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*Review Article*

# A Review On Analytical Methods For Determination of Losartan Potassium And Pioglitazone In Different Dosage Form

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**ABSTRACT**

Nowadays antihypertensive drugs like Losartan Potassium and Antidiabetic drugs like Pioglitazone represent the first choice in the treatment of patients with type 2 diabetic nephropathy. Losartan Potassium reduced the degree of proteinuria while Pioglitazone act as efficient insulin sensitizers. Generally the Combination of Losartan Potassium and Pioglitazone are used for patients suffering from the diabetes mellitus which leads to end stage renal disease. This article narrates different chromatographic (HPLC, HPTLC, LC) & different Spectrophotometric method (UV) for Statin class single drug as well as combination with other drug. Thus, this paper will help in the selection and development of proper analytical methodologies for estimation of Losartan Potassium and Pioglitazone to achieve satisfactory results.

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**Key-words:** Losartan Potassium, Pioglitazone, UV Spectroscopy, Different Chromatography (HPLC, HPTLC, LC).

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**Introduction** [1-2]:

Pioglitazone proliferator-activator receptor agonist. Pioglitazone is an oral drug that reduces the amount of glucose (sugar) in the blood. It is in a class of anti-diabetic drugs called thiazolidinedione that are used in the treatment of type 2 diabetes. Patients with type 2 diabetes cannot make enough insulin, and the cells of their body respond less to the insulin that is produced. Since insulin is the hormone that stimulates cells to remove glucose from the blood, the reduced amount of insulin and its reduced effect cause cells to take up less glucose from the blood and the level of glucose in the blood to rise. Pioglitazone often is referred to as an "insulin sensitizer" because it attaches to the insulin receptors on cells throughout the body and cause the cells become more sensitive (more responsive) to insulin. As a result, more glucose is removed from the blood, and the level of glucose in the blood falls. At least some insulin must produce by the pancreas in order for pioglitazone to work. Pioglitazone also lower the level of glucose in the blood by reducing the production and secretion of glucose into blood by the liver.so Pioglitazone is widely used in the treatment of diabetes & diabetes mellitus. In addition, pioglitazone may alter the blood concentrations of lipids (fats) in the blood. Specifically, it decreases triglycerides and increases the "good" (HDL) cholesterol.

Losartan Potassium is non-peptide angiotensin II antagonist. Losartan Potassium is a member of class I antihypertensive agent. Losartan Potassium also indicated for the treatment of essential hypertension & left ventricular hypertrophy and end stage renal disease and reduce proteinuria. It is effectively used for the treatment of hypertension and heart disease either singly or sometime with the combination of diuretics. It is also recommended for the patient having type II diabetic disease with proteinuria and stroke prevention. This drug is white crystalline, Soluble in aqueous medium, selective, non-peptide and angiotensin II receptor antagonist.

It is observed in many cases the patients suffers from diabetes mellitus which leads to end stage renal disease. So, the combination of Losartan Potassium and Pioglitazone are used for patients suffering from the diabetes mellitus which leads to end stage renal disease.

This study was performed to ascertain whether losartan combined with pioglitazone is superior to losartan alone in delaying the progression of chronic renal failure in patients with type 2 diabetic nephropathy.

This Review Article offers an overview of various analytical methods for estimation of Losartan potassium and Pioglitazone. Different methods have been developed for estimation of Statins like UV-Spectroscopy, Liquid Chromatography, HPTLC and RP-HPLC

**Reported methods are categorized depending on the following considerations.**

1. Single component analyzed by UV-spectroscopy methods and chromatographic method.

2. Analysis of Losartan Potassium and Pioglitazone combination with other class drugs by UV-Spectroscopy methods and Chromatographic method.

