Literature review

Maria Del Rosario B\textsuperscript{11} \textit{et al.} developed and validated column switching high performance liquid chromatographic (HPLC) method for determination of losartan, telmisartan, and valsartan in human urine. Urine samples were diluted on the extraction mobile phase and a volume of 20 µl of this mixture were directly injected onto the HPLC system. The analytes were extracted from the matrix using an on-line solid phase extraction procedure involving a precolumn packed with 25 µm C18 alkyl diol support (ADS), and a solution 2% methanol in 5mM phosphate buffer (pH 3.8) at a flow-rate of 0.8 mL min\(^{-1}\). The enriched analytes were back flushed after, onto the analytical column with a mixture of 5mM phosphate buffer (pH 3.8): acetonitrile: methanol (65:20:15, v/v/v) at a flow-rate of 3.0 mL min\(^{-1}\) and detected using fluorescence at 259 and 399nm as excitation and emission wavelength respectively. The separation of losartan, telmisartan and valsartan was achieved on a Chromolith RP-18e monolithic column. The LOD for losartan, telmisartan, and valsartan at a signal to noise ratio of 5:1 were 0.002, 0.0002 and 0.001 µg mL\(^{-1}\) when a sample volume of 20 µl was injected.

Yogesh G\textsuperscript{12} \textit{et al.} developed RP-HPLC method for the simultaneous estimation of ramipril and telmisartan in tablet dosage forms, using ODS column hypersil, (250X4.6 mm, 5 µm) in a low pressure gradient mode, with mobile phase acetonitrile: NaH\textsubscript{2}PO\textsubscript{4} buffer (pH 4.5) (65:35 v/v). The flow rate was 1.0 mL min\(^{-1}\) and eluents were monitored at 210 nm. The retention time were found to be 4.25 min and 7.99 min for ramipril and telmisartan respectively. They were found to be linear over a range of 4-16 µg mL\(^{-1}\) and 32-128 µg mL\(^{-1}\) for ramipril and telmisartan respectively.

Kurade V P\textsuperscript{13} \textit{et al.} developed and validated HPLC method for the simultaneous estimation of ramipril and telmisartan in combined dosage form using Genesis C18 column (4.6X250 mm 5

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µm) in an isocratic mode, with mobile phase 0.01 M potassium dihydrogen phosphate buffer (pH 3.4 using orthophosphoric acid): methanol: acetonitrile (15:15:70 v/v/v). The flow rate was 1.0 mL min⁻¹ and the eluents were monitored at 210 nm. The retention time were found to 3.68 min and 4.98 min for ramipril and telmisartan respectively. The ramipril and telmisartan were found to be linear in the range of 3.5-6.5 µg mL⁻¹ and 28.0-52.0 µg mL⁻¹, respectively.

Bankey S¹⁴ et al. developed spectrophotometric method for simultaneous determination of telmisartan, ramipril and hydrochlorthiazide in combined tablet dosage form. The wavelength selected were 218 nm, 271 nm and 296 nm respectively using methanol as solvent. They were found to be linear between 4-28 µg mL⁻¹, 0.5-3.5 µg mL⁻¹ and 1.25-8.75 µg mL⁻¹ for TEL, RAM and HCT respectively. The concentrations of these drugs were evaluated in laboratory mixture and marketed formulation. Accuracy was determined by recovery studies from tablet dosage forms and range from 99.09-99.52%.

Belal F¹⁵ et al. developed HPLC method for the simultaneous determination of ramipril and hydrochlorothiazide using Clobazam as an internal standard in their dosage forms. The separation was achieved using supelcosil™ LC-8 (5X150 mm, 4.6 mm) column with mobile phase containing acetonitrile: 0.1 M sodium perchlorate solution (pH 2.59 with phosphoric acid) (46:54 v/v). The flow rate was 1.5 mL min⁻¹ with spectrophotometric detector at 210 nm. The method was also applied for the determination of ramipril in the presence of its degradation products. They were found to be linear in the range of 4.5-45 and 0.6-14 mg mL⁻¹, for ramipril and hydrochlorothiazide respectively. LOD were 180 and 23 ng mL⁻¹ for ramipril and hydrochlorothiazide, respectively.

