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Review Article

A Review on Analytical Techniques for the Determination of Anti-diabetic Drugs in Pharmaceutical Dosage Forms

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ABSTRACT

Diabetes mellitus (DM) has emerged as a major global health challenge. Current data indicate that around 8.5% of the world's adult population is affected, and this figure is projected to rise to 10.9% by 2030. In the pharmaceutical industry, quality remains paramount. Pharmaceutical analysis involves both qualitative and quantitative evaluation of drugs and formulations, covering everything from raw materials to finished dosage forms. In modern medical practice, analytical techniques are not only used to assess drug quality but also to monitor chemical constituents within the human body. Shifts in these concentrations often serve as diagnostic markers for disease. Moreover, such methods help in studying drugs and their metabolites within biological systems. Since the efficacy, safety, and reliability of pharmaceutical products directly impact patient health, rigorous analysis is essential. Anti-diabetic Drugs such as Tolbutamide, Gliclazide, Metformin Glipizide, Glimepiride and Glibenclamide require accurate analytical methods to ensure their quality, safety, and therapeutic effectiveness. Many antidiabetic drugs exhibit poor solubility, low dosage levels, or stability issues, making the development of reliable analytical methods essential. This review highlights advanced analytical approaches for glimepiride, including UV-Visible spectroscopy, High Performance Liquid Chromatography (HPLC), High Performance Thin Layer Chromatography (HPTLC), and Liquid Chromatography-Mass Spectroscopy. These techniques are applicable to both active pharmaceutical ingredients (APIs) and combination drug formulations.

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To ensure consistent quality, the Quality by Design (QbD) framework plays a crucial role in maintaining high standards across pharmaceutical development and manufacturing.

INTRODUCTION

Diabetes mellitus (DM) is becoming an important global health problem. Current estimates suggest that the prevalence of the disease is 8.5% of the world's adult population, and this is expected to rise to 10.9% by 2030. The number of people affected is expected to increase significantly, putting pressure on healthcare systems across the world.[1]

The development of Diabetes Mellitus is complex and may occur in many ways, so any system of classification is to some extent flexible. However, classification is important because it helps the healthcare professional to understand the disease and to choose the most appropriate treatment. The current classification system includes the etiology of diabetes and the pathogenesis and is useful in diagnosis and clinical management. In this system, diabetes is generally classified into four broad categories: Type 1 Diabetes, Type 2 Diabetes, Gestational Diabetes, and other types of diabetes caused by specific medical conditions, disorders, or underlying pathologies.[2]

