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Review Article

Emerging and Established Methods for Voglibose Quantification: A Detailed Review

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ABSTRACT

Voglibose (VGB) is an α-glucosidase inhibitor used in the management of type 2 diabetes mellitus. It works by delaying the absorption of carbohydrates from the gastrointestinal tract, thereby reducing postprandial blood glucose spikes. This mechanism of action helps to control blood sugar levels without causing hypoglycemia, making it particularly useful for patients with fluctuating blood glucose levels. VGB has shown efficacy in improving glycemic control when used as monotherapy or in combination with other antidiabetic agents. This review aims to provide a comprehensive analysis of the pharmacological properties, therapeutic applications, and clinical efficacy of VGB. It also examines the bioanalytical methods used to measure VGB concentrations in plasma, particularly focusing on spectroscopy methods and its role in ensuring accurate pharmacokinetic and pharmacodynamic studies. Special emphasis is placed on the challenges of method validation, sample extraction, and plasma analysis, which are critical for assessing the drug's effectiveness and safety profile. Despite its benefits, further studies are needed to explore long-term outcomes and the potential for VGB to be integrated into broader diabetes management strategies.

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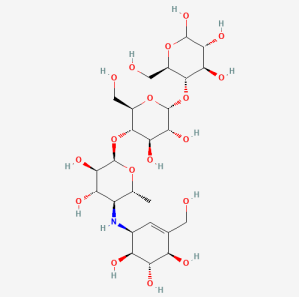
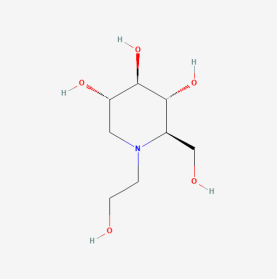
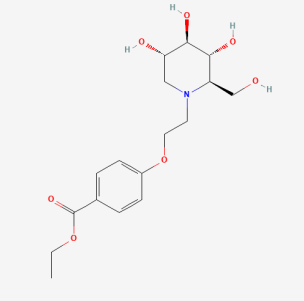
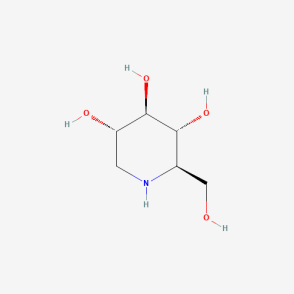
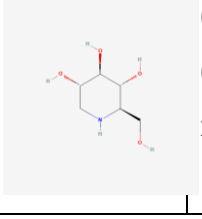
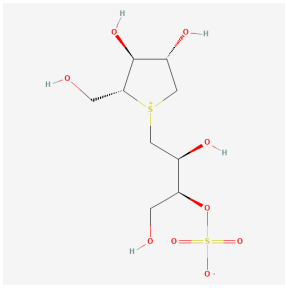
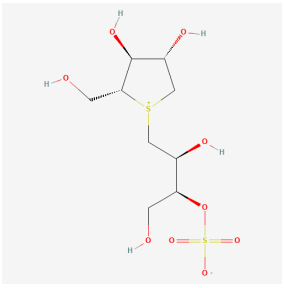
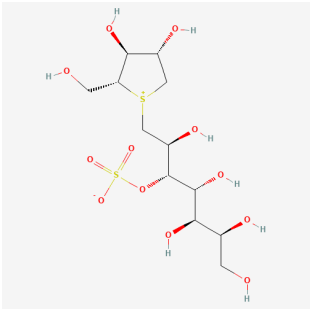
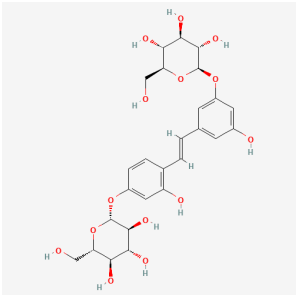
Introduction:

Voglibose (VGB) is α-glucosidase inhibitor widely used in the treatment of type 2 diabetes mellitus to control postprandial hyperglycemia. Unlike other oral antidiabetic agents, VGB works by inhibiting action of the α-glucosidase enzymes present in the small intestine, which delays the digestion and absorption of carbohydrates. This results in a slower and more controlled release of glucose into the bloodstream following meals, helping to prevent sharp spikes in blood sugar levels. VGB is particularly beneficial for patients who experience significant postprandial glucose excursions, making it a valuable addition to a comprehensive diabetes treatment regimen, either as monotherapy or in combination with other drugs [1-3]. Although effective, VGB clinical use requires careful monitoring to ensure optimal dosing and to prevent gastrointestinal side effects such as bloating and flatulence. Furthermore, the bioanalytical assessment of VGB concentrations in plasma is crucial for evaluating its pharmacokinetics and pharmacodynamics in Table 1. Spectroscopy techniques have become essential for the precise quantification of the VGB in biological samples, allowing for more accurate monitoring of drug levels and aiding in method validation for clinical studies. This review aims to provide the in-depth analysis of the VGB pharmacological profile, its therapeutic efficacy in type 2 diabetes management, and the bioanalytical methodologies employed to monitor its use. By exploring both the benefits and challenges of VGB, this review offers a comprehensive perspective on its role in modern diabetes care [4-5].

