 3.921 ± 0.02min<br>Glimepiride : 5.102 ± 0.02 min<br>**Flow rate:** 1.4 ml/min<br>**Linearity range:**<br>Ezetimibe : 60 -140 mcg<br>Glimepiride : 6 -14 mcg<br>**Limit of detection (LOD) :**<br>Ezetimibe : 3.09 µg / ml<br>Glimepiride : 0.23 µg / ml<br>**Limit of quantification (LOQ) :**<br>Ezetimibe : 9.37 µg / ml<br>Glimepiride : 0.69 µg / ml<br>**%Recovery :**<br>Ezetimibe : 98.79%<br>Glimepiride : 98.82% | 30 |
| 26 | Glimepiride And Ezetimibe In Bulk And Tablet Dosage Form | Stability Indicating RP-HPLC Method | **Detection wavelength:** 237nm.<br>**Mobile Phase:** Phosphate in water as buffer pH adjusted to 4.8 with tri ethylamine, acetonitrile in proportion ratio 30:70(v/v)<br>**Stationary Phase:**<br>Hypersil ODS $C_{18}$(150mm x 4.6 mm, 5m) column<br>**Retention time:**<br>Glimepiride : 3.328 min<br>Ezetimibe : 2.322 min<br>**Flow rate:** 1.0 ml/min<br>**Linearity range:** Glimepiride: 2.5-15 µg/ml<br>Ezetimibe : 25-150 µg / ml<br>**Total run time** : 6 min | 31 |

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|---|---|---|---|---|
| 27 | Rosuvastatin Calcium and Glimepiride in Tablet Dosage Form | UV Spectrophotometric Method | **Detection wavelength:** 241nm and 231nm<br>**Solvent :** 0.1 N NaOH<br>**Linearity range:** 10-22µg/ml<br>**Accuracy(%Recovery):**Rosuvastatin Ca.: 99.04%<br>Glimepiride **:** 100.94% | 32 |
| 28 | Glimepiride and sildenafil citrate in rat plasma | RP-HPLC method And application to pharmacokinetic studies | **Detection wavelength:** 230nm<br>**Mobile Phase:** Methanol: Water (85:15 v/v)<br>**Stationary Phase:** C18 column<br>**Retention time:**<br>Glimepiride: 2.5min<br>Sildenafil : 4min<br>**Flow rate:** 1.0ml/min<br>**Total run time :** 7 min | 33 |
| 29 | Sildenafil and Glimepiride in Rat Plasma | LC-MS Method and their Applications in Pharmacokinetic Interactions | **Linearity range:** 100-12 000 ng/ml.<br>**Mobile phase:** A mixture of 70% methanol, 30% of 0.1% formic acid in water<br>**Stationary phase:** ACE 5 C18 column<br>**Flow rate:** 0.5 mL/min<br>**Autosampler injection volume:** 5 µL,<br>**Internal standard:** Clarithromycin<br>**%Accuracy:**<br>Glimepiride: 99.7%<br>Sildenafil: 98.9%<br>**Correlation coefficient:** 0.994 to 1 | 34 |
| 30 | Atorvastatin and Glimepiride in Human Plasma | LC-MS/MS Method and Its Application to a Pharmacokinetic Study | **Linearity range:**<br>Atorvastatin: 0.2-30 ng / ml<br>Glimepiride : 1-250 ng/ml<br>**Mean Extraction Recoveries :**<br>Atorvastatin: 80.34 ± 9.43<br>Glimepiride : 88.19 ± 7.13<br>**Intra & Inter-run Mean %Accuracy:**85% - 115%<br>**% Imprecision :** ≤15% | 35 |
| 31 | Carvedilol, Glimepiride Or Glibenclamide In Binary Combinations | RP-HPLC Method And Its Application For In Vitro - Interaction Studies | **Detection wavelength:** 220nm.<br>**Mobile Phase:** Methanol: 0.2M phosphate buffer (pH 3.5) : 70:30 (v/v)<br>**Stationary Phase:** C18 column<br>**Column temperature** adjusted to 30 oC.<br>**Flow rate:** 1.0ml/min<br>**Assay percent range** :99.49- 99.95 %<br>**Linearity range:**<br>Carvedilol : 2-75 µg/mL<br>Glimepiride and Glibenclamide : 5-300 µg/mL | 36 |
| 32 | Glimepiride, Pioglitazone and Metformin In Pharmaceutical Dosage Forms | RP-HPLC Method | **Detection wavelength:** 228nm<br>**Mobile Phase:**<br>Buffer(pH5):Acetonitrile:Tetrahydrofuran**:** (40:50:10)<br>**Stationary Phase:** Inertsil ODS-3V(250mm× 4.6mm, 5µm)<br>**Resolution Run time:** Glimepiride: 5 min<br>Pioglitazone: 3.9min<br>Metformin :1.3 min<br>**Flow rate:** 1.7 ml/min<br>**Linearity** : 150%, 125%, 100%, 75%, and 50% solutions | 37 |
| 33 | Metformin, Glimepiride and Pioglitazone in Tablet dosage form | RP-HPLC Method | **Detection wavelength:** 238nm<br>**Mobile Phase:** Methanol: Phosphate buffer(pH3.6 with OPA) (75: 25v/v)<br>**Stationary Phase:** C18 column (100 mm × 4.6 mm, 5 µm)<br>**Flow rate:** 1.0 ml/min<br>**Linearity range** :<br>Metformin : 400-600 µg/ml<br>Glimepiride: 1.5-3.5 µg/ml<br>Pioglitazone: 10-25 µg/ml<br>**Limit of detection (LOD):**<br>Metformin : 0.15 µg/ml<br>Glimepiride : 0.02 µg/ml<br>Pioglitazone: 0.12 µg/ml<br>**Limit of quantification (LOQ)**:<br>Metformin : 0.45 µg/ml<br>Glimepiride : 0.06 µg/ml<br>Pioglitazone: 0.36 µg/ml | 38 |