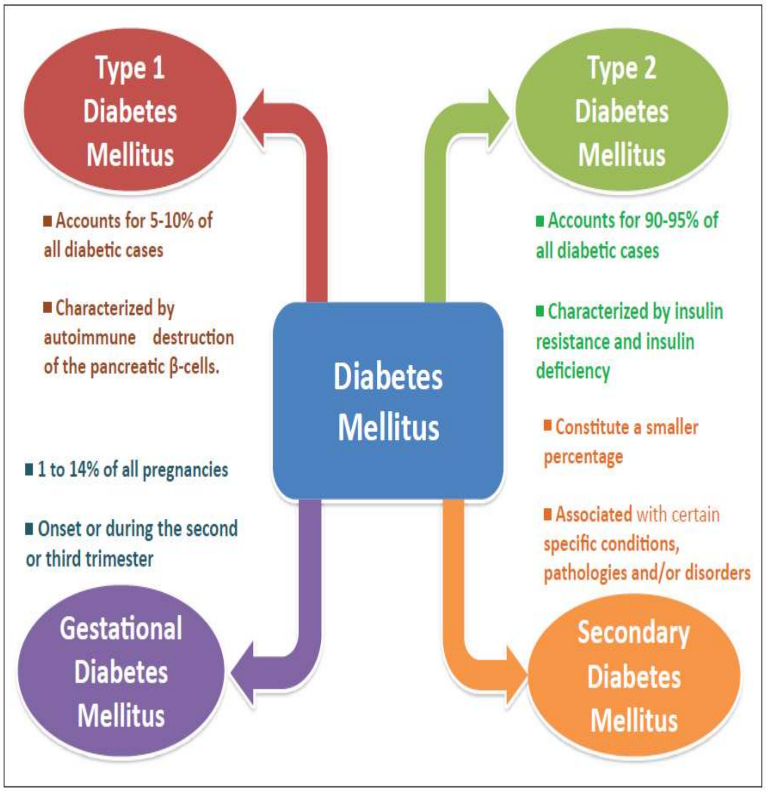

Fig No. 1 Types of Diabetes Mellitus

Diabetes is a long-term condition where the body can't manage blood sugar (glucose) properly. This may be because the pancreas does not make enough insulin, or because the body cannot use insulin well. Insulin is a hormone that is produced by special cells in the pancreas (called beta cells). Its main function is to help control the level of sugar in the blood by letting it into the cells, where it can be used as fuel. In many people with diabetes especially type 2 diabetes the body develops a condition called insulin resistance. That means the cells in the body no longer respond well to insulin. This makes it hard for glucose to get into the cells and it starts to build up in the blood.[3]

Type 2 diabetes is a common metabolic condition that occurs when two major problems happen at the same time: the pancreas doesn't make enough insulin, and the body's tissues don't respond to insulin as they should. This means that the body has more difficulty regulating blood sugar levels effectively. There are several factors that can increase the risk of developing this condition such as high blood sugar levels over time, being overweight, high triglyceride levels, poor eating habits, lack of physical activity, aging, and a family history of diabetes. Factors can also include feelings like stress, anxiety, and depression. Type 2 diabetes usually requires a mix of treatments to manage. This can include insulin therapy and medications such as metformin and other drugs that help lower blood sugar levels, along with lifestyle changes to support overall health.[4]

Analytical chemistry is the branch of chemistry that deals with figuring out what matter is and how much of it there is. Analytical chemistry is not an independent discipline within chemistry; rather, it is the practical application of chemical principles. Pharmaceutical Analysis is the process of using analysis to find out how pure, safe, and high-quality a drug or chemical is. "Quantitative pharmaceutical chemistry" is another name for "pharmaceutical analysis." Pharmaceutical analysis encompasses both qualitative and quantitative evaluations of drugs and pharmaceutical substances, ranging from bulk drugs to final dosage forms. In quantitative analysis, the method used is based on the quantitative performance of appropriate chemical processes. This involves either measuring the amount of reagent needed to complete the reaction or finding out how much reaction product was made.[5]

1. Quality by design: [6]

Quality is the most important thing when it comes to drugs. The effectiveness, safety, and quality of pharmaceutical products have a direct effect on the health and safety of patients. QbD is a cutting-edge method that focuses on building quality into processes and products from the start, rather than just testing finished products. It is an important part of making sure that pharmaceutical goods always meet these high standards. QbD was first used in the pharmaceutical industry, but now it is being used in many other fields, such as biotechnology, chemical manufacturing, and food production, because it is a systematic and scientific way to make sure quality.

2.1 Benefits of QbD

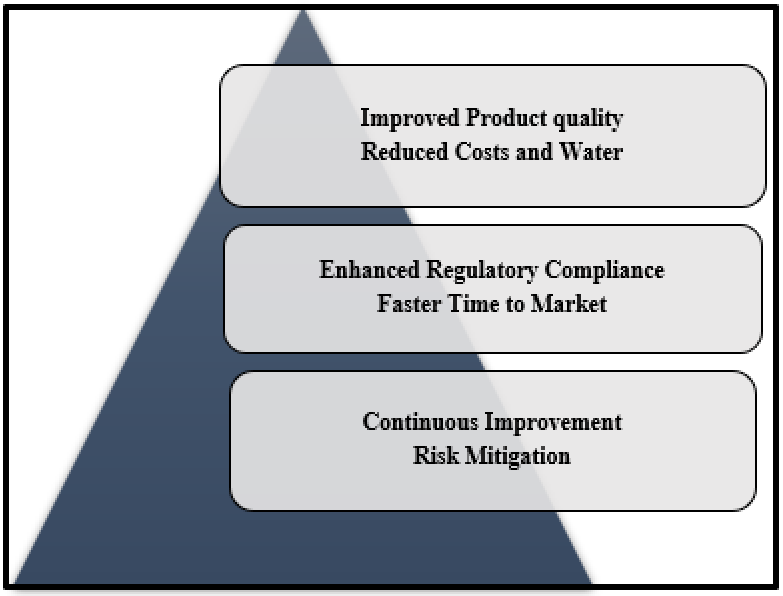

Fig No.2 Benefits of QbD

2.2 Key Principles of QbD

QbD is based on several key principles that guide its implementation:

2.2.1 Gaining an understanding of the product and process:

To do Qbd, you need to know a lot about the product and how it is made. This means figuring out what quality traits you want and what can change them.

