SPOTLIGHT feature

Refractometry & Polarimetry

Polarimeters - A known standard for precision in pharmaceutical quality control

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This article highlights the continuing importance of polarimetric analysis, with an emphasis on its critical role in the pharmaceutical industry. It explores the principles of optical activity, application areas, benefits of polarimetric measurement, and functionalities for error prevention. It also examines methods to achieve data integrity and compliance in a highly regulated environment. An example using amino acids demonstrates its practical applications and possible future use in the analysis of amino acids on the way to final products.

Polarimetry is a long-established analytical technique, with its origins dating back to exploration of optical activity in the 19th century. Over time, it has become an indispensable device for quality control across various industries. Polarimeters, the instruments central to polarimetric analysis, provide rapid and precise measurements, making them essential for quality assurance, especially in pharmaceutical applications.

The pharmaceutical industry prescribes polarimetry for analysing active pharmaceutical ingredients (APIs), as prescribed in international pharmacopoeias like USP 781 and EUP Annex 2.2.7. These standards ensure that optical rotation measurements contribute to verifying API purity, concentration, and stereochemical properties.

Principles of optical rotation: Understanding the basics

Why is optical rotation important in pharmaceuticals?

Pharmaceuticals that are optically active have a molecule that is their mirror image. This molecule can have different pharmacological effects, toxicity, or have no effect at all. The optically active pharmaceutical and its mirror image are referred to as enantiomers. They might possess identical physical properties – however their physiological properties might differ dramatically. Enzymes have an active center which can prefer one substrate's enantiomer over the other, as the induced fit of different enantiomers of the same substrate differs.

Enantiomer-specific effects necessitate rigorous quality control to ensure the desired therapeutic outcome. Polarimetry enables precise enantiomeric analysis, making it critical for:

- **New substance development:** determining stereochemical properties crucial for biological activity
- **Quality control:** verifying API compliance with purity standards
- **Purity determination:** detecting minor impurities that could affect drug efficacy and safety

Modern polarimeters, such as Anton Paar's MCP series, are designed to meet international pharmacopoeia standards and ensure compliance with FDA 21 CFR Part 11 and GMP Volume 4 Annex 11.

High reliability with minimal effort and cost

Anton Paar's MCP polarimeters deliver reliable, non-destructive measurements with minimal maintenance. Unlike high-performance liquid chromatography (HPLC), which requires regular upkeep, MCP polarimeters feature robust construction and advanced optics that ensure consistent performance.

Their user-friendly interfaces and automated features allow for seamless integration into laboratory workflows, reducing operator error and operational costs.

Advancing polarimeter technology: Measure, comply, perform

Meeting the demands of regulated industries

Working in highly regulated industries comes with certain expectations. Passing audits is a must.

Even small issues require time-intensive follow-up. Big ones are business-critical. Either way, that's extra stress and costs.

Measure with the high-performing, automated MCP polarimeter series from Anton Paar. It eliminates errors before they can even occur, bringing you maximum efficiency and reduced costs.

Accuracy up to <±0.0020° OR. Zero errors. Full compliance. Results in seconds.

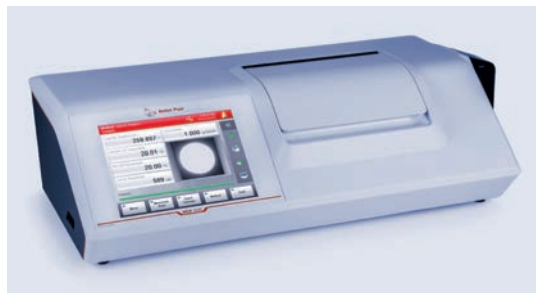
Comply by complementing the capabilities of MCP polarimeters with the available high-performance data handling tools. The sophisticated software solutions provide a centralised platform for data collection, storage, and analysis, empowering pharmaceutical companies to manage vast amounts of data with ease and efficiency. No matter if the instrument is operated standalone, or remote-controlled with the Anton Paar desktop software or in combination with the central data hub AP Connect, more than just compliance with regulatory requirements such as 21 CFR Part 11 and GMP Volume 4 Annex 11 can be taken as granted.

Perform by having perfect results in seconds for the highest efficiency in your lab

Guided workflows keep training efforts low and optimise operation

The Toolmaster™ function recognises measuring cells and automatically transfers data to the instrument, which eliminates human error.

(Semi-)automated workflows for system suitability tests (SST) and calibration improve analysis efficiency.



Ensuring compliance and audit readiness

Qualification and validation

Compliance in regulated industries is often seen as a major burden since it's considered time-consuming, and requires effort and a good understanding of key concepts. These days, manufacturers of laboratory instruments not only aim to provide excellent measuring technology, tools, services, and documentation, but also – and this is becoming more and more crucial – instrument software features that support you in your daily laboratory operations and, at the same time, help you fulfil compliance regulations.