**Table: 1. Analysis of single component Losartan Potassium and Pioglitazone by UV-spectroscopy methods.** [3-7]

| SR.NO | DRUG | METHOD | DESCRIPTION | REF NO. |
|---|---|---|---|---|
| 1 | Losartan Potassium Tablet | UV- Spectrophoto Meter | **Solvent**: Water<br>**Detection**: 234 nm.<br>**Correlation coefficient** (r2) =0.9996 | 3 |
| 2. | Losartan Potassium in Tablet | UV derivative spectrophotometric | **Solvent:** Methanol<br>**Detection:** 234 nm.<br>**Correlation coefficient:** 0.9996<br>**Conc. Range:** 4.00-14µg/ml | 4 |
| 3. | Pioglitazone | UV- Spectrophoto Meter | **Solvent:** Methanol<br>**Detection:** 234 nm<br>**Correlation coefficient:** 0.996<br>**Conc. Range:** 2.00-12 µg/ml. | 5 |

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| 4. | Pioglitazone in Pharmaceutical dosage form | UV- Spectrophoto Meter | **Solvent:** Ethanol<br>**Detection:** 224.4<br>**Conc. Range:** 5-25 µg/mL<br>. | 6 |
| 5. | Pioglitazone hydrochloride in bulk and tablet dosage form. | UV- Spectrophoto Meter | **Solvent**: Methanol: Water: HCl (250:250:1)<br>**Concentration range**: 10-70 µg/ml.<br>**Molar absorptivity**: 9.6013 ×104 L/mol.cm.<br>**λmax**: 269 nm | 7 |

**Table: 2. Analysis of Losartan Potassium and Pioglitazone in combined dosage form by UV-Spectroscopy [8-14]:**

| SR NO. | DRUG | METHOD | DESCRIPTION | REF.NO |
|---|---|---|---|---|
| 6. | Losartan potassium,Hydroch Lorthaizide & Amlodipine besilate in Tablet Dosage Form. | UV- Spectrophoto Meter | **1st UV:**<br>Detection:<br>Amlodipine besilate:236.5<br>Losartan Potassium:254<br>Hydrochlorthiazide:271<br><br>Conc. Range:<br>Amlodipine besilate:5-25µl<br>Losartan Potassium:10-50µl<br>Hydrochlorthiazide:5-25µl<br><br>**2st UV:**<br>Detection:<br>Amlodipine besilate:231.5-241.5<br>Losartan Potassium:266-276<br>Hydrochlorthiazide:249-259<br><br>Conc. Range:<br>Amlodipine besilate:5-25µl<br>Losartan Potassium:10-50µl<br>Hydrochlorthiazide:5-25µl<br><br>**Solvent**: 0.025 M phosphate buffer(pH 3.7):Acetonitrile (57:43 v/v) | 8 |
| 7. | Losartan Potassium and Atenolol in combined dosage form | UV- Spectrophoto Meter (Q-Absorption ratio method) | **Solvent:** Methanol<br>**Detection:**<br>Losartan Potassium:280nm<br>Atenolol:275 nm<br>**Correction coefficient:**0.999<br>**Conc. Range:**5-50µg/ml<br>**LOD:** 0.72µg/ml at 275nm & 0.74 µg/ml at 280nm<br>**LOQ**:2.45µg/ml at 275nm & 1.78µg/ml at 280 nm | 9 |