2.2.2 Building quality into product:

The goal is to create a process that naturally guarantees quality, so there is less need for a lot of testing and quality checks after production. The focus is on creating processes that naturally guarantee quality, which reduces the need for extensive testing and quality checks after production.

2.2.3 Risk management:

QbD means finding and controlling risks at every stage of a product's life. This proactive approach helps to find and fix problems before they affect the quality of the products.

2.2.4 Design of experiment:

Structured experiments that look into the links between process factors, product factors, and product qualities make process optimization possible.

2.2.5 Continuous improvement:

To make the products better and more efficient. QbD is an ongoing process that includes watching, evaluating, and improving processes.

2.3 ICH Guidelines:

Guidelines: The ICH has developed several guidelines that incorporate QbD, including:

ICH Q8: Pharmaceutical development

ICH Q9: Quality risk management

ICH Q10: Pharmaceutical quality system

Objectives: ICH guidelines aim to harmonize regulatory expectation across regions, promoting a unified approach to pharmaceutical quality.

2.4 Role of QbD in Analytical Method Development:

Analytical method development is the process of coming up with ways to accurately measure compounds or properties. When developing analytical methods with QbD, you make sure that they are reliable, reproducible, and fit for their intended use.

2.5 Benefits of Using QbD in Analytical Method Development:

- ✓ Improved understanding of methods
- ✓ Enhanced method robustness
- ✓ Reduction of variability
- ✓ Efficiency in development

2.6 Key aspects of QbD includes: [7]

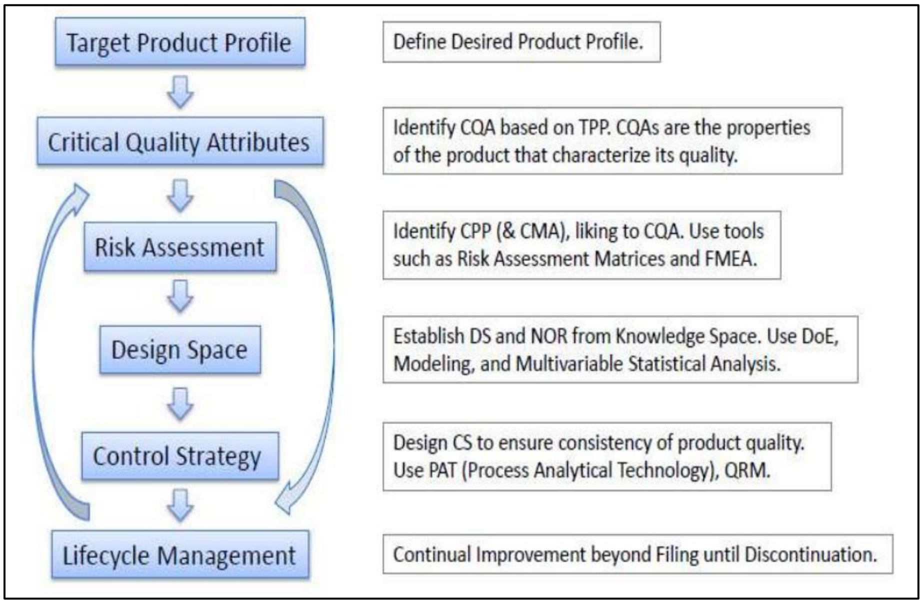

Fig No. 3 Key aspects of QbD

2.7 Tools and Techniques in QbD for Analytical Method Development:

2.7.1 Statistical software:

- JMP: Offers powerful visualization and analysis tools.
- Minitab: Widely used for statistical analysis in various industries.
- Design-Expert: Specializes in the DoE and optimization.

2.7.2 Risk assessment tools:

Fishbone Diagram: Identifies potential causes of variability.

Failure mode and effect analysis: Risks are systematically assessed together with their effects using FMEM.

Risk ranking and filtering: Prioritizes risk based on severity and probability.