Santaji N¹⁶ et al. developed stability indicating UPLC method for the simultaneous determination of telmisartan, amlodipine besylate and hydrochlorothiazide from poly pill dosage...
form in the presence of degradation products. The separation was achieved using C18 (100X 2.1 mm, 1.7 μm) column with a gradient method. The mobile phase composed of mixture of A [sodium perchlorate 0.053M (pH 3.2): acetonitrile (90:10, v/v)] and B [sodium perchlorate 0.053M (pH 3.2): acetonitrile in the ratio (20:80, v/v)] in gradient program (T/%B) is set as 0/5, 1.2/5, 1.6/40, 4/40, 4.1/5 and 4.5/5 with the flow rate of 0.6 mL min⁻¹. The detection was performed at 271 nm for hydrochlorothiazide and telmisartan and 237 nm for Amlodipine. The retention time of telmisartan, amlodipine and hydrochlorothiazide were 3.6, 3.2 and 0.9 min respectively the developed method was validated following ICH guidelines.

Sathe S R¹⁷ et al. developed HPTLC method for separation and quantitative analysis of losartan potassium, atenolol, and hydrochlorothiazide in bulk and in pharmaceutical dosage form. The sample and standard solution were applied after to prewashed silica gel plates after extraction with methanol and developed with toluene: methanol: triethylamine (6.5:4:0.5 v/v) as mobile phase. Scanning were performed densitometrically at 274 nm the Rf values of losartan potassium, atenolol, and hydrochlorothiazide were 0.60, 0.43, and 0.29 respectively. They were found to be linear in the range 1000-5000 ng per band for losartan potassium and atenolol and 250-1250 ng per band for hydrochlorothiazide.

Nagavalli D¹⁸ et al. developed four different spectrophotometric methods for simultaneous estimation of losartan potassium, amlodipine besilate and hydrochlorothiazide in bulk drugs and in formulations. Overlapped data was quantitatively resolved by using chemometric methods, classical least squares (CLS), multiple linear regression (MLR), principal component regression (PCR) and partial least squares (PLS). Calibrations were constructed using the absorption data matrix corresponding to the concentration data matrix, with measurements in the range of 230.5-350.4 nm (Δλ= 0.1 nm) in their zero order spectra. They were found linear over a range of 8-40,
1-5 and 3-15 μg mL⁻¹ for losartan potassium, amlodipine besilate and hydrochlorothiazide, respectively.

Karunanidhi S L et al. developed and validated HPTLC method for separation and quantitative analysis of losartan potassium, amlodipine, and hydrochlorothiazide in bulk and in pharmaceutical formulations. The sample and standard solutions were applied to silica gel plates and developed with mobile phase containing chloroform: methanol: acetone: formic acid (7.5:1.3:0.5:0.03 v/v/v/v) after extraction with methanol. They were scanned Zones densitometrically at 254 nm. The Rf values of amlodipine besylate, hydrochlorothiazide, and losartan potassium were found to be 0.35, 0.57, and 0.74, respectively. They found to be linear in the ranges 500-3000 ng/spot for losartan potassium, amlodipine and hydrochlorothiazide. The method was validated in accordance with the pharmaceutical regulatory standards.

Satheesh K S et al. developed stability indicating HPLC method for the simultaneous estimation of aspirin, atorvastatin, atenolol and losartan potassium in a poly pill fixed dose combination containing three or more drugs in a single pill. They were determined quantitatively in a poly pill in the presence of degradation products. The separation was achieved on a C18 column, mobile phase containing acetonitrile: 0.1% orthophosphoric acid (pH 2.9) in a gradient mode and detection was carried out at 230 nm with a flow rate of 1.0 mL min⁻¹. The retention times of atenolol, aspirin, losartan potassium, and atorvastatin were 3.3, 7.6, 10.7 and 12.9 min respectively. The combination drug product were exposed to thermal, acid/base hydrolytic, humidity and oxidative stress conditions, and the stressed samples were analyzed by proposed method. The drugs were linear in the range of 37.5-150.0, 5.0-20.0 and 25.0-100.0 μg mL⁻¹ for aspirin, atorvastatin, atenolol and losartan potassium respectively.
Oskar G et al. developed LC–MS/MS with electrospray ionization (ESI), method for simultaneous analysis of atenolol, bisoprolol, hydrochlorothiazide, chlorthalidone, salicylic acid, enalapril and its active metabolite enalaprilat, valsartan and fluvastatin in human plasma working in multiple reaction monitoring mode (MRM). They achieved separation using Luna C18 (150×4.6 mm, 3 µm) column using a gradient elution mode with mobile phase composed of acetonitrile: water containing 0.01% formic acid and 10 mM ammonium formate (pH 4.1) were pravastatin used as an internal standard. Sample were precipitated using acetonitrile. The method was validated as per ICH guidelines.