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| 8. | Pioglitazone and Glimepiride in Tablet Dosage Form | UV Derivative Spectrophoto Metric methods | **Solvent**: methanol<br><br>**λmax**:<br>GLIM: 225.6 nm<br>PIO: 267.2 nm | 11 |
| **9.** | Atenolol in combination with losartan potassium and hydrochlorothiazide in bulk and tablet formulation | Spectrophotometric method for simultaneous estimation. | **Solvent:** Dissolve in methanol and dilute with water.<br>**Detection:**<br>LosartanPotassium:251.60 nm<br>Atenolol: 224.20nm<br>Hydrochlorothiazide:271nm<br>**Correlation coefficient:**<br>Losartan Potassium:0.9991<br>Atenolol:0.9993<br>Hydrochlorothiazide:0.9995 | 10 |
| 10. | Pioglitazone HCl with Glimepiride, Metformin HCl In Bulk And Marketed Formulation. | UV Derivative Spectrophoto Metric methods | **Solvent**: 0.1 N NaOH solution and distilled water (50:50)<br>**Detection Range**: 237 nm<br>Pioglitazone::265.5 nm<br>Glimepiride:227 nm<br>Metformin: 233 nm | 12 |
| 11. | Pioglitazone HCl with Glimepiride, Metformin HCl In Bulk And Marketed Formulation. | UV Derivative Spectrophoto Metric method | **Solvent**: Methanol: Water(50:50)<br>**Detection Range:**<br>Metformin HCl: 236.5 nm<br>Glimepiride: 226.4 nm<br>Pioglitazone HCl : 227.3 nm | 13 |
| 12. | Pioglitazone HCl & Atorvastatin calcium In Its Multicomponent Dosage Forms. | UV Simultaneous Spectroscopy | **Solvent:** Ethanol<br>**Concentration Range:**<br>ATV: 1-5µg/ml.<br>PIO: 3-15µg/ml.<br>**λmax:**<br>ATV: 210nm<br>PIO: 225 nm | 14 |

**Table: 3. Analysis of single component Losartan Potassium and Pioglitazone by chromatographic method.**

| SR.NO | DRUG | METHOD | DESCRIPTION | REF NO. |
|---|---|---|---|---|
| 13. | Losartan Potassium (USP) | LC (Dissolution Test 2) | **Column**: 4.6 mm× 15 cm, 5µm Packing L10<br>Column Temp. :45°<br><br>**Flow rate**: 1.5 ml/min<br><br>**Injection size** :10 µl<br><br>**Detection**: 265 nm<br>**Mobile Phase**: Methanol: acetonitrile: Buffer (20:20:60)<br><br>**Tailing Factor**:NMT 2.0<br><br>**RSD** :NMT 2.0% | 15 |

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| 14. | Losartan Potassium | LC (Uniformity of dosage units) | **Column**: 4.6 mm× 5 cm, 10µm packing L7<br>**Column efficiency**: NLT 3000 Theoretical plates.<br><br>**Detection**: 230 nm<br><br>**Flow rate**: 1.4 ml /min<br><br>**Injection size**: 20µl<br><br>**Mobile Phase**: Acetonitrile: Buffer (Dissolve 1.36 mg/ml of monophasic potassium phosphate in water. Adjust with phosphoric acid to a pH OF 2.5) (3:2)<br><br>**RSD**: NMT 2% | 15 |
| 15. | Losartan Potassium Tablets. | LC | **Column**: 3.9 mm× 15 cm; 5µm packing L7<br><br>**Flow rate**: 1.o ml/min<br><br>**Injection size**:10 µl<br><br>**Detection**: 250 nm<br><br>**Mobile Phase**: Acetonitrile: Buffer (3:17). | 15 |
| 16. | Losartan Tablet (IP) | LC (Dissolution) | **Column**: stainless steel (25cm ×4mm) packed with octadecylsilane bonded to porous silica (5 mm). (such as Lichrosphere RP8e)<br><br>**Mobile Phase**: Buffer (770 mg of ammonium acetate in 1000 ml water + 2 ml triethylamine, Adjust pH 6.5 with glacial acetic acid): acetonitrile (75:25).<br><br>**Flow rate**:1.5 ml/min<br><br>**Detection**: 235 nm<br><br>**Injection volume**: 10µl | 15 |
| 17. | Losartan Potassium Tablet. | LC | **Column**: stainless steel (25 cm × 4 mm) packed with octylsilane bonded to porous silica (5mm).<br><br>**Mobile Phase**: 0.005 M | 15 |