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| | | | **Detection wavelength:** 240nm using a UV-SPD-10AVP detector<br>**Mobile Phase:**<br>Methanol:Acetonitrile: 15 mM potassium dihydrogen phosphate (pH 4) 40:35:25 (v/v)<br>**Stationary Phase:** Phenomenex-ODS-3 (C-18) column (250 × 4.60 mm, 5 µm) | |
| 34 | Metformin, pioglitazone, & Glimepiride In pharmaceutical dosage forms | Liquid chromatography | **Retention time:**<br>Metformin : 2.85 ± 0.03 min<br>Pioglitazone: 4.52 ± 0.03 min<br>Glimepiride : 7.08 ± 0.02min<br>**Flow rate:** 1.0ml/min<br>**Linearity Range :**<br>Metformin : 0.2–50 µg/ ml<br>Pioglitazone & Glimepiride : 0.2–30 µg/ml<br>**Accuracy :**<br>Metformin : 99.66 ± 0.14<br>Pioglitazone: 98.46 ± 0.40<br>Glimepiride : 98.62 ± 0.39 | 39 |
| 35 | Metformin, Glimepiride and Pioglitazone in Human Plasma | LC–MS–MS Method and Its Application to a Bioequivalence Study | **Stationary Phase:**<br>C18 (33 9 4.6 mm, 5 l particle size) column<br>**Isocratic Mobile Phase:**<br>A mixture of methanol:water (containing 0.5% formic acid) 8:2<br>**The primary stock solutions** (2.0 mg mL-1 ) of the analytes<br>**For the preparation of calibration curve:**<br>**Solvent :** Methanol<br>**Metformin:** 100, 250, 500, 1,000, 2,500, 5,000, 10,000 and 15,000 ng mL-1<br>**Glimepiride:** 25, 50, 100, 200, 500, 1,000, 2,000 and 5,000 ng mL-1<br>**Pioglitazone:** 25, 50, 100, 500, 1,000, 2,500, 6,000 and 10,000 ng mL-1 | 40 |
| 36 | Glimepiride, Metformin and Pioglitazone In Tablet Dosage form | UPLC MS Method Using Internal Standard | **Detection wavelength:** 220nm.<br>**Mobile Phase:** Acetonitrile (A) & 1% Ammonium acetate buffer (B) (pH 2.5 adjusted with trifluoro acetic acid) with gradient mode<br>**Stationary Phase:** Waters Acquity HSS C18, (1.8 µm, 2.1x50 mm) column<br>**Flow rate:** 0.4 mL min-1<br>**Column maintainance :** 250C<br>**Injection volume :** 2 µl.<br>**Retention time:** Glimepiride: 3.17 min<br>Metformin: 0.425 min<br>Pioglitazone: 2.3 min<br>**Rectilinearity range :**<br>Glimepiride: 2-12 ng mL-1<br>Metformin: 500-3000 ng mL-1<br>Pioglitazone: 15-90 ng mL-1 | 41 |
| 37 | Metformin, Voglibose, Glimepiride in Bulk and Combined Tablet Dosage Form | Gradient RP-HPLC | **Detection wavelength:** 230nm using Photodiode array detector.<br>**Mobile Phase:** 0.02M phosphate buffer(pH 2.5): Acetonitrile(v/v)<br>**Stationary Phase:** Inertsil ODS 3V(150x4.6mm, 5µm) column in a gradient mode.<br>**Retention time:**<br>Metformin: 2.423min<br>Voglibose : 8.191min<br>Glimepiride : 11.708min<br>**Flow rate:** 1.0ml/min<br>**Linearity range :**<br>Metformin: 200-600 µg/ml<br>Voglibose : 0.08-0.24 µg/ml<br>Glimepiride: 0.8-2.4 µg/ml | 42 |
| 38 | Glimepiride, Rosiglitazone and Pioglitazone Hydrochloride in the Pharmaceutical Dosage Form | RP-HPLC Method | **Detection wavelength:** 215nm.<br>**Mobile Phase:** Water HPLC grade adjusted to pH 3.0 using diluted orthophosphoric acid and acetonitrile (80:20 v⁄v)<br>**Stationary Phase:**<br>Nucleodur C–18 column (250mm x 4.6 mm, 5µ)<br>**Retention time:**<br>Glimepiride : 17.9 min<br>Rosiglitazone : 6.31 min<br>Pioglitazone :8.24 min<br>**Flow rate:** 0.8 ml/min | 43 |
| 39 | Combination of Metformin HCl, Atorvastatin Calcium and Glimepiride | RP-HPLC Method and Stress Degradation : Application to Nanoparticles | **Detection wavelength:** 230nm<br>**Mobile Phase:** Phosphate buffer (pH 2.9)–Organic phase : (70:30v/v).<br>[Organic phase :- methanol–acetonitrile (90:10)]<br>**Stationary Phase:** 5-µm Qualisil gold, C18 column (4.6 mm × 250 mm).<br>**Flow rate:** 1.0ml/min<br>**Linearity range:** Metformin : 10–60 µg/ ml<br>Atorvastatin calcium : 2-20 Glimepiride : 5–30 µg/ml | 44 |