Table 1: provides information about nucleoside analogues.

Drug	Structure	IUPAC Name	Molecular weight	Solubility
Acarbose		(3R,4R,5S,6R)-5-[(2R,3R,4R,5S,6R)-5-[(2R,3R,4S,5S,6R)-3,4-dihydroxy-6-methyl-5-[[(1S,4R,5S,6S)-4,5,6-trihydroxy-3-(hydroxymethyl)cyclohex-2-en-1-	645.6 g/mol	Soluble in water

		yl]amino]oxan-2-yl]oxy-3,4-dihydroxy-6-(hydroxymethyl)oxan-2-yl]oxy-6-(hydroxymethyl)oxane-2,3,4-triol		
Miglitol		(2R,3R,4R,5S)-1-(2-hydroxyethyl)-2-(hydroxymethyl)piperidine-3,4,5-triol	207.22 g/mol	Soluble in water
Emiglitate		ethyl 4-[2-[(2R,3R,4R,5S)-3,4,5-trihydroxy-2-(hydroxymethyl)piperidin-1-yl]ethoxy]benzoate	355.4 g/mol	Insoluble in water, Soluble in DMSO
Deoxynojirimycin		(2R,3R,4R,5S)-2-(hydroxymethyl)piperidine-3,4,5-triol	163.17 g/mol	Soluble in water, dimethyl sulfoxide and methanol
1-Deoxymannojirimycin		(2*R*,3*R*,4*R*,5*S*)-2-(hydroxymethyl)piperidine-3,4,5-triol	199.63 g/mol	Soluble in DMSO

N-butyldeoxynojirimycin		[(2S,3S)-4-[(2R,3S,4S)-3,4-dihydroxy-2-(hydroxymethyl)thiolan-1-ium-1-yl]-1,3-dihydroxybutan-2-yl] sulfate	334.4 g/mol	Soluble in water
Salacinol		[(2S,3S)-4-[(2R,3S,4S)-3,4-dihydroxy-2-(hydroxymethyl)thiolan-1-ium-1-yl]-1,3-dihydroxybutan-2-yl] sulfate	334.4 g/mol	Soluble in DMSO
Kotalanol		[(2S,3S,4R,5R,6S)-1-[(2R,3S,4S)-3,4-dihydroxy-2-(hydroxymethyl)thiolan-1-ium-1-yl]-2,4,5,6,7-pentahydroxyheptan-3-yl] sulfate	424.4 g/mol	Soluble in Methanol
Mulberroside A		(2S,3R,4S,5S,6R)-2-[3-hydroxy-4-[(E)-2-[3-hydroxy-5-[(2S,3R,4S,5S,6R)-3,4,5-trihydroxy-6-(hydroxymethyl)oxan-2-yl]oxyphenyl]ethenyl]phenoxy]-6-(hydroxymethyl)oxane-3,4,5-triol	568.5 g/mol	Soluble in DMSO

Voglibose

This review briefly discusses regarding VGB. The chemical name is (1S,2S,3R,4S,5S)-5-[(1,3-dihydroxypropan – 2 – yl)amino] – 1-(hydroxymethyl)cyclohexane-1,2,3,4-tetrol (Fig.1), VGB, an α-glucosidase blocker, is used for the treatment of type 2 diabetes mellitus to manage postprandial hyperglycemia. It works by inhibiting the activity of α-glucosidase enzymes in the small intestine, delaying the breakdown of complex carbohydrates into glucose. This results in a slower & more controlled absorption of glucose into the bloodstream, preventing rapid spikes in blood sugar levels after meals [6]. Unlike other antidiabetic medications, VGB does not induce hypoglycemia and is often used in combination with other oral hypoglycemic agents. While effective in reducing postprandial blood glucose, it can cause gastrointestinal side effects such as bloating, flatulence, and diarrhea. VGB is typically prescribed to individuals who struggle with postprandial glucose excursions and can be a useful adjunct to lifestyle modifications like diet and exercise [7].

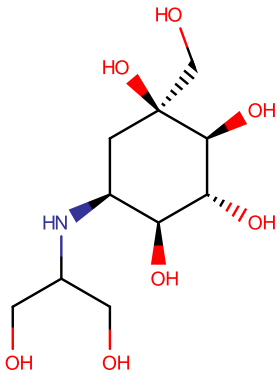


Figure 1. Chemical Structure of Voglibose

Importance of Analytical Estimation

Analytical method development and validation (AMDV) are found critical processes in pharmaceutical industry & other scientific fields, ensuring that analytical techniques are found to be robust, reliable, and suitable for their intended purposes. This discussion highlights the importance of AMDV, its key components, and its implications for drug development and quality assurance [8-10].

Importance of Analytical Method Development

❖ **Establishing Methodology**

Analytical method development involves creating and refining techniques to accurately measure and analyze the components of a product. This can include both the development of advanced methods & the improvement of existing ones. The aim is to established that the methods used was appropriate for the specific characteristics of the substances

being tested, such as their identity, purity, potency, and stability [11-12].

❖ **Regulatory Compliance**

Validation of these methods is not just a best practice; it is a regulatory requirement. Regulatory authorities worldwide mandate that analytical methods used in clinical trials and for marketing authorization must be validated to demonstrate their accuracy, specificity, precision, and robustness. This is essential for gaining approval for new drugs and ensuring that they are safe and effective for patient use [13].