Kavitha J et al. developed HPLC and Dissolution methods for the analysis of Atenolol, Hydrochlorothiazide and Losartan potassium in tablet formulation. The chromatographic separation were achieved by using reverse phase Phenomenex Princeton Spher C18 (250×4.6 mm, 5 µm) column using acetonitrile: 50 mM potassium dihydrogen ortho phosphate (pH 3.5) ratio 50:50 as mobile phase with a flow rate of 1 mL min⁻¹ and isocratic elution with a total run time of 14 min. Sulphadoxine was selected as an internal standard. The retention time of Atenolol, Hydrochlorothiazide, Losartan potassium and Internal Standard was found to be 5.55, 3.28, 7.37 and 12.39 min respectively at a wavelength of 270 nm.

Santaji N et al. developed stability indicating UPLC method for the simultaneous quantitative determination of telmisartan, amlodipine besylate and hydrochlorothiazide from their poly pill combination drug product in the presence of degradation products. The separation was achieved by using C18 (100×2.1 mm, 1.7 µm) column by simple gradient method the mobile phase A contains a mixture of sodium perchlorate 0.053M (pH 3.2): acetonitrile (90:10 v/v) and mobile B contains a mixture of sodium perchlorate 0.053M (pH 3.2): acetonitrile (20:80 v/v). The flow rate was 0.6 mL min⁻¹ and the column temperature was maintained at 55°C. The gradient
program (T/%B) is set as 0/5, 1.2/5, 1.6/40, 4/40, 4.1/5 and 4.5/5. They were detected at a wavelength of 271 nm for hydrochlorothiazide and telmisartan and 237 nm for amlodipine. The retention times of telmisartan, amlodipine, and hydrochlorothiazide were 3.6, 3.2 and 0.9 min respectively.

**Chaturvedi P K**24 et al. developed RP-HPLC method for simultaneous estimation of metformin hydrochloride, pioglitazone hydrochloride, and glibenclamide in a tablet dosage. The separation was achieved using Phenomenex Luna C18 (250X 4.6 mm, 5 μm) column with mobile phase acetonitrile: potassium dihydrogen phosphate buffer (pH adjusted to 3.0 with 5% orthophosphoric acid) (55:45 v/v) at a flow rate of 1.5 mL min\(^{-1}\). The detection was performed at 230 nm with run time 10 min. The retention time of metformin hydrochloride, pioglitazone hydrochloride and glibenclamide were 1.36, 3.41, and 7.39 min respectively. They were found to be linear over a range of 200-1000, 200-1000 and 50–300 μg mL\(^{-1}\) for metformin hydrochloride, pioglitazone hydrochloride and glibenclamide respectively. The LOD were 6.3, 15.4, and 8.2 ng mL\(^{-1}\) and LOQ were 19.09, 46.66, and 24.84 ng mL\(^{-1}\) for metformin hydrochloride, pioglitazone hydrochloride, and glibenclamide, respectively.

**Chaturvedi, P**25 et al. developed two spectrophotometric methods using Shimadzu UV 1700, for simultaneous estimation of three drugs pioglitazone HCl, metformin HCl, and glibenclamide in a tablet formulation. In method I, absorbance of the sample solution was measured at 285 nm and 300 nm for the estimation of pioglitazone HCl and glibenclamide, and at 237 nm for estimation of metformin hydrochloride, respectively. Method II was based on a multiwavelength spectroscopic method. Recording the absorbances of standard solutions at 237, 268, 280, and 300 nm were processed by means of statistical calculations and results of the sample solution were obtained. The drugs obey Beer’s law in the concentration ranges used for the methods. The
result of the analysis for both methods were tested and validated in accordance to ICH guidelines.