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|---|---|---|---|---|
| 40 | Metformin Hydrochloride, Atorvastatin and Glimepiride in Bulk Drug and Formulation | HPTLC Method | **Preparation of standard stock solution :** 1000µg/mL were prepared in methanol<br>**Diluted mixed standard solution** : 100µg/mL<br>**Mobile phase for TLC** :<br>Water: Methanol: Ammonium sulphate (1:1:4, v/v/v)<br>**Linearity Range :**<br>Metformin : 200, 300, 400, 500, 600, 700 ng/spot<br>Atorvastatin & Glimepiride : 600, 900, 1200, 1500, 1800, 2100 ng/spot<br>**Detection wavelength:** 243nm. | 45 |
| 41 | Metformin,Glimepiride And Atorvastatin In Combined Tablet Dosage Form | UPLC Method | **Mobile Phase:** Phosphate buffer(pH adjusted to 3 with orthophosphoric acid) and acetonitrile (40:60 v/v)<br>**Stationary Phase:** BEH C18 (1.7 x 100mm, 2.1 µm)<br>**Flow rate:** 0.4 ml/min<br>**Retention time:**<br>Metformin Hydrochloride:0.551min<br>Glimepiride : 1.924 min<br>Atorvastatin:1.541 min<br>**Linearity range :**<br>Metformin Hydrochloride: 40 - 120µg/ml<br>Glimepiride : 0.8 - 2.4 µg/ml<br>Atorvastatin: 0.16 – 0.48 µg/ml<br>**Detection wavelength:** 230nm | 46 |
| 42 | Pioglitazone, Glimepiride And Glimepiride Impurities In Combination Drug Product | Stability Indicating RP-HPLC Method | **Mobile Phase:** Potassium dihydrogen phosphate buffer: Acetonitrile (50:50 v/v)<br>**Stationary Phase:** C18 column (250mm × 4.6mm, 5µm)<br>**Flow rate:** 0.8 ml/min<br>**Sample Concentration:** 0.1 µg/ml<br>**Injection Volume:** 25 µL<br>**Retention time:**<br>Pioglitazone HCl: 31.93 min<br>Glimepiride : 38.73 min<br>Glimepiride impurity A: 21.99 min<br>Glimepiride impurity B: 19.82 min<br>**%RSD:**<br>Pioglitazone HCl: 1.1<br>Glimepiride : 1.3<br>Glimepiride impurity A: 4.1<br>Glimepiride impurity B: 3.2 | 47 |

## CONCLUSION

This review depicts the reported Spectrophotometric and Chromatographic methods; developed and validated for the estimation of Glimepiride. According to this review, it was concluded that for Glimepiride (Sulfonyl urea) different Spectroscopic & Chromatographic methods are available for the 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. For chromatographic method flow rate was observed in the range of 0.8-1.5 ml/min to get good retention time. For most of the Spectroscopic methods, common solvent was Methanol. Hence this all methods found to be simple, accurate, economic, precise, and reproducible in nature.

**Acknowledgement**

The authors are thankful to Dr. K. Pundarikakshudu, Director of L. J. Institute of Pharmacy, Ahmedabad, India for providing all the facilities and encouragement to carry out the research work.

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**How to cite this article:**

Nusratbanu K. Shaikh *et al*.2016, Review on Analytical Method For Determination of Glimepiride In Bulk And In Different Dosage Forms. *Int J Recent Sci Res.* 7(10), pp. 13515-13524.