2.7.3 Process analytical technology:

PAT involves using real-time data to monitor and control processes, ensuring compliance with quality standards.

2. RP-HPLC Method development and validation of Anti-diabetic drugs.

This review focus on HPLC method development and validation of Anti-diabetic drugs in BCS Class II : [8]

Table No.1 Anti-diabetic Drugs in BCS Class II

Drug	Formula	IUPAC Name	Structure Type
Tolbutamide	$C_{12}H_{18}N_2O_3S$	1-butyl-3-(4-methylphenyl)sulfonylurea	Sulfonylurea
Gliclazide	$C_{15}H_{21}N_3O_3S$	1-(hexahydrocyclopenta[c]pyrrol-2-yl)-3-(4-methylphenyl)sulfonylurea	Sulfonylurea
Metformin	$C_4H_{11}N_5$	3-(diaminomethylidene)-1,1-dimethylguanidine	Biguanide
Glipizide	$C_{21}H_{27}N_5O_4S$	N-[2-[4-(cyclohexylcarbamoylsulfamoyl)phenyl]ethyl]-5-methylpyrazine-2-carboxamide	Sulfonylurea
Glimepiride	$C_{24}H_{34}N_4O_5S$	4-ethyl-3-methyl-N-[2-[4-(4-methylcyclohexyl) carbamoylsulfamoyl]phenyl]ethyl]-5-oxo-2H-pyrrole-1-carboxamide	Sulfonylurea
Glibenclamide	$C_{23}H_{28}ClN_3O_5S$	5-chloro-N-[2-[4-(cyclohexylcarbamoylsulfamoyl)phenyl]ethyl]-2-methoxybenzamide	Sulfonylurea

There are many methods developed for anti-diabetic drugs RP-HPLC methods in API and combination drugs. This method seems to be economic than other methods.

Table No.2 RP-HPLC Method development and validation of anti-diabetic drugs

Sr. No	Title	Description	Reference
1	Development and Validation of RP-HPLC method for Quantitative analysis Tolbutamide in Pure and Pharmaceutical formulation	Mobile Phase = Methanol: 0.1 % Orthophosphoric acid: Acetonitrile (10:30:60) $\lambda max = 231\ nm$ Flow rate = 1.0 ml/min Linearity ≈ 0.9984	[9]
2	A RP-HPLC method development and validation for the estimation of Gliclazide in bulk and pharmaceutical dosage forms	Mobile phase = Methanol: Phosphate buffer (50: 50 v/v) λ max $= 210nm$ Flow rate = 1.2 ml/min Linearity = 0.999	[10]
3	Development and Validation of a new analytical HPLC method for simultaneous determination of the	Mobile Phase = Ammonium formate buffer (pH 3.5): Acetonitrile (45:55 v/v)	[11]

	antidiabetic drugs, metformin and gliclazide	λ max = 227 nm Flow rate = 1ml/min Linearity ≈ 0.9980	
4	Analytical Method Development and Validation of Gliclazide using RP-HPLC from Pharmaceutical Dosage Form	Mobile phase = Phosphate buffer: Acetonitrile (10:90 v/v) λ max = 228 nm Flow rate = 1.0 ml/min Linearity= 0.9990	[12]
5	HPLC Method for Estimation of Metformin hydrochloride in formulated Microspheres and Tablet Dosage form	Acetonitrile: phosphate buffer (65:35) λ max = 233nm Flow rate= 1.0 ml/min Linearity = 0.9990	[13]
6	A Novel RP-HPLC Method and Validation for the Quantification of a Potential Anti-Diabetic Drug Metformin hydrochloride in Tablet Dosage Form	Mobile Phase= Buffer: Acetonitrile (70:30) λ max = 232nm Flow rate = 0.5 ml/min Linearity= 0.999	[14]
7	Bioanalytical RP-HPLC Method Development and Validation for the Determination of Metformin hydrochloride in Spiked Human Plasma	Mobile Phase= Acetonitrile: Sodium dodecyl sulphate (40:60 % v/v) λ max = 235nm Flow rate= 2.0 ml/min Linearity= 0.9989	[15]
8	Development and Validation of Sensitive RP-HPLC Method for the Estimation of Glibenclamide in Pure and Tablet Dosage forms	Mobile Phase= Disodium hydrogen phosphate buffer: Methanol (75:25 v/v) λ max = 236nm Flow rate =1.0 ml/min Linearity = 0.9989	[16]
9	Method Development and Validation of Glibenclamide in Tablet Dosage form by using RP-HPLC	Mobile phase = Acetonitrile: 20 mM Ammonium acetate buffer pH 4.5 (50:50) λ max = 300 nm Flow rate = 1.0 ml/min Linearity = 0.9997	[17]
10	Development and Validation of RP-HPLC Method for Estimation of Glibenclamide in Nano emulsion formulation	Mobile Phase=Acetonitrile: Water (60:40 v/v) λ max =228nm Flow rate =1.0 ml/min Linearity ≤ 0.9998	[18]
11	Development and Validation of HPLC Method for Estimation of Metformin HCl and Anagliptin in its Synthetic Mixture	Mobile Phase= Buffer: Acetonitrile pH 3.0(80: 20) λ max = 232 nm ; **Metformin HCl**	[19]