❖ **Quality Assurance**

The reliability of analytical methods directly impacts the quality of pharmaceutical products. Validation establishes that a method consistently produces results that meet predefined criteria, which is vital for quality control and assurance throughout the drug development process. This includes assessing active pharmaceutical ingredients (APIs), excipients, and degradation products to ensure that they meet safety and efficacy standards [14-15]

Key Components of Analytical Method Validation

Analytical method validation involves several critical parameters:

- ✓ **Accuracy:** The closeness of the calculatedqualityto the observed value.
- ✓ **Precision:** The degree to which repeated measurementsidentical findings are obtained from under unchanged conditions shows the same results.
- ✓ **Limit of Detection; LOD & Limit of Quantification; LOQ:** The lowest analyte concentration that can be accurately measured or detected.
- ✓ **System Suitability Testing:** Ensuring that the analytical system is operating correctly before analysis.
- ✓ **Specificity:** The method's capacity to measure the analyte while additional analytes are present.
- ✓ **Robustness:** The method's capacity to remain functional independently of small variations in method parameters.

Steps in Method Development and Validation

- ✓ **Assessment of Existing Methods:** Determine if current methods are sufficient or if new methods need to be developed.
- ✓ **Experimentation:** Conduct experiments to test the new or improved methods against established standards.
- ✓ **Theory Application:** Utilize theoretical frameworks to predict outcomes and analyze data.
- ✓ **Real-World Application:** Apply the methods to actual samples to validate their effectiveness

Role in Pharmaceutical Industry

The development and validation of advanced analytical methods act an important role in the pharma industry, assuring that drugs are safe, effective, and of high quality. These processes are integral to the overall drug development lifecycle, from initial research through to clinical trials and manufacturing [16]. An overview of their significance, processes involved, and regulatory considerations are narrated below.

Regulatory Guidelines

The validation of analytical methods and development is associated with guidelines established by various regulatory bodies. These include:

- **ICH Q2(R1):** Provides guidelines for the validation of analytical procedures.
- **FDA Guideline for Industry:** Outlines expectations for Validation of analytical techniques and processes for pharmaceuticals and biologics.

These guidelines help standardize the validation process across the industry, ensuring that all pharmaceutical products meet safety and efficacy standards.

Analytical Techniques for Estimation

Pharmaceutical Analysis Techniques in figure 2:

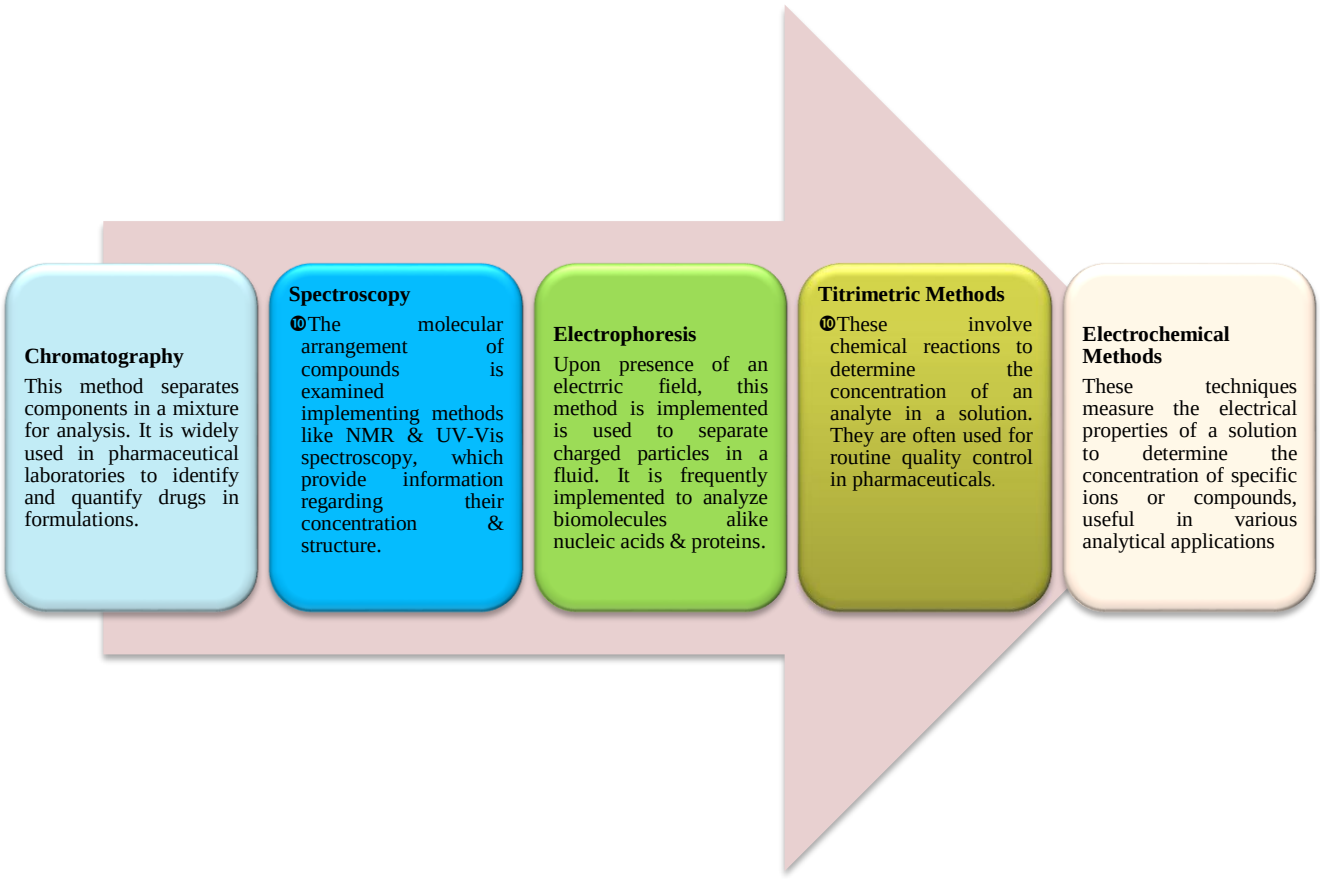


Figure 2. Different techniques for Analysis

The choice of analytical technique for estimation depends on the specific requirements of the project or analysis being conducted. Every approach has advantages and disadvantages, and frequently a mix of both of techniques is employed to achieve the most accurate and reliable results [17-18]. Understanding these techniques is crucial for effective project management, data analysis, and pharmaceutical research in Table 2 & 3.

Spectroscopic Techniques

Table 2. Determination of stability methods

Sl. No	Solvent	λmax	Description	Reference
1	Methanol (Taurine and Sodium periodate)	282 nm	Linearity range: 10-80 µg/ml	19
2	Water (Taurine and Sodium periodate)	222 nm	Linearity range: 0.003-0.024 µg/ml LOD: 0.00263 LOQ: 0.0079	20

Table 3. Comparative study results for VGB in combination by using Spectrophotometric

Sl. No	Solvent	λmax		Lineraity		LOD (µg/ml)		LOQ (µg/ml)		Reference
		VGB	MET	VGB	MET	VGB	MET	VGB	MET	
1	Methanol (Taurine and Sodium periodate)	242nm	220nm	2-10	10-50	0.62	0.86	2.25	5.11	21

Table 4. Comparative study results for VGB using HPLC

Sl. No	Mobile Phase (v/v)	Stationary Phase	Linearity (µg/ml)	LOD (µg/ml)	LOQ (µg/ml)	RT	Reference
1	Acetonitrile and water (50:50)	C18 (250 x 4.6 mm, 5 µm) column	10-100	2.91	9.7	3.264 min	22
2	0.025M potassium dihydrogen phosphate pH 2.5: acetonitrile:methanol (40:55:5)	Hibar RT column (250×4.6mm)	100 – 500	30	100	2.6 min	23
3	Acetonitrile: water (20:80 v/v)	Agilent TC C18 (250 × 4.6 mm) 5µm column	10-70	0.037	0.114	3.17±0.1 min	24
4	Acetonitrile: water (70:30 v/v)	C18 column (250 mm x 4.6 mm, 5 µm)	10-60	0.054	0.16	3.08 min	25

Applications of analytical tools in drug development

Analytical tools play a crucial role in drug development, enhancing various stages from discovery to clinical trials. This overview highlights key applications of analytical methods and technologies in the pharmaceutical industry [26].

A. ML; Machine Learning &AI; Artificial Intelligence

The implementation of artificial intelligence; AI and machine learning; ML algorithms in drug discovery & development procedures are expanding [27]. These technologies facilitate in figure-3.