Instruments and systems need to operate in a fully qualified environment, with validated processes and instrument-/system-specific qualification packages, as well as qualified installation support. Such packages need to follow guidelines in USP <1058> regarding analytical instrument system qualification.

This initial activity and possible requalification and compliant maintenance over the complete instrument lifecycle guarantee audit readiness, documented step by- step with the system qualification status available at a glance.

The comprehensive and audit-proven qualification documents from Anton Paar streamline the qualification process, reducing the workload for in-house personnel by up to 70%.

This simplifies the qualification process and helps you attain and retain system productivity more quickly.

Enjoy the complete package of professional instrument and system qualification to integrate the instrument quickly into your workflow and guidelines.

- FDA 4Q model: covering design, installation, and operational and performance qualifications
- Risk assessment: addressing potential compliance issues
- 21 CFR Part 11 compliance: ensuring software and systems meet stringent regulatory standards
- Traceability and reporting: facilitating audit readiness with traceability matrices and qualification summaries

Training and adoption: Empowering users

Successful adoption of new technology depends heavily on user acceptance and proper training.

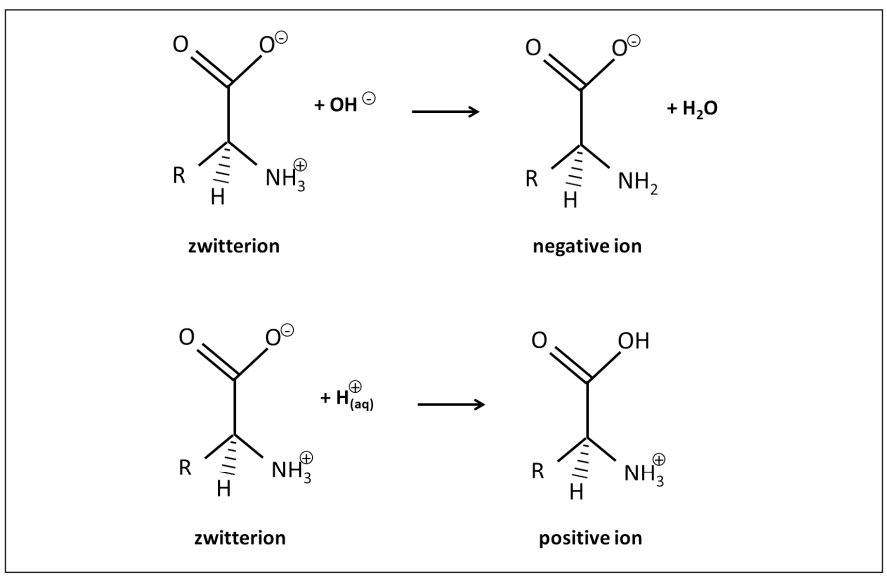
Training programs: Polarimeters are easy to operate and almost self-explaining. However, comprehensive training for laboratory personnel on using polarimeters ensures accurate and reliable measurements.

Ease of adoption: Due to its straightforward operation, polarimetry can be quickly learned and integrated into daily laboratory routines, minimising disruption.

- Embedded and desktop software allows flexible configuration to seamlessly adapt to existing SOPs.

Application: polarimetric analysis of amino acids

Amino acids as optically active zwitterions



More than 50 years ago, amino acids were found to be an important component in metabolism. That's why they play a major role in the pharmaceutical and food industry. Amino acids, as optically active compounds, are frequently analysed using polarimetry to determine their purity and concentration. For example, L-glutamine, a key amino acid used in pharmaceutical formulations and nutritional supplements, exhibits specific optical rotation values under defined conditions.

In recent times, the biopharmaceutical industry has been growing strongly, and amino acids are a key ingredient, e.g., for recombinant proteins.

Amino acids are a group of organic compounds, classified into essential and non-essential (Table 1). Essential amino acids cannot be synthesised within the human body; they have to be taken from outside sources in animal or plant food forms.

Table 1: Overview of amino acids.

Essential AA Obtained from Nutrition	Non-essential AA Synthezised by the Body	Conditionally Essential AA	Precursors of Conditionally Essential AA
Leucine	Alanine	Arginine	Glutamine / glutamate / aspartate
Isoleucine	Asparagine	Cysteine	Methionine / serine
Histidin	Aspartic Acid	Glutamine	Glutamic acid / ammonia
Lysine	Glutamic Acid	Glycine	Serine / choline
Methionine	Serine	Proline	Glutamate
Phenylalanine		Tyrosine	Phenylalanine
Threonine			
Tryptophan			
Valine			

Practical considerations

Each amino acid comprises two different forms called the L- and D-form. The L-form of amino acids is usually the biologically reactive form.

Being a zwitterion, a molecule with an equal number of positively and negatively charged functional groups, the overall charge of an amino acid strongly depends on the pH value. These characteristics affect the molecule's geometrical structure and therefore also the optical rotation of the light

The specific rotation $[a]_D^{20}$ is a measure of the optical rotation (α) at a defined concentration (c) of 1 g / 100 mL, a path length (l) of 1 dm, a wavelength of 589 nm (sodium D line), and a temperature of 20 °C:

As a result, international pharmacopoeias require the measurement of amino acids in defined acidic or basic solutions, to assure the generation of comparable results; see an example in *Figure 1*.