		λ max = 247 nm ; **Anagliptin** Flow rate = 1.0 ml/min Linearity =0.999	
12	Development and validation of RP-HPLC Method for The Analysis of Metformin	Mobile Phase= Methanol: Water (30:70 v/v) $\lambda max = 233\ nm$ Flow rate= 0.5 ml/min Linearity=0.9995	[20]
13	HPLC Method for Determination of Gliclazide in Human Serum	Mobile phase= Acetonitrile: Methanol: Water (50:30:20, v/v) $\lambda max = 227 - 230\ nm$ Flow Rate=1.0 ml/min Linearity= 0.999	[21]
14	Development and Evaluation of Robust RP-HPLC Method for Gliclazide Estimation Integrating Box Behnken Design	Mobile phase= Methanol:0.02M Potassium dihydrogen orthophosphate (70:30 v/v) $\lambda max = 210\ nm$ Flow rate= 1.2 ml/min Linearity=0.999	[22]
15	HPLC Estimation of Gliclazide in Formulation and In Pharmacokinetic Studies	Mobile Phase= Mixture of water containing 0.1 % w/v Sodium phosphate monobasic: Acetonitrile (34:66) $\lambda max = 230\ nm$ Flow rate= 1 ml/min Linearity= 0.9999	[23]
16	Analytical Method Validation of Gliclazide related Substances by High Performance Liquid Chromatography Method	Mobile Phase= Acetonitrile: Water (45:55) $\lambda max = 235\ nm$ Flow rate =0.9 ml/min Linearity = 0.99998	[24]

This review emphasis on different method development and validation of glimepiride as follows:

3. Drug Profile:

Table No. 3 Drug Profile of Glimepiride

Name	Glimepiride
IUPAC Name	4-ethyl-3-methyl-5-oxo-N-[2-[4-[[2,3,5,6-tetradeuterio-4-(trideuteriomethyl) phenyl] carbamoylsulfamoyl] phenyl] ethyl]-2H-pyrrole-1-carboxamide
Molecular formula	$C_{24}H_{28}N_4O_5S$
Molecular weight	491.6 g/mol
Category	Sulfonylurea (second-generation)

Activity	Type II Diabetes Mellitus
Melting point	207-209 ^{0}C
Mechanism	Glimepiride binds to sulfonylurea receptors (SUR1 and SUR2A) on pancreatic beta cells, closing ATP- sensitive K+ channels, which depolarizes the membrane and triggers insulin granule exocytosis.
Pharmacokinetics	Onset & peak: Absorbed rapidly after oral dosing; peak effect within about 2-3 hours. Duration: Long acting, with a duration of action up to approximately 24 hours, allowing once-daily dosing.
Metabolism	Mainly by CYP2C9
Contraindication	Hypoglycemia
Drug Interaction	Alcohol, diuretics and other medications can affect effectiveness and increase risks.