**Musmade P B**\(^26\) *et al.* developed and validated bioanalytical method for simultaneous determination of pioglitazone and glimepiride in rat plasma. The separation were achieved using C18 column using mobile phase acetonitrile: ammonium acetate (pH 4.5) in the ratio of 55:45%. The drugs were detected using UV detector and plasma samples clean-up was carried out using solid phase cartridges. The drugs were found to be linear in the range of 0.05-8 and 0.05-2 \(\mu g/mL\) for PIO and GLM respectively. Moreover they found that PIO and GLM were stable in plasma, up to 30 days of storage at -70 \(^{0}\)C.

**Udaykumar R**\(^27\) *et al.* developed RP-HPLC method for the stability indicating assay of Glipizide Glibenclamide and Glimepiride in the presence of Metformin hydrochloride (MET) in pharmaceutical dosage forms using ion pair-reversed phase liquid chromatographic Technique. The ion pairing agent used was tetrabutyl ammonium hydrogen sulphate (TBHS). The chromatographic separations were performed microbondapak C18 (300X 3.9 mm, 10 \(\mu m\)) column, eluted with mobile phase composed of 0.030 M TBHS (pH 6.0 with 1 N NaOH): acetonitrile (50:50 v/v) with flow rate of 1.0 mL min\(^{-1}\). The wave length used was 225 nm the linearity range was between 100- 300 \(\mu L\) min\(^{-1}\) for Glipizide Glibenclamide and Glimepiride respectively.

**Praveenkumar R B**\(^28\) *et al.* developed HPLC method for the simultaneous estimation of pioglitazone and glimepiride in pharmaceutical dosage form. The separation were achieved using phenomenex Luna C18 (4.6x150mm) column, mobile phase composed of acetonitrile: Potassium dihydrogen orthophosphate buffer (60:40%v/v) (pH 6) at a flow rate of 1.5 mL min\(^{-1}\) with detection at 230nm. The retention time of pioglitazone and glimepiride were 4.4 and 2.7 minutes.
respectively. They were found to be linear in the range of 240-360 μg mL\(^{-1}\) and 32-48 μg mL\(^{-1}\) for pioglitazone and glimepiride respectively. The developed method was validated following ICH guidelines.

**Navaneethan G\(^{29}\) et al.** Stability indicating RP-HPLC method was developed and validated for the simultaneous estimation of pioglitazone, glimepiride and glimepiride impurities i.e., related compound B and related compound C from combination drug product containing pioglitazone, glimepiride and metformin HCl. The chromatographic separation was achieved on a CN (250 x 4.6mm, 5.0 µ particles) column with mobile phase combination delivered in gradient mode at a flow rate of 0.8 mL min\(^{-1}\) at 230nm. In the developed method, the compound of glimepiride related compound B and related compound C was found more than 6.5 resolutions. This method is capable to detect glimepiride related compound B and related compound C at a level below 0.005% with respect to glimepiride sample concentration of 0.1µg mL\(^{-1}\) for a 25 µL injection volume.

**Venkatesh P\(^{30}\) et al.** developed RP-HPLC method for the simultaneous estimation of six anti-diabetic drugs viz., glibenclamide (GLB), gliclazide (GLC), glipizide (GLZ), pioglitazone (PGL), repaglinide (RPG) and rosiglitazone (RGL) in pharmaceutical formulations and in biological samples. They spiked human plasma with anti-diabetic drugs and internal standard (IS). The separation was achieved Intertisl ODS 3V (4.6X250 mm, 5 µm) column at ambient temperature at a flow rate of 1 mL min\(^{-1}\). The mobile phase consisted of 0.01 M formic acid (pH 3.0): acetonitrile: Milli Q water: methanol. Celecoxib was used as an IS. They were monitored at a wavelength of 260 nm. The retention times were 11.4, 13.3, 14.8, 17.6, 20.78, 22.1 and 25.4 min, for of RGL, PGL, GLZ, GLC, GLB, IS and RGL respectively. The linearity range was...
ranged from 0.1 to 100 µg mL\(^{-1}\) for all analytes with the exception of GLB, where the range was 0.3-100 µg mL\(^{-1}\). The developed method were validated.

**Lalit K\(^3\) et al.** developed two spectrophotometric methods for the simultaneous estimation of Pioglitazone (PIO) and Glimepiride (GLIM). First method used was simultaneous equation method, in this two wavelengths (216 and 225 nm) were selected for the measurement of absorbance. The second method was absorption ratio method in which measurements are made based on the absorptivity at the isobestic point (228 nm) and absorption maxima of PIO (216 nm). The absorption maximum wavelengths of PIO, GLIM were observed at 216 and 225 nm respectively and the isobestic point at 228 nm. Linearity ranges from 5-25 µg mL\(^{-1}\) for both drugs. The proposed was validated according to the ICH guidelines.