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| | | | ammonium acetate : acetonitrile: methanol: triethyamine,adjust the pH to 6.6 with glacial acetic acid.(65:30:5:0.2)<br><br>**Flow rate**: 1ml/min<br><br>**Detection**: 237nm. | |
| 18. | Losartan Potassium | LC | **Column**: stainless steel (25 cm × 4 mm) packed with octylsilane bonded to porous silica (5mm).<br><br>**Mobile Phase** :( A) 0.1% w/v solution of ortho-phosphoric acid in water & filter, (B) acetonitrile.<br>Gradient programme.<br><br>**Flow rate**: 1ml/min<br><br>**Detection**:254nm | 15 |
| 19. | Losartan Potassium in Pharmaceutical Formulation. | HPLC | **Column**:Shimadzu CLC-C8<br><br>**Mobile Phase:** Triethylamine solution(0.5%) pH 2.4 & acetonitrile 60:40(v/v)<br><br>**Detection**:225nm<br><br>**Conc. Range**:15-45µg/ml. | 16 |
| 20. | Pioglitazone HCl | LC | **Column**: Stainless steel (25 cm ×4.6cm) packed with octadecylsilane bonded to porous silica.<br><br>**Mobile phase**:0.01 M potassium dihydrogen phosphate : acetonitrile (50:50)<br><br>**Flow rate**: 1ml/min<br><br>**Detection**:225 nm | 17 |
| 21. | Pioglitazone Tablet | LC<br>(Pioglitazone HCl in solvent mixture) | **Column**: Stainless steel (25 cm× 4.6 cm) packed with octadecylsilane bonded to porous silica.<br><br>**Mobile phase**: potassium dihydrogen orthophosphate (1.36 gm.) & di ammonium hydrogen phosphate (1.15 gm.) | 17 |

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| | | | In 1000 ml water.<br><br>**Flow rate**:1.5 ml/min<br><br>**Detection**:270 nm | |
| 22. | Pioglitazone HCL in bulk and Pharmaceutical formulation | HPLC | **Column:** 5 µm symmetry C18 column (250×4.6 mm i.d)<br><br>**Mobile Phase**: 0.01 M potassium dihydrogen phosphate buffer (pH 6.0):ACN (50:50, v/v)<br><br>**Detection:** 225 nm<br><br>**Flow rate**:1.0 ml/min | 18 |
| 23. | Pioglitazone | RP-HPLC | **Column:** reversed-phase Intersil ODS C18 (150 mm × 4.6 mm, 5µm)<br><br>**Mobile phase**: Ammonium acetate buffer with Acetonitrile and Glacial acetic acid in the ratio 50:50:1 (v/v)<br><br>**Detection** :269 nm<br><br>**Flow rate:** 0.7 ml/min | 19 |
| 24. | Pioglitazone in Human Plasma | RP-HPLC | **Column:** Nova-Pak C8<br><br>**Mobile phase**: acetonitrile–140mM K2HPO4 (40:60, v/v, pH = 4.45)<br><br>**Detection:**269 nm<br><br>**Flow rate:**1.4ml/min | 20 |

**Table: 4. Analysis of Losartan Potassium and Pioglitazone in combined dosage form by chromatographic methods.**

| SR.NO | DRUG | METHOD | DESCRIPTION | REF. NO. |
|---|---|---|---|---|
| 25. | Losartan Potassium & Hydrochlorothiazide in Binary mixtures. | RP-HPLC | **Column:** Phenomenex C18 column (250x4.6mm, 5µ).<br><br>**Mobile Phase**: methanol and Phosphate buffer pH 6.7 (80:20v/v).<br><br>**Flow rate**: 1ml/min.<br><br>**Detection**: 225 nm. | **21** |