SPECIFIC TESTS

→ **Optical Rotation,** *Specific Rotation* (781S)
Sample solution: 80 mg/mL in 6 N hydrochloric acid
Acceptance criteria: +24.0° to +26.0°, at 20°

Figure 1: Determination of the specific rotation of L-aspartic acid according to the US Pharmacopeia.

Use of amino acids in biopharmaceuticals

Biopharmaceuticals, often referred to as biologics, represent a revolutionary class of medicines that rely on biological systems to produce therapeutic or diagnostic substances. These protein- or nucleic acid-based pharmaceuticals are at the forefront of modern medicine, addressing complex diseases with unmatched precision.

What Are Biopharmaceuticals?

Biopharmaceuticals are pharmaceutical substances derived from living organisms. Unlike conventional drugs that are chemically synthesised, biopharmaceuticals are produced using genetically modified cells such as bacteria, yeast, animal or human cells, or even plants. These cells are engineered to produce therapeutic compounds encoded by inserted genetic material.

One of the most significant advancements in this field is recombinant protein expression. This technique involves the insertion of human DNA into a host organism, enabling it to produce peptides or proteins identical to their human counterparts. For example, the production of insulin – a peptide hormone crucial for regulating blood sugar – has been revolutionised by this method.

The importance of amino acids in biopharmaceuticals

Amino acids are the fundamental building blocks of proteins, and their role in biopharmaceuticals is indispensable. Every biopharmaceutical protein is composed of a specific sequence of amino acids, which determines its structure and function. The precision with which these amino acids are assembled is critical for the therapeutic efficacy and safety of the final product.

Key aspects of amino acids in biopharmaceuticals include:

1. **Protein structure and stability:** The sequence and arrangement of amino acids determine the three-dimensional structure of the protein. This structure is essential for the protein's biological activity and stability under physiological conditions.
2. **Post-translational modifications:** Amino acids can undergo modifications such as glycosylation and phosphorylation, enhancing protein function and therapeutic potential.
3. **Cell culture media:** Amino acids are essential nutrients in the media used to grow genetically modified cells. They support cell growth, protein synthesis, and overall productivity of the biopharmaceutical manufacturing process.

Benefits of biopharmaceuticals

Biopharmaceuticals offer numerous advantages over traditional small-molecule drugs, making them a game-changer in healthcare.

1. **Structural similarity to human compounds:** Biopharmaceuticals closely mimic natural human proteins, reducing the likelihood of adverse reactions. This structural compatibility allows them to cure diseases rather than merely manage symptoms. For instance, monoclonal antibodies can precisely target specific disease markers, providing a level of specificity unattainable with conventional drugs.
2. **Fewer side effects:** Traditional medications often act on multiple systems, leading to a range of side effects. In contrast, biopharmaceuticals are highly specific, interacting only with their intended targets.
3. **Sustainability:** Unlike chemical synthesis processes that generate significant environmental waste, biopharmaceuticals are produced in living systems. The use of genetically modified organisms eliminates the need for environmentally harmful synthesis steps, offering a sustainable alternative for drug production.

Case Study: Insulin Production

Diabetes mellitus, a chronic condition characterised by high blood sugar levels, exemplifies the transformative potential of biopharmaceuticals. With this disease, insufficient insulin activity leads to metabolic imbalances.

Insulin, a peptide hormone produced by the beta cells of the pancreas, regulates carbohydrate, fat, and protein metabolism. Before the advent of recombinant DNA technology, insulin was extracted from animal pancreases, a process fraught with challenges such as limited supply and immunogenic responses.

Today, recombinant insulin is produced by introducing the human insulin gene into bacteria or yeast. These microorganisms efficiently synthesise insulin, which is then purified and formulated for therapeutic use. This approach ensures a consistent supply of high-quality insulin, significantly improving the lives of millions of diabetes patients worldwide.

Future perspectives

As the field of biopharmaceuticals continues to evolve, amino acids will remain central to innovations in drug design and manufacturing. Advances in protein engineering, cell line development, and synthetic biology promise to further enhance the therapeutic potential of biologics. Additionally, the integration of artificial intelligence and machine learning into protein sequence optimisation will likely streamline the development of next-generation biopharmaceuticals.

Conclusion

Polarimetry remains a vital analytical technique for regulated industries, particularly pharmaceuticals. Anton Paar MCP polarimeters combine advanced technology with intelligent data management, ensuring precision, reliability, and compliance. From analysing amino acids to supporting biopharmaceutical production, these instruments exemplify innovation in quality control.

The Anton Paar MCP polarimeters offer tailored solutions for these applications, with compact models like MCP 100/150 for limited lab space and high-end MCP 4100/5100/5500 models for flexible, modular setups.