**Pinaki S\(^3\) et al.** developed and validated LCMSMS method for the simultaneous quantitation of antidiabetic drugs metformin, glimepiride and pioglitazone in human plasma using glipizide as an internal standard. Quantitation was performed on a triple quadrupole mass spectrometer employing electrospray ionization technique, operating in multiple reaction monitoring and positive ion mode. Inter-batch and intra-batch coefficient of variation across four validation runs for the quality control samples was less than 7%. The accuracy determined at quality control levels was within 92.81–105.13%. Developed method was validated following FDA guidelines.

**Bandarkar F S\(^3\) et al.** developed UFLC method for simultaneous separation and quantification of three anti-diabetic drugs, viz., glibenclamide, gliclazide, and metformin hydrochloride. The separation was achieved using XR-ODS C18 column (30°C) with a mobile phase comprised of acetonitrile: water: trifluoroacetic acid: triethylamine (54:46:0.1:0.1v/v) in isocratic elution mode at a flow rate of 0.38 mL min\(^{-1}\) and detected at 230 nm. The method was validated according to
FDA and ICH guidelines. The retention time were 0.98 min, 4.10 min and 6.40 min for metformin, gliclazide and glibenclamide respectively.

Aburuz S et al. developed two RP-HPLC method for the simultaneous estimation of antidiabetic drugs in method 1 metformin and Glibenclamide or Glimperide using Pioglitazone as an internal standard. In method 2 simultaneous determination of metformin and Glipizide or Gliclazide using tolbutamide as an internal standard. In both the case separation were achieved by using Discovery C18 Supelco (250X4.6 mm, 5 µm) column using mobile phase composed of 2mM sodium dodecyl sulphate: acetonitrile (37.5%) and 0.0125 M potassium dihydrogen phosphate (62.5%). For method 1 pH 7.3 (adjusted with NaOH) and for Method 2 pH 5.3 (adjusted with HCl) for optimal separation. The analytes were measured at 223 nm. The LOD were 3.0 (method 1), 9.9 (method 2), 4.0, 4.5, 4.5 and 13.5 ng mL\(^{-1}\) and LOQ were 5.0 (method 1), 16.5 (method 2), 7.0, 7.5, 7.5 and 22.5 for metformin (method 1 & 2) Glibenclamide, Glimperide, Glipizide and Gliclazide respectively. The retention time were 4.7, 12.5, 8.4 and 6.2 min for metformin, pioglitazone, Glimperide and Glibenclamide respectively. In method 2 the retention time were 5, 8.1, 15.6 and 10.1 min for metformin, glipizide, gliclazide, and tolbutamide respectively.

Shaodong J et al. Charged aerosol detection (CAD), a new kind of universal detection method, has been widely employed in the HPLC system. In this study, four kinds of anti-diabetic drug standards, glipizide, gliclazide, glibenclamide and glimepiride were determined by ultraviolet (UV) detection, evaporative light scattering detection (ELSD) and the aforementioned CAD. The results were compared with reference to linearity, accuracy, precision and limit of detection (LOD). All of the experiments were performed on a reverse phase column with water and acetonitrile as the mobile phase. Separations were achieved under the same chromatographic
conditions for each detection method. As a result, CAD generated nearly uniform responses compared with UV detection and ELSD. It showed the best accuracy and LOD among 3 detectors and had similar precision with UV detection at higher concentrations while UV detection showed a better precision at lower concentrations than did CAD or ELSD. The LOD of CAD, in fact, can be up to two times higher than that of ELSD. The UV and ELSD linearity was.

**Lakshmi K S** et al. Reverse phase high performance liquid chromatographic method for the determination of Pioglitazone (PIO) and Glimepiride (GLM) was developed on a Shimadzu Class vp series HPLC system with a phenomenex C18 column (150x4.6mm, 5μ) using a mobile phase mixture containing methanol and ammonium acetate buffer (pH-3.5) in the ratio of 55: 45. The flow rate was 0.5mL min\(^{-1}\) and effluents were monitored at 252 nm and retention time for PIO and GLM were 5.63 min and 7.18 min respectively. The linearity range were found to be 25-25000 ng mL\(^{-1}\) and 10-10000 ng mL\(^{-1}\) for PIO and GLM. The assay was validated, the drugs were extracted from rat plasma by simple liquid-liquid extraction using diethyl-ether as extraction solvent.