4. Method Development and Validation

I) Method Development

There are many methods developed for glimepiride by UV Visible Spectroscopy, HPLC, HPTLC, LCMS methods in API and combination drugs. This method seems to be economic than other methods.[25]

5.1 By using UV-Visible Spectroscopy:

Table No. 4 UV-Visible Spectroscopy Method for Glimepiride

Sr.no	Title	Description	Reference
1	Analytical method development and validation of Glimepiride in bulk and tablet dosage form using UV Spectrophotometer	Solvent=NaOH λmax = 231 nm R^2 = 0.999732 LOD =25.93 µg/ml LOQ = 86.44 µg/ml	[26]
2	Analytical method development and validation of Glimepiride in pharmaceutical dosage form by UV visible spectrophotometric method	Solvent= 0.1 N NaOH λmax = 233nm R^2 = 0.999 LOD = 0.5 µg/ml LOQ = 1.5 µg/ml Intraday & Inter day precision = 1 & 0.95 %	[5]
3	Stability Indicating UV Spectrophotometric Method Development and Validation for Simultaneous Estimation of Pioglitazone hydrochloride and Glimepiride in Bulk drug and Pharmaceutical Formulation	Solvent = Methanol **Glimepiride**, λmax =227 nm **Pioglitazone hydrocholride** , λmax =266 nm R^2= 0.999	[27]

4	Development and Validation of UV Spectrophotometric method for simultaneous estimation of Lobeglitzone Sulfate and Glimepiride in combined dosage form	Solvent = Methanol Method I, **Simultaneous estimation**, **Lobeglitzone** , λmax = 250 nm **Glimepiride**, λmax = 227 nm Method II, **2nd order derivatives,** **Lobeglitzone**, λmax = 297 nm **Glimepiride**, λmax = 259 nm Con. = 3-13 µg/ml (LS) Con. = 6-26 µg/ml (GLM) R^2 = 0.999	[28]
5	Development and Validation of an UV-Derivative Spectrophotometric Method for Determination of Glimepiride in Tablets	λmax = 220 – 300 nm Solvent= 5*10^{-3} mol $^{L-}$ NaOH R^2 = 0.999	[29]
6	Development and Validation of a Spectrophotometric Method for Quantification and Dissolution Studies of Glimepiride in Tablets	Solvent = 0.1 M NaOH & Methanol λ max = 225 nm R^2 = 0.999 Con.= 6.0-14.0 µg/ml % Recovery = 99.32-100.98 %	[30]

5.2 By using HPLC:

Table No. 5 HPLC Method for Glimepiride

Sr.no	Title	Description	Reference
1	Reverse-Phase High-Performance Liquid Chromatography Method Development and Validation for Estimation of Glimepiride in Bulk and Tablet Dosage Form	Mobile Phase= Monobasic sodium phosphate in water: acetonitrile Flow rate= 1 ml/min λ max = 225 *nm* Linearity = 0.999,	[31]
2	Analytical Method Development and Validation by RP-HPLC for Quantitative Determination of Glimepiride in pharmaceutical formulation	Mobile Phase= Methanol: Phosphate buffer (pH 4.0) Flow rate= 0.5 ml/min λ max = 225 nm Linearity= 10-50 µg/ml	[32]
3	Method Development and Validation of Glimepiride in Tablet Dosage form by RP-HPLC Method	Mobile Phase= Acetonitrile: Disodium hydrogen o-phosphate (70:30 v/v, pH 4) Flow rate= 1 ml/min λmax = 228 nm Linearity= 0.999	[25]

4	Analytical Method Development and Validation for The Simultaneous Estimation of Pioglitazone and Glimepiride in Tablet Dosage form by RP-HPLC	Mobile Phase=Phosphate buffer (pH 4.5): Acetonitrile (45:55, v/v) Flow rate= 1 ml/min λ max = 225 nm Linearity=0.9854 **PIO** 0.9926 **GLM**	[33]
5	Development of a quality by design-based hybrid R-HPLC method for Glimepiride: Bioanalytical and industrial application	Mobile Phase= Acetate buffer: Acetonitrile (40:60) Flow rate= 0.8 ml/min Linearity= 0.999	[34]
6	Method Development and Method Validation of Glimepiride in Formulation by HPLC in Reverse Phase Method	Mobile Phase= Acetonitrile: 0.1 % formic acetic acid (55:45, v/v) Flow rate= 1 ml/min $\lambda max = 250$ nm Linearity= 0.999	[35]
7	Deduction of the operable design space of RP-HPLC technique for the simultaneous estimation of metformin, pioglitazone and glimepiride	Mobile Phase= Methanol: KDHP (pH 3.7) Flow rate 1.2 ml/min λmax = 227 nm Linearity= 0.999	[36]

