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Review on Reported Analytical Method Development by Uplc and Hplc of Selected Anti-Diabetic Drugs

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ABSTRACT: In this review article determines the different analytical methods for the establishment of selected Anti-Diabetic drugs such as **(Glibenclamide, Liraglutide, Nateglinide, Sitagliptin, Tolbutamide)** by using HPLC and UPLC.

UPLC is a modern technique which gives a new direction for liquid chromatography. UPLC refers to ultra performance liquid chromatography, which enhance mainly in three areas: "speed, resolution and sensitivity. Ultra performance liquid chromatography (UPLC) applicable for particle less than 2µm in diameter to acquire better resolution, speed, and sensitivity compared with high-performance liquid chromatography (HPLC). In twenty first centenary pharmaceutical industries are focusing for new ways to in economy and shorten time for development of drugs. UPLC analysis at the mean time gives the better quality of their products and analytical laboratories are not exception in this trend. The separation and quantification in UPLC is done under very high pressure (up to 100M Pa). As compare to HPLC, under high pressure it is observed that not any negative influence on analytical column and also other components like time and solvent consumption is less in UPLC.

High performance liquid chromatography (HPLC) is an important qualitative and quantitative technique, generally used for the estimation of pharmaceutical and biological samples. It is the most versatile, safest, dependable and fastest chromatographic technique for the quality control of drug components.

This article was prepared with an aim to review the comparison of the reported analytical methods of HPLC and UPLC of the selected Anti Diabetic drugs such as GLIBENCLAMIDE[(6)(10)], TOLBUTAMIDE[(2)(13)], NATEGLINIDE[(1)(7)], SITAGLIPTIN[(9)(12)], LIRAGLUTIDE[(8)(11).]

KEYWORDS: Method Development, High Performance Liquid Chromatography (HPLC), (Glibenclamide, Liraglutide, Glipizide, Sitagliptin, Tolbutamide), Ultra Performance Liquid Chromatography; High Separation Efficiency; Cost Effective; High Pressure.

I. INTRODUCTION AND REPORTED ANALYTICAL METHODS FOR SELECTED ANTIDIABETIC DRUGS:

Comparison- HPLC vs. UPLC INSTRUMENTATION:

	HPLC	UPLC
COLUMN	C18,50*46mm,4µm particle	BEH C18,50*2.1mm,1.7µm particles
FLOW RATE	3.0ml/min	0.6ml/min
INJECTION VOLUME	20µl	3µl partial loop fill or 5µl full loop fill
TOTAL RUN TIME	10min	1.5min
TOTAL SOLVENT CONSUMPTION	Acetonitrile:10.5ml Water:21.0ml	Acetonitrile:0.53ml Water:0.66ml
PLATE COUNT	2000	7500
USP RESOLUTION	3.2	3.4
LOQ	-0.2µg/ml	-0.54µg/ml

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II. REPORTED UPLC METHODS:

LIRAGLUTIDE:

Taposh Gorella et.al **(2019)** reported **"UPLC-MS/MS Determination of GLP-1 Analogue, Liraglutide A Bioactive Peptide in Human Plasma"**. Chromatographic separation was achieved with an ACQUITY UPLC Peptide BEH C18, 300 Å, 1.7 µm, 2.1 × 150 mm Column, using a linear gradient (Table 1) with 0.3% formic acid in water and acetonitrile: methanol (50:50) mobile phases at a flow rate of 0.3 mL/min. Total cycle time was 8 minutes. Retention time 4.77min.

GLIBENCLAMIDE:

Mohd Aftab Alam et.al **(2018)** reported **"Rapid, Validated UPLC-MS/MS Method for Determination of Glibenclamide in Rat Plasma".** Glibenclamide was eluted on an Acquity UPLC®BEH C18 1.7 µm, 2.1 x 50 mm column. The mobile phase consisted of component (A) acetonitrile (0.1 % formic acid) and component (B) water (0.1% formic acid). Mobile phase was pumped at 150 µl/min in gradient mode. Total sample run time was 2.0 min. The 10 µl sample was injected and the temperature of autosampler was kept at 20 ± 3°C. The parent sodium ion [Na^+] adduct of glibenclamide was observed at m/z 516.11. The parent sodium ion [Na^+] adduct of glimepiride was observed at m/z 513.19. The molecular masses of daughter fragments of glibenclamide sodium ion adduct (m/z 516.11) were 391 and 417.Retention time is 0.80min.