**Deepti J** et al. developed RP-HPLC method for the simultaneous estimation of metformin hydrochloride, pioglitazone hydrochloride and glimepiride present in multicomponent dosage forms. The separation was achieved by using Inertsil-ODS-3 C18 (250X 4.60 mm, 5 μm) column by isocratically with a mobile phase composed of methanol: phosphate buffer (pH 4.3) (75:25 v/v) at a flow rate of 1 mL min\(^{-1}\). The detection was carried out at 258 nm. The retention times for metformin hydrochloride, pioglitazone hydrochloride and glimepiride were 2.66, 7.12, and 10.17 min, respectively. They were found to be a linear in range of 10-5000, 10-150 and 1-10 μg mL\(^{-1}\) for metformin hydrochloride, pioglitazone hydrochloride and glimepiride respectively.

**Shraddha P** et al. developed and validated LC method for the simultaneous determination of
glimepiride and metformin in sustained release formulation. The separation was achieved by using Nucleosil 100-5SA column, with mobile phase composed of 1.7 % ammonium dihydrogen phosphate buffer (pH 3.0): acetonitrile (70:30 v/v) at a flow rate of 1.0 mL min\(^{-1}\). The detection was performed at 230 nm. The retention time for glimepiride and metformin were 5.1 and 11.3 min respectively.

Vinay P\(^{39}\) et al. developed and validated RP-HPLC method for simultaneous estimation metformin hydrochloride, pioglitazone hydrochloride and glimepiride. The chromatographic separation was performed by using a Phenomenex ODS-3 C18 (250X4.60 mm, 5 µm) column with a mobile phase consisting of methanol: acetonitrile: 15 mM potassium dihydrogen phosphate (pH 4 glacial acetic acid) (40:35:25 v/v) at a flow rate of 1 mL min\(^{-1}\). The detection was performed at UV-SPD 10AVP detector at 240 nm. The drugs were found to be in the range of 0.2-50 µg mL\(^{-1}\) for metformin hydrochloride and 0.2–30 µg mL\(^{-1}\) for pioglitazone hydrochloride and glimepiride respectively. The retention time for metformin hydrochloride, pioglitazone hydrochloride and glimepiride were 2.85, 4.52 and 7.08 min respectively.

Karthik A\(^{40}\) et al. Isocratic HPLC method was developed for the separation and quantification of pioglitazone and glimepiride in bulk drug and pharmaceutical dosage form. The quantification was carried out using Inertsil ODS (250 X 4.6 mm, 5µ) column and mobile phase comprised of acetonitrile and 20 mM ammonium acetate (pH 4.5 with glacial acetic acid) (60:40 v/v). The flow rate was 1.0 mL min\(^{-1}\) and the effluent was monitored at 230 nm. The retention time of pioglitazone and glimepiride were 7.0 and 10.2 min respectively. The drugs were found to be linear in the range of 2.0 to 200.0 µg mL\(^{-1}\) and 0.5-50 µg mL\(^{-1}\) for pioglitazone and glimepiride respectively.
**Jing Y** et al. developed Isocratic RP-HPLC method for screening counterfeit medicines and adulterated dietary supplement products. The separation of six anti-diabetic drugs glipizide, gliclazide, glibenclamide, glimepiride, gliquidone, repaglinide achieved on Alltima C18 (150X 4.6 mm, 5µm) column with an isocratic mobile phase composed of methanol : 0.01 mol L\(^{-1}\) phosphate buffer (pH 3.0) (70:30 v/v) at a flow rate of 1.0 mL min\(^{-1}\) and the detection was performed at 230 nm. They were found to be linear in the range of 1-100 µg mL\(^{-1}\) for glipizide, gliclazide, glibenclamide, glimepiride, gliquidone and 5-100 µg mL\(^{-1}\) for repaglinide. The LOD were found to be 0.1, 0.2, 0.24, 0.26, 0.35 µg mL\(^{-1}\) and LOQ were found to be 0.34, 0.38, 0.77, 0.88, 0.5 and 3.95 for glipizide, gliclazide, glibenclamide, glimepiride, gliquidone and repaglinide respectively.