5.3 By using LC-MS/MS

Table No. 6 LC-MS/MS Method for Glimepiride

Sr.no.	Title	Description	Reference
1	Simultaneous determination of atorvastatin, metformin and glimepiride in human plasma by LC-MS/MS and its application to a human pharmacokinetics study	Mobile Phase =Acetonitrile: Ammonium acetate (60:40 v/v) Flow rate=1.1 ml/min $R^2 = 0.9980$ Con.; 1)0.50-150.03 ng/ml; **Atorvastatin** 2)12.14-1207.50 ng/ml; **Metformin** 3) 4.98-494.29 ng/ml; **Glimepiride**	[37]

5.4 By using UPLC-MS/MS

Table No. 7 UPLC-MS/MS Method for Glimepiride

Sr.no	Title	Description	Reference
1	UPLC-MS/MS Method for Simultaneous Quantification of Glimepiride and Metformin in Human Plasma	Mobile Phase= 0.1% Formic acid: Methanol (3:7 v/v) Linearity= 0.999	[38]

		Con., 1) 50-2000 ng/ml; **Metformin hydrochloride** 2) 0.1-1000 ng/ml; **Glimepiride**	

II) Validation

The methodical process of evaluating and presenting unbiased proof that particular requirements for a given intended use are satisfied is known as validation. It entails assessing a method's effectiveness and proving that it can satisfy particular requirements. Validation basically gives you a thorough understanding of what your method can consistently produce, especially when working with low doses or difficult conditions in analytical methods.[5]

Method Validation

Method validation is the process to confirm that analytical procedure employed for a specific test is suitable for its intended use. Method needs to be validated or revalidated;

- Before their introduction into routine use
- Whenever the conditions change for which, the method has been validated, e.g., instrument with different characteristics
- Whenever the method is changed, and the change is outside the original scope of the method.

All the variables of the method should be considered, including sampling procedure, sample preparation, chromatographic separation, detection and data evaluation chromatographic methods used in analytical applications there is more consistency in validation practice with key analytical parameters.[5]

The process of evaluating an analytical method's performance uniqueness and compliance with the requirements for its intended use is known as validation, and it is established through laboratory studies. The first step in the validation process for analytical procedures is the applicant's deliberate and methodical collection of validation data to support the analytical procedure.[39]

Parameters

The following are typical analytical performance characteristics which may be tested during methods validation:

- ➢ Accuracy
- ➢ Precision
- ➢ Linearity and Range
- ➢ Detection limit
- ➢ Quantitation limit
- ➢ Specificity
- ➢ Robustness
- ➢ Ruggedness
- ➢ System suitability determination
- ➢ Stability studies

1. Accuracy

It is the degree to which the method's test results closely resemble the actual value. Using a known quantity of standard drug solution added to the sample solution, recovery studies were conducted using the standard addition method.[4]

2. Precision

The degree of agreement or scattering between a series of measurements made under particular conditions from multiple samplings of the same homogeneous material is known as precision in the context of analytical methods. Precision is a crucial parameter for evaluating the reproducibility of the entire analytical process. Repeatability and intermediate precision are the two parts of precision.

The variation that a single analyst experiences on a single instrument is known as repeatability. It does not differentiate between variance resulting from the instrument or system and variance brought about by the sample preparation process. The fluctuation that takes place in a laboratory on different days, with different instruments, and involving different analyses is referred to as intermediate precision.[17]

3. Linearity

The ability of an analytical procedure to yield test results that are exactly proportionate to the analyte concentration in the sample, within a given range, is known as linearity. It is essential to assess this linear relationship throughout the analytical technique's range. To directly demonstrate linearity on the drug substance, the suggested method entails diluting a standard stock solution containing the components of the medical product.[17]

4. Detection limit

The most fundamental indicator of an analyte in a sample that can be identified but not precisely quantified is the detection limit of a single analytical technique. This limit, which serves as a key indicator of the method's sensitivity, is the lowest concentration at which the analyte's presence can be consistently detected.[17]

5. Quantification limit

The lowest amount of analyte in a sample that can be precisely and accurately measured quantitatively is known as the quantitation limit of a particular analytical system. The quantitation limit serves as a threshold for accurate quantitative measurements in analytical techniques and is essential for detecting contaminants and/or impurities in samples.[17]