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| 26. | Losartan Potassium & Hydrochlorothiazide Tablets. | HPLC | **Column:** stainless steel (30cm× 3.9 mm) packed with octadecylsilane bonded to porous silica (10µm).<br><br>**Mobile Phase**: Buffer( 0.78gm of sodium dihydrogen orthophosphate in 500 ml water, adjusted to pH 2.5 with orthophospheric acid) :Acetonitrile.(60:40)<br><br>**Flow rate**: 1ml/min<br><br>**Detection**: 220nm.<br><br>**Injection volume**: 20µl. | **22** |
| 27. | Losartan Potassium & Hydrochlorothiazide in Tablet Dosage Form | RP-HPLC | **Column**: Shim-pack CLC-ODS (250mm×4.6mm,5µ)<br><br>**Mobile Phase**:0.025 M phosphoric acid solution: acetonitrile(60:40 v/v ,pH adjusted with 80% phosphoric acid)<br><br>**Flow rate**:1.5 ml/min<br><br>**Detection**:254nm<br><br>**Retention time**:<br>Losartan Potassium::8.790 min<br>Hydrochlorothiazide: 3.748 min | **23** |
| 28. | Losartan Potassium & Amlodipine Besylate Tablets. | HPLC | **Column**: Inertsil ODS-4 HP (3 µm, 50 x 4.6 mm I.D.)<br><br>**Mobile phase**: A) CH3OH B) CH3CN C) 0.7 % Triethylamine (pH 3.0, H3PO4 ) A/B/C =7/3/10, v/v/v.<br><br>**Flow rate**: 1.0 mL/min Column.<br><br>**Temp**. : 25 °C 1<br>**Detection**: UV 237 nm<br>**Injection Vol**.: 5 µL | **24** |
| 29. | Losartan potassium,Hydroch lorthaizide & Amlodipine besilate in Tablet Dosage Form. | HPLC | **HPLC:**<br>**Column:**Kromasil C18 (4.6mm i.d×250mm)<br><br>**Detection** :232nm<br><br>**Conc. Range:**<br>Amlodipine besilate:2-14µl | **25** |

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| | | | Losartan Potassium:20-140µl<br>Hydrochlorothiazide:5-40µl<br><br>**Mobile Phase**: 0.025 M phosphate buffer(pH 3.7):Acetonitrile (57:43 v/v) | |
| 30 | Losartan Potassium & Ramipril in Combined Dosage Form. | RPHPLC | **Column**: Hypersil ODS C18, 4.6×250mm, 5µm in Isocratic mode.<br><br>**MobilePhase**:acetonitrile:methanol:10mM tetra butyl ammonium hydrogen sulphate in water.(30:30:40)<br><br>**Flow rate**:1.0ml/min<br><br>**Detection**:210nm<br><br>**Retention times:**<br>Losartan Potassium:4.7<br>Ramipril:3.3<br><br>**Linearity range:**<br>Losartan Potassium:0.004-100µg/ml<br>Ramipril:0.2-300µg/ml. | **26** |
| 31. | Losartan, Hydrochlorothiazide & Amlodipine in Bulk & Formulation. | RPHPLC | **Column**: Hypersil Gold(250mm× 4.6mm, 5µ)<br><br>**Mobile Phase:**methanol:water (95:5%v/v)<br><br>**Flow rate**:0.8ml/min<br><br>**Detection:**230nm | **27** |
| 32. | Losartan Potassium, Hydrochlorothiazide & Atenolol in Tablet Formulation. | RPHPLC | **Column**:Phenomenex C18<br><br>**Mobile Phase**: acetonitrile: 50mM potassium dihydrogen ortho phosphate (pH 3.5)(50:50)<br><br>**Flow rate**: 1mL/min<br><br>**Detection**:270nm | **28** |
| 33. | Amlodipine Besylate, Losartan Potassium, Valsartan & Atorvastatin in Pharmaceutical Formulation. | HPLC | **Column**: Spherical monomeric C18 (250×4.6 mm, 5µ)<br><br>**Mobile Phase**: Ammonium acetate (Ph5.5,0.01M) :acetonitrile(45:55 v/v)<br><br>**Flow rate**:1.5 ml/min at 40°C | **29** |