TOLBUTAMIDE:

Yan Liu et.al **(2013)** reported "**UPLC–MS-MS Method for Simultaneous Determination of Caffeine, Tolbutamide, Metoprolol, and Dapsone in Rat Plasma and its Application to Cytochrome P450 Activity Study in Rats"** The chromatographic separation was carried out using an Acquity UPLC–MS-MS and performed on a Waters Acquity UPLC BEH HILIC C18 column (2.1 × 50 mm, 1.7 µm). The column temperature was maintained at 40°C. The chamber temperature in the autosampler was kept at 10°C. The mobile phase consisted of acetonitrile and water (containing 0.1% formic acid) (15:85, v/v) at a flow rate of 0.25 mL/min, and the total run time for each injection was 5 min. Retention time is 3.10.

NATEGLINIDE:

Basavaiah Kanakapura et.al **(2012)** reported **"RP-UPLC Method Development And Validation For The Determination Of Nateglinide In Bulk Drug And Pharmaceutical Formulations: A Quality By Design Approach"** The chromatographic column used was Acquity UPLC BEH C-18 (100 × 2.1) mm with 1.7 µm particle size. Isocratic elution process was adopted throughout the analysis. Mobile phase used was 40:60 (buffer:acetonitrile) v/v (buffer-potassium dihydrogen orthophosphate of pH 2.8) The isocratic flow rate of mobile phase was maintained at 0.40 mL min–1. The column temperature was adjusted to 35°C. The injection volume was 2 µL. Eluted sample was monitored at 210 nm and the run time was 6.0 min. The retention time of the sample was about 2.8 min.

SITAGLIPTIN:

Chellu S N Malleswararao et.al **(2012)** reported **"Simultaneous Determination of Sitagliptin Phosphate Monohydrate and Metformin Hydrochloride in Tablets by a Validated UPLC Method".** Acquity UPLC BEH C8 (100 × 2.1 mm, 1.7 µm) was used as stationary phase. The mobile phase composition used was the buffer 10mM potassium dihydrogen phosphate and 2 mM hexane-1-sulfonic acid sodium salt (pH adjusted to 5.50 with diluted phosphoric acid) and acetonitrile with gradient program [Time(min)/% acetonitrile): 0/8, 2/8, 4/45, 6/45, 8/8, 10/8]. Prior to use, the mobile phase was filtered by using 0.2 µm filter. The flow rate of the mobile phase was maintained at 0.2 mL min^{-1} and water was used as sample diluent. The column temperature was 25°C and eluents were monitored at 210 nm. The injection volume for samples and standards was 0.5 µL. The total analysis run time was 10 min. The retention times of MH and SP were found to be 2 min and 7 min.

III. REPORTED HPLC METHODS:

NATEGLINIDE:

Prasanthi Chengalva et.al **(2016)** reported **"Development And Validation Of RP - HPLC Method For Metformin Hydrochloride And Nateglinide In Bulk And Combined Dosage Form"** The developed method used a reverse phase C18 column, Waters Inertsil ODS 3V (250x4.6 mm, 5µ), a mobile phase of phosphate buffer (pH 4.0): Acetonitrile: methanol (30:60:10), flow rate of 1.0 ml/min and a detection wavelength of 221 nm using a UV detector. Total run time is 20min.The developed method resulted in elution of Metformin hydrochloride at 2.45 min and Nateglinide at 4.21 min.

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SITAGLIPTIN:

Vasanth P M et.al **(2013)** reported **"Method development and validation of sitagliptin and metformin using reverse phase HPLC method in bulk and tablet dosage form"** A mobile phase has a composition of potassium dihydrogen orthophosphate and methanol(50:50v/v),adjusted the pH 8.5 with o-phosphoric acid was used and flow rate 1.0ml/min. The elution is observed using a PDA detector at 215 nm and the injection volume was 10 µL. HPLC device Waters model 2695 with Empower software version 2.0.Detector waters 2996 PDA Detector. Elico Ph meter, Sartorius – Digital balance (0.1 mg – 205 gm).separation was achieved on a Hypesil BDS C18 Column (100 x 4.6 mm, 5µm particle size. Total run time is 25 min. Retention times of Sitaglipitin and Metformin were 2.3 min and 17.113 min respectively.