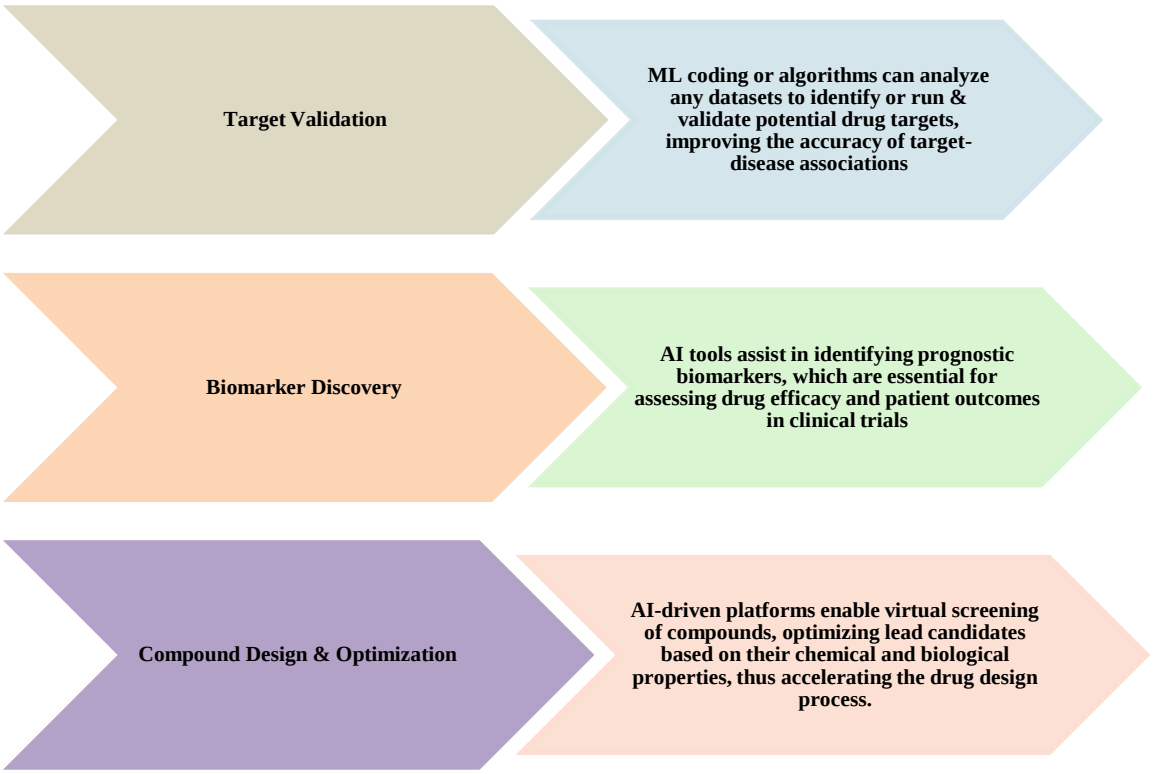


Figure 3. An analytical tool for technology facility

B. Analytical Method Development

Analytical methods are vital for ensuring drug quality and safety. Key techniques include in figure 4:

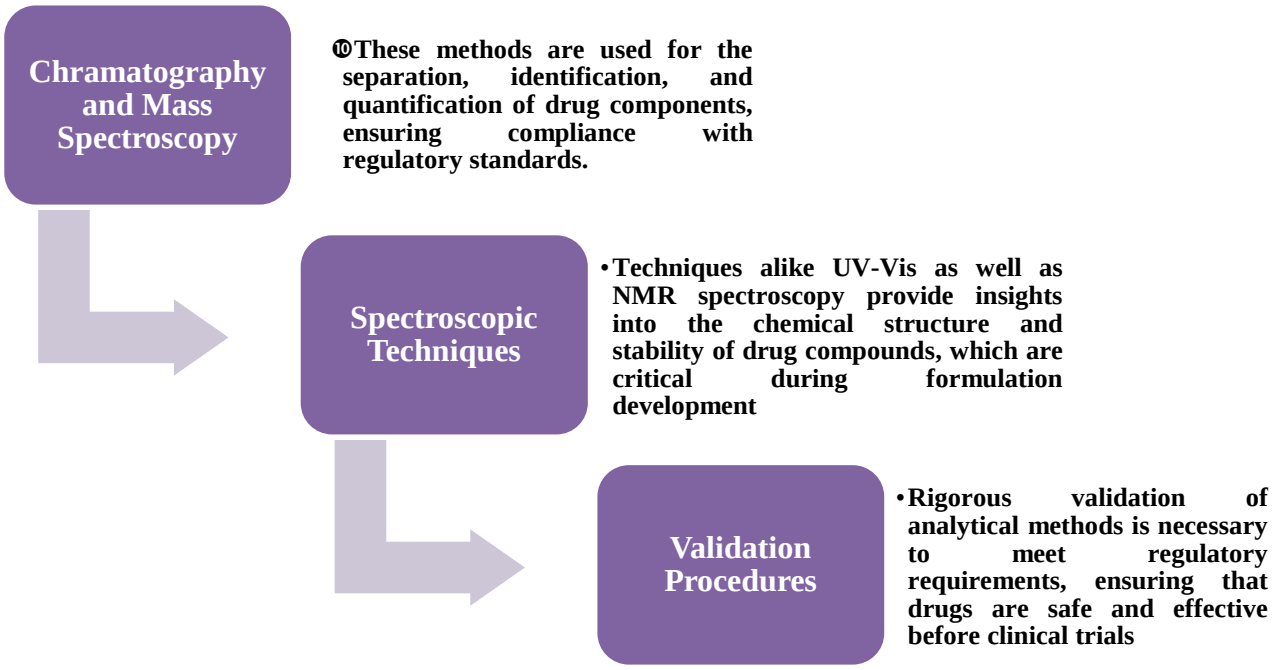


Figure 4. Key techniques for analytical methods are vital for ensuring drug quality and safety

C. Process Analytical Technology (PAT)

PAT is a methodology that enhances the quality and efficiency of pharmaceutical manufacturing. It involves in figure 5:

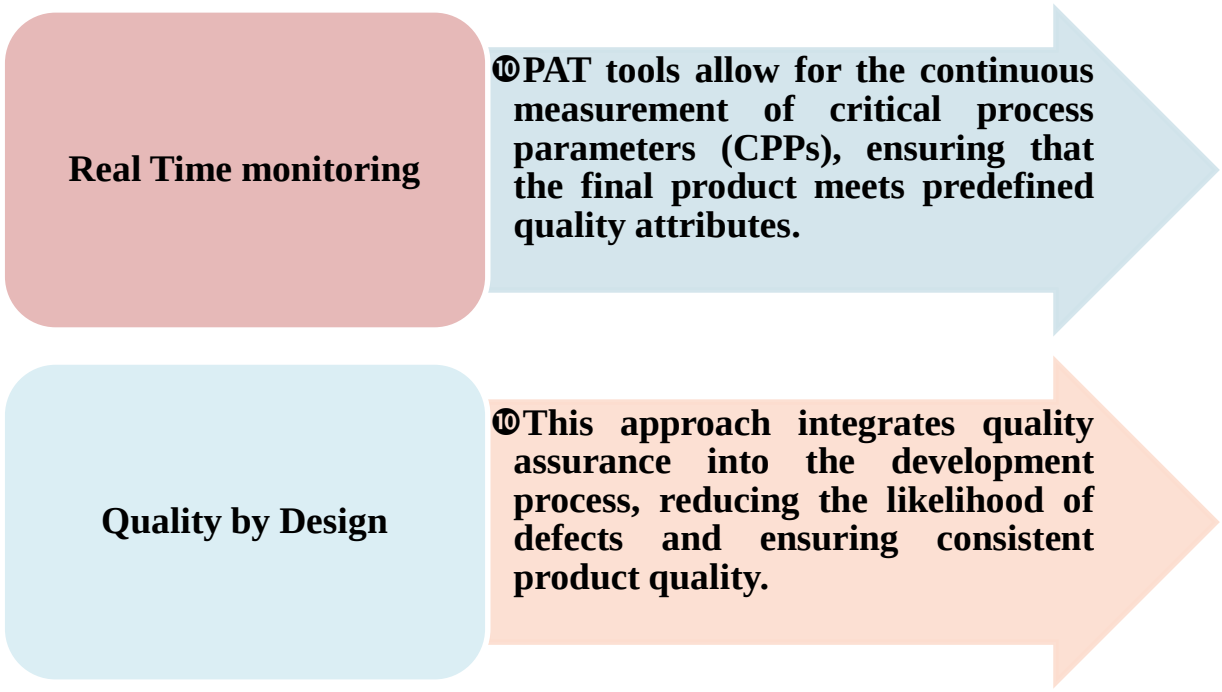


Figure 5. Enhances the quality and efficiency of pharmaceutical manufacturing

D. Data Analytics

Pharmaceutical companies leverage data analytics to inform various aspects of drug development in figure 6:

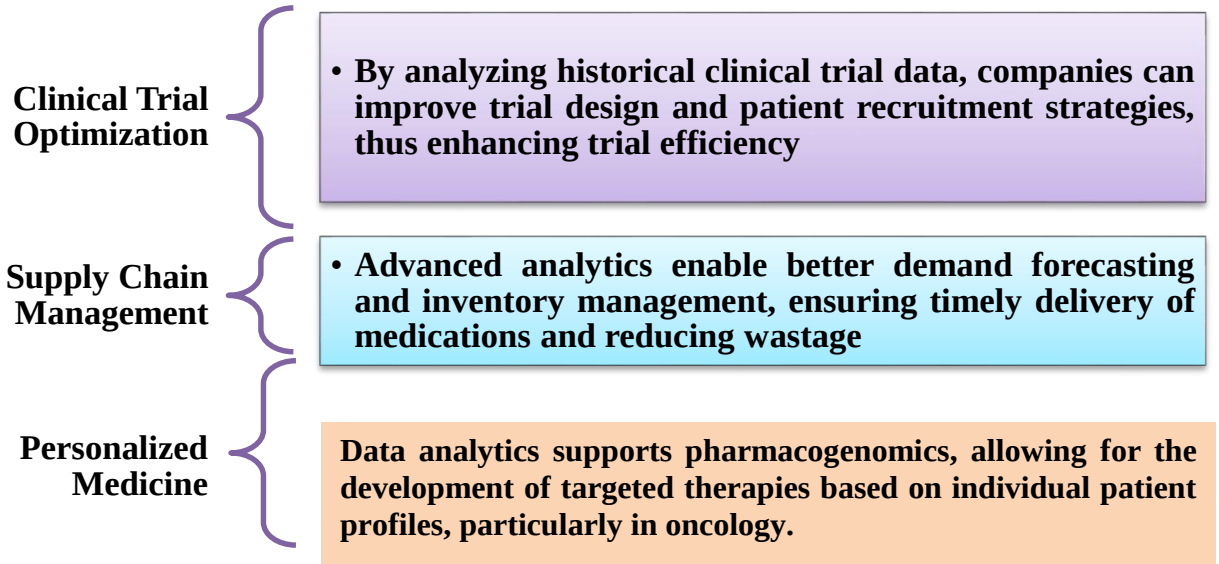


Figure 6. Leverage data analytics to inform various aspects for drug development

E. Quality Control and Compliance

Ensuring compliance with stringent regulatory standards is paramount in drug development. Analytical tools help in figure 7:

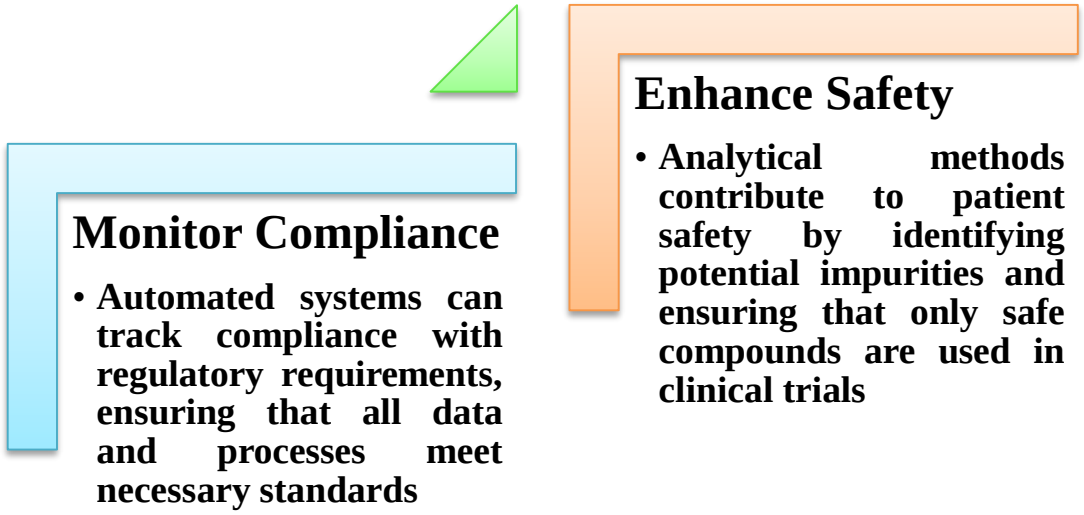


Figure 7. Stringent regulatory standards are paramount in drug development

Formulation Development

Importance of Analytical Method Validation in Formulation Development

- **Ensuring Drug Quality:** The initial goal of any development program of pharmaceutical industries is to produce high-quality outcomes. Analytical method validation helps in understanding the composition of chemical compounds, which is crucial for the development of new drugs [28-29]. This process allows for the identification of critical attributes that affect the drug's efficacy and safety.
- **Regulatory Compliance:** Regulatory authorities, such as the FDA and EMA, require that analytical methods be validated before they can be used in clinical trials or marketed. A poorly documented chemistry, manufacturing, and controls (CMC) section can hinder the approval process for clinical trials[39-41]. Thus, having validated analytical methods simplifies regulatory compliance and provides clear information about the drug's quality.
- **Patient Safety:** Patient safety is paramount in drug development. Analytical methods ensure that only safe compounds are used in clinical trials, which is essential for protecting human subjects during early-phase studies[42-44]. The validation of these

methods helps guarantee that the drugs administered are of the highest quality and efficacy.

The validation procedure for analytical methods typically involves several key steps in figure 8:

Steps in Analytical Method Validation

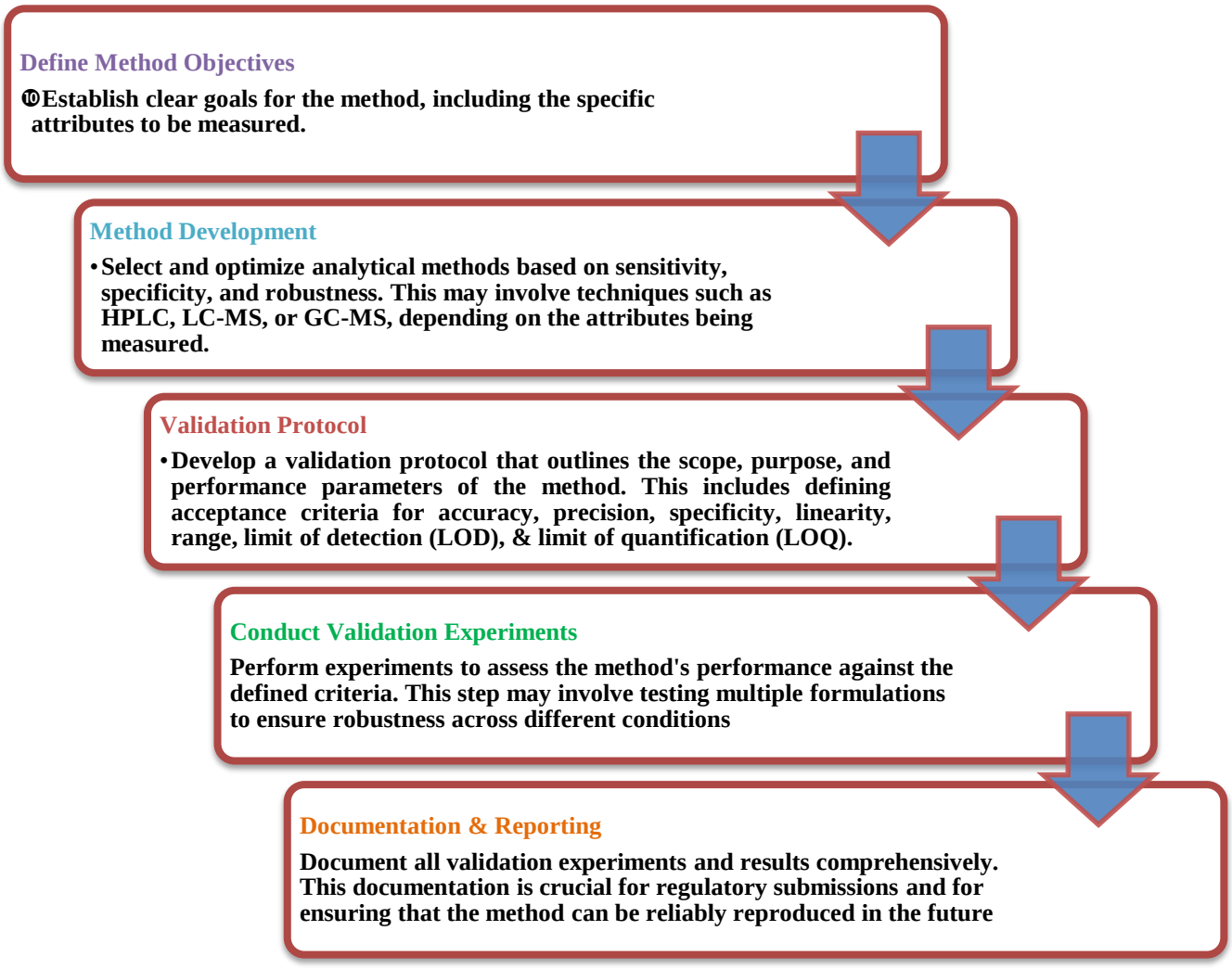


Figure 8. Validation procedure for analytical methods

CHALLENGES AND FUTURE PERSPECTIVES

A. Challenges

Complexity of Drug Formulations:

The intricate nature of pharmaceutical formulations, which often include multiple active ingredients and excipients, complicates the analytical method development process. This complexity can lead to issues with specificity and sensitivity, making it difficult to accurately quantify the active pharmaceutical ingredients (APIs) like CFP [30-32].

Regulatory Compliance:

Adhering to stringent regulatory requirements set by organizations such as

the FDA and ICH is a vital guidelines. The advancing of nature of these regulations necessitates continuous updates to analytical methods to ensure compliance, which can be resource-intensive.

Method Transfer and Validation:

The transfer of methods from research and development (R&D) to quality control (QC) labs can introduce variability. Ensuring that analytical methods maintain their performance across different settings is crucial but often problematic [33]. This requires thorough validation processes that can be time-consuming and costly.

Technological Limitations:

While advancements in analytical instrumentation (e.g., UHPLC, MS) have improved the capabilities of analytical methods, there are still limitations regarding the sensitivity and specificity of these techniques when applied to complex biological matrice [34]. This can hinder the detection of low-level impurities or degradation products in formulations.

Sample Preparation Challenges:

The need for efficient sample preparation techniques that minimize matrix effects while maximizing recovery of the analytes is paramount. Inadequate sample preparation can lead to inaccurate results, necessitating further method optimization [35-37].

B. Future Perspectives

Integration of Advanced Technologies:

Future developments in analytical methods may increasingly rely on the integration of futuristic technologies such as AI and ML. These technologies can optimize method development processes, enhance data analysis, and improve the predictability of method performance [37-40].

Focus on Robustness and Flexibility:

There is a growing emphasis on developing robust analytical methods that can withstand variations in sample composition and analytical conditions. This includes adopting systematic approaches to evaluate method robustness, such as design of experiments (DoE) methodologies, which can provide insights into how method parameters affect performance [41-44].

Regulatory Evolution:

As regulatory frameworks evolve, there will be a need for continuous education and adaptation of analytical methods to meet new guidelines. This includes a focus on the validation of methods for biopharmaceuticals, which may require different considerations compared to traditional small-molecule drugs [45-49].

Collaboration across Disciplines:

Enhanced collaboration between analytical chemists, formulation scientists, and regulatory affairs professionals will be essential. This interdisciplinary approach

can facilitate the development of more effective and compliant analytical methods that are aligned with the overall drug development strategy [50-54].

Sustainability Considerations:

The future of analytical method development will likely include a focus on sustainability, with an emphasis on reducing waste and energy consumption in analytical processes. This aligns with broader industry trends toward environmentally responsible practices in pharmaceutical development [55-56].

CONCLUSION

In conclusion, VGB is a valuable therapeutic option for managing postprandial hyperglycemia in patients with type 2 diabetes mellitus. The unique mechanism of inhibiting α-glucosidase enzymes in the small intestine helps to control glucose absorption, thus preventing sharp rises in blood sugar after meals. While it is effective in improving glycemic control, particularly when used in combination with other antidiabetic agents, it is important to monitor for gastrointestinal side effects that may limit its use in some patients. VGB role in diabetes management remains significant, especially for patients with difficulty controlling postprandial glucose levels, and ongoing research into its long-term benefits and optimal use will further solidify its place in modern diabetes care.

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Conflict of Interest: None

Aberrations

VGB: Voglibose

VZV: varicella-zoster virus

HSV: herpes simplex virus

LC/MS: liquid chromatographic techniques coupled with mass spectrometry

AMDV: Analytical method development and validation

LOD: Limit of Detection

LOQ: Limit of Quantification

ML: Machine Learning

AI: Artificial Intelligence

CMC: chemistry, manufacturing, and controls

APIs: active pharmaceutical ingredients

R&D: research and development

QC: quality control

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