**Nanduri Ramana V V S** et al. developed two method for the simultaneous estimation of Voglibose by HPLC method. The first method was based on the pre-column derivatization of Voglibose followed by visible detection and second method involves mass spectrometric detection. In chromatographic method, voglibose was derivatized with sodium metaperiodate and 3-methyl-2-benzothiazolinone hydrazone hydrochloride monohydrate (MBTH). The derivatized color product of voglibose was eluted through Novapak C18 (300X 3.9 mm, 4 µm) column using 0.01M mixture of sodium di hydrogen orthophosphate and disodium hydrogen orthophosphate, buffer (pH 6.0): acetonitrile (35:65 v/v). The eluted derivatized voglibose was monitored at 667 nm. The derivatized voglibose was confirmed by mass spectral analysis. In LC-MS method, voglibose was passed through Venusil XBPH (150X 4.6 mm, 5 µm) column with mobile phase containing 0.01% formic acid and methanol (95:5 v/v).

**Jong Soo W** et al. developed RP-HPLC by post-column derivatization for estimation of voglibose using fluorescence detection in pharmaceutical dosage form and LC-MS method.
estimation without derivatization. The sample pre-treatment include a simple extraction and centrifugation without pre-column derivatization. Taurine and sodium periodate dissolved in water were used as a post-column reagent. Detection was performed by excitation and emission wavelength at 350 nm and 430 nm. Elution were performed by using Cosmosil® 5NH2-MS (150X4.6 mm, 5 μm) column, with mobile phase containing acetonitrile: 30 mM NaH2PO4 (pH 6.5) (2:1, v/v). Voglibose was detected by LC-MS method by an electrospray ionization (ESI) mode with single ion recording (SIR, m/z 268.1). They found to be linear in the range of 50-1000 ng mL⁻¹ and LOD and LOQ were 9.4 and 29 ng mL⁻¹ for LC and 18 and 52 ng mL⁻¹ for LC-MS method respectively. Both methods could be successfully applied to the quantification of voglibose in commercially available tablets.

**Mithlesh R et al.** developed and validated LC/MS/MS method for the determination of voglibose in the pharmaceutical formulation. Separation and analysis of the analyte was carried out on Waters X Terra MS C18 (100X 2.1 mm, 5 μm) column with a mobile phase composed of A (1 mL formic acid in 1000 mL water): B (1 mL in 1000 mL of methanol) (50:50 v/v). It is found to be linear in the range of 25-1200 ng mL⁻¹ respectively. The retention time were found to be 1.06 min. the LOD and LOQ for voglibose were found to be 1.5 and 3.0 ng mL⁻¹ respectively. The monitoring of parent to product ion transitions for voglibose [m/z 268.1 to 78.86] using triple quadrupole in the MRM mode.

**Mallikarjuna Rao N et al.** developed deravitized RP-HPLC method for the determination of voglibose in bulk and tablet dosage forms. The separation was achieved by using RP-18e, Hibar RT (250X4.6mm, 0.5 μm) column with a mobile phase composed of 0.025M potassium dihydrogen phosphate (pH 2.5): acetonitrile: methanol (40:55:5 v/v/v) in isocratic mode at a flow rate of 1mL min⁻¹. Voglibose was derivatized with Taurine and sodium periodate, the retention
time was 2.6 min and mefanamic acid used as an internal standard and the detection was monitored at 282 nm. The linearity range was from 100 to 500 ng mL\(^{-1}\). The LOD and LOQ for voglibose were found to be 30 ng mL\(^{-1}\) and 100 ng mL\(^{-1}\) respectively.

**Guo D**\(^{46} \textit{et al.}** established RP-HPLC method for the simultaneous determination of four highly polar anti-diabetic drugs, metformin hydrochloride, phenformin hydrochloride, acarbose, and voglibose, in Chinese traditional patent medicines. The separation was achieved by using Thermo NH\(_2\) (4.6X 250 mm, 5 µm) column with the mobile phase consisted of 30% A and 70% B, where A included 0.06% potassium dihydrogen phosphate and 0.028% disodium hydrogen phosphate, B was acetonitrile. The flow rate was 1 mL min\(^{-1}\), the detection was performed at 195 nm, and the column temperature was 30 °C. It was found to be linear in the range of 1000-30,000 µg mL\(^{-1}\) respectively.