TOLBUTAMIDE:

D. Madhu Latha et.al **(2013)** reported **"Development and Validation of RP - HPLC Method for Quantitative Analysis Tolbutamide in Pure and Pharmaceutical Formulations"**. Analysis was carried on Zodiac C18 column (250 mm × 4.6 mm × 5 µ particle size) using Methanol: 0.1% Orthophosphoric acid: Acetonitrile (10: 30: 60) as mobile phase. Detection was carried out by U.V atS 231 nm. Flow rate 1.0ml/min and Total run time is 10min. Retention time 4.60 min.

LIRAGLUTIDE:

P.V.V. Satyanarayana et.al **(2012)** reported **"Validated RP - HPLC Method For The Estimation Of Liraglutide In Tablet Dosage"** Mobile phase Methanol:Acetonitrile:0.1% OPA(35:60:5)PH 5.1,UV detection 245nm,Analytical column C18,Flow rate 1.0ml/min, Temperature ambient, Injection volume 20µl,Runtime 10 min, Retention time 6.11 min.

GLIBENCLAMIDE:

S. D. Rajendran et.al **(2007**) reported **"RP - HPLC method for the estimation of glibenclamide in human serum"** The chromatographic separations of glibenclamide and internal standard (glimepride) were accomplished using a 250 mm×4.6 mm ID Luna phenomenex 5u C18 analytical column (Phenomenex , USA). A Guard-Pak precolumn module (Phenomenex, USA) containing an ODS cartridge insert was placed serially just before the analytical column. The mobile phase consisted of acetonitrile: 25 mM phosphate buffer (pH: 3.5) in a combination of 60:40 v/v. The mobile phase was pumped at an isocratic flow rate of 1 ml/min at room temperature. The UV detection wave length was set at 253 nm. The wavelength of 253 nm represented the UV maximum of glibenclamide in acetonitrile: water in 1:1 ratio. Analytical run time was less than 12 min and the retention time was 8.12min

IV. RESULT AND DISCUSSION:

Name of the drug	UPLC			HPLC		
	Flow Rate	Run Time	Retention Time	Flow Rate	Run Time	Retention Time
LIRAGLUTIDE	0.3ml/min	8min	4.77min	1ml/min	10min	6.11min
GLIBENCLAMIDE	150µl/min	2min	0.80min	1ml/min	11min	8.12min
TOLBUTAMIDE	0.25ml/min	5min	3.10min	1ml/min	10min	4.60min
NATEGLINIDE	0.40ml/min	6min	2.8min	1ml/min	20min	4.21min
SITAGLIPTIN	0.2ml/min	10min	7min	1ml/min	25min	17.113min

In UPLC chromatogram, it is found that better resolution and separation are found as compared to HPLC along with performed more sensitive analysis, reduced consumption of solvent and has high speed of analysis.

A completely new system design with advanced technology has been developed, called Ultra High Performance Liquid Chromatography (UPLC).

The advantages of short turnaround time, method reliability, method sensitivity and drug specificity justify the use of LC techniques for various groups of the drug active compounds.

This review describes some of the principles of UPLC and HPLC, validation of these methods, system suitability tests for the methods, and application of methods to pharmaceutical analysis.

In LIRAGLUTIDE, compared to HPLC method, UPLC method provides reduced flow rate (0.3ml/min), runtime (8min), retention time (4.77min).

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In GLIBENCLAMIDE, compared to HPLC method, UPLC method provides reduced flow rate (150µl/min), run time (2min), retention time (0.80min).
In TOLBUTAMIDE, compared to HPLC method, UPLC method provides reduced flow rate (0.25ml/min), run time (2min), retention time (3.10min).
In NATEGLINIDE, compared to HPLC method, UPLC method provides reduced flow rate (0.40ml/min), run time (6min), retention time (2.8min).
In SITAGLIPTIN, compared to HPLC method, UPLC method provides reduced flow rate (0.2ml/min), run time (10min), retention time (7min).

V. CONCLUSION:

UPLC have proved to expand the utility of separation science when the conventional HPLC have almost reached separation barriers. Since most pharmaceutical companies try to reduce the R&D timings and cost, a faster and better UPLC separation can decrease the time and other resources. Using the UPLC technique, it is possible to run higher resolution methods, using shorter columns, smaller size of packing particles, with higher flow rates under high pressure. A significant decrease in solvent consumption and column equilibration time is also achieved while working on UPLC systems. Injection volume is drastically reduced than HPLC.

The high price of the instrument is the main disadvantage of UPLC. Moreover, the increased back pressure reduces the column life. But the advantages of UPLC, such as low solvent consumption, faster separation with better selectivity and sensitivity overcome its disadvantages. From this review we can conclude that UPLC provides more advantages compared to HPLC.

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