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| | | | **Detection**: 240nm. | |
| 34. | Losartan & perindopril in pure Form & Tablet Formulation. | RPHPLC | **Column:** LUNA C18 Isocratic mode<br><br>**Mobile phase:** Methanol and phosphate buffer (pH 6.8) (85:15)<br><br>**Flow rate**:0.8 ml/min<br><br>**Detection**: 210nm | **30** |
| 35. | Losartan & Ramipril in Pharmaceutical Dosage Form. | HPTLC | **Mobile phase**: methanol: ethyl acetate: toluene: glacial acetic acid (1:9:1:0.2 v/v/v/v).<br><br>**Detection:** 210 nm. | **31** |
| 36. | Losartan Potassium & Enalapril maleate in Pharmaceutical Dosage Form | RPHPLC | **Column**: C-18 BDS Hypersil column (250mm × 4.6 mm id 5µm)<br><br>**Mobile phase**: Buffer-Acetonitrile(60:40 v/v) pH4.5 adjusted With o-Phosphoric Acid<br><br>**Flow rate**: 1.0 ml/min<br><br>**Detection** :235nm | **32** |
| 37. | Pioglitazone HCl With Metformin HCl in Combined Tablet Dosage Form. | RPHPLC | **Mobile phase**: acetonitrile:water:aceticacid (60:40:0.3)<br><br>**Detection**: 230 nm<br><br>**Flow rate**:1 ml/min | **33** |
| 38. | Pioglitazone with Metformin & Glimepiride in Pharmaceutical Dosage Forms. | HPLC | **Column**: Phenomenex-ODS-3 (C-18) column (250 × 4.60 mm, 5 µm)<br><br>**Mobile phase**: methanol: acetonitrile:15 mM potassium dihydrogen phosphate (pH 4) (40:35:25 (v/v))<br><br>**Flow rate** : 1 ml/min<br><br>**Detection**: 240 nm | **34** |
| 39. | Pioglitazone with Glimepiride and metformin in Pharmaceutical Dosage Forms | RPHPLC | **Column**: Inertsil ODS -3V (250 mm × 4.6 mm, 5µm) column.<br><br>**Mobile phase**: acetonitrile, tetra hydro furan, and buffer at | **35** |

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| | | | pH 5<br><br>**Flow rate**: 1.7 ml/min<br><br>**Detection**: 228 nm | |
| 40. | Pioglitazone and Glimepiride in Tablet Dosage Form | RPHPLC | **RP-HPLC-Column**: $C_{18}$ (250 × 4.6,5µm)<br><br>**Mobile Phase**: Methanol: Water (72:28)<br><br>**Flow rate**: 1.0 ml/min | **11** |
| 41. | Pioglitazone and Alogliptin in bulk and dosage form | HPLC | **Column**: Hypersil C18, 250mm × 4.6mm, 5µ (particle size)<br><br>**Mobile Phase**: Buffer pH 3.5: Methanol (70:30)<br><br>**Detection**:271 nm<br><br>**Column Temp**.:25º C<br><br>**Flow rate**: 1.0 ml/min<br><br>**Conc. Range:**<br>Pioglitazone: 3.75-18.75µg/ml<br>Alogliptin: 6.25-31.25 µg/ml<br><br>**Correlation Coefficient:**<br>Pioglitazone:o.9997<br>Alogliptin:0.9993 | **36** |

**Conclusion:**

This review represents the reported spectrophotometric and chromatographic methods developed and validated for determination Losartan Potassium and Pioglitazone. According to the literature review it can be concluded that for Losartan Potassium and Pioglitazone in single component and its combination with other drug spectroscopy and chromatography methods available. This all methods are found to be simple, accurate, economic, precise, and reproducible in nature. Comparing various validation parameters of already reported methods, it can be concluded that different analytical methods like spectrophotometric, HPTLC and HPLC can be developed for Losartan Potassium and Pioglitazone showing its simplicity, sensitivity (low LOD and LOQ values) linearity and accuracy. As per Review most of work have used the reversed-phase HPLC and UV absorbance detection because this provided with best available reliability, repeatability, analysis time and sensitivity. There is a great scope for development of newer analytical methods for drugs such as Losartan Potassium and Pioglitazone combination.

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