6. Specificity

The ability of an analytical method to precisely measure an analyte in the presence of interference, such as synthetic precursors, excipients, enantiomers, and known (or likely) degradation products that might be expected to be present in the sample matrix, is known as selectivity.[40]

7. Robustness

It is described as a measure of an analytical method's capacity to show its dependability under typical use while remaining unaffected by slight but intentional changes in method parameters (e.g., pH, mobile phase composition, temperature, and instrumental settings). The methodical process of changing a parameter and assessing the impact on the procedure by keeping an eye on system suitability and/or sample analysis is known as robustness determination.[40]

8. Ruggedness

The sample solutions were prepared and examined under various analytical conditions, such as different laboratory settings, and the findings are presented.[4]

9. System suitability determination

Testing for system suitability is a common procedure in liquid chromatography. They act as a guarantee that the resolution, detection sensitivity, and repeatability of the chromatographic system are adequate for the planned analysis. These tests are predicated on the idea that the instruments, electronics, analysis procedures, and samples to be tested are all parts of a bigger system that can be evaluated collectively.

Key parameters such as peak resolution, the number of theoretical plates, peak tailing and capacity are examined during system suitability tests to assess the adequacy and performance of the employed analytical method.[17]

10. Stability studies

In order to determine whether special storage conditions, such as refrigeration or light protection, are required, the stability of standards and samples is established during validation under normal conditions, normal storage conditions, and occasionally in the instrument.

6. Difference between UV Visible and HPLC

Table No. 8 Difference between UV-Visible spectroscopy and HPLC

Sr.No.	UV Visible	Components	HPLC
1	Limited	Selectivity	High, very good separation capabilities
2	Goods for Simple Assays	Sensitivity	Superior, detects low level impurities
3	Low cost and simple setup	Cost and Equipment	High cost but Complex Instrumentation
4	Very Simple	Sample Preparation	Need optimizes mobile phase, column
5	Minimal	Need of Solvent	Very High
6	Limited Expertise	Expertise	Skilled personnel
7	Fast	Analysis Time	Moderate
8	Higher (Less Sensitive)	LOD (Limit of Detection)	Lower (more sensitive)
9	Higher	LOQ (Limit of Quantification)	Lower

7. FUTURE ASPECTS

Future research in the method development of anti-diabetic drugs (BCS Class II) should focus on the advancement of more sensitive, rapid, and eco-friendly analytical techniques. The integration of high-performance methods such as LC-MS/MS and UPLC can significantly enhance detection sensitivity and reduce analysis time. Expanding bioanalytical applications for pharmacokinetic and bioequivalence studies represents another important direction. Furthermore, the incorporation of automation and artificial intelligence in method optimization can improve efficiency and reproducibility. Overall, future developments should align with updated regulatory guidelines to ensure accuracy, precision, and global applicability.

8. CONCLUSION

Analytical method development and validation remain essential components of pharmaceutical quality assurance for antidiabetic medications. A wide range of analytical techniques, including UV-visible spectroscopy, RP-HPLC, LC-MS/MS, and UPLC-MS/MS, have been successfully utilized for the qualitative and quantitative determination of antidiabetic drugs in bulk materials, pharmaceutical formulations, and biological matrices. The available evidence indicates that these methods provide satisfactory accuracy, precision, sensitivity, and robustness in accordance with regulatory expectations. Among the antidiabetic drugs reviewed, glimepiride exhibited the highest number of reported analytical method development and validation studies. This extensive research activity may be attributed to its clinical significance, low-dose formulation requirements, and analytical complexity associated with its limited aqueous solubility. The large number of published methods reflects the continuous need for reliable and sensitive analytical procedures to support formulation development, quality control, stability assessment, and bioanalytical investigations. The integration of Quality by Design principles into analytical method development has further enhanced method understanding, robustness, and lifecycle management. Future research should focus on environmentally sustainable analytical approaches, advanced chromatographic techniques, automation, and artificial intelligence-assisted method optimization to improve analytical efficiency and regulatory compliance. Overall, the reviewed analytical methodologies provide a strong scientific foundation for the continued development and quality evaluation of antidiabetic pharmaceutical products.

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