Determination of Optical Rotation and Specific Rotation

Analyte:	Optically active pharmaceutical substances
Matrices:	Not specified
Apparatus:	MCP 300/500
Customers:	Pharmaceutical industry
Reference Customers:	Bayer AG, Schering AG
Approved by:	International Pharmacopeia
Method No.	n.a.
Scope:	Determination of Optical Rotation and Specific Rotation
Field of Application	Production and Quality Control of optically active substances

Description

Substances which rotate in the plane of linear polarized light are called optically active. In pharmaceutical applications the measurement of optical activity is mainly used for identifying the substance, to determine the purity of the substance or as a general test procedure.

Definitions

Optical Rotation

The optical rotation is the angle by which the plane of linear polarized light is rotated when passing through the sample.

Depending on the direction in which the plane of light is rotated the substances are called dextrorotatory (clockwise) or levorotatory (counterclockwise). The view of the observer is towards the light source.

Dextrorotation is designated (+) and levorotation is designated (-).

In the *International Pharmacopoeia* the optical rotation (α) is expressed in angular degrees. In the SI, the angle of optical rotation is expressed in radians (rad).

The optical rotation is measured on a layer of suitable thickness (optical path length *l*) at the wavelength λ and temperature T specified in the monograph. A typical optical path length is 100 mm, the most common wavelength is 589 nm (Sodium D-Line), while the reference temperature is usually between 20-25 °C.

Some substances have large temperature coefficients and with them special care should be taken to adjust the temperature indicated.

According to the following formula, optical rotation depends on:

$$\alpha = [\alpha]_T^{\lambda} \frac{c \cdot l}{100}$$

c = Concentration [g/100 cm^3]

$$[\alpha]_T^{\lambda} = Specific\ Rotation \left[\frac{^{\circ}}{dm \cdot g \cdot cm^{-3}} \right]$$

l = Optical path length (Sample cell length [dm])

T = Temperature

λ = Wavelength

Specific Rotation

The specific rotation of a substance is defined as the observed angle of optical rotation α when linear-polarized light is passed through a sample cell of 1 decimeter (=100 mm) optical path length at a sample concentration of 1 gram per 1 deciliter (=100 mL).

Specific rotation of a pure material is a physical property of that material at a given wavelength and temperature and can be looked up in literature.

From above, the following calculation applies:

$$[\alpha]_T^{\lambda} = \alpha \frac{100}{c \cdot l}$$

c = Concentration [g/100 cm3]

$$[\alpha]_T^{\lambda} = Specific\ Rotation \left[\frac{^{\circ}}{dm \cdot g \cdot cm^{-3}} \right]$$

l = Optical path length (Sample cell length [dm])

T = Temperature

λ = Wavelength

In the *International Pharmacopoeia* the specific rotation is expressed as $[\alpha]^{\lambda}_{T}$ where T is the temperature and *λ* the wavelength. For solid substances the solvent, if different from water, and the concentration are further described.

Apparatus

Optical rotation is measured with a polarimeter. The zero point of the polarimeter is determined with the tube empty. The tube is closed for measuring liquid substances and filled with the specified solvent for solutions of solid substances.

The required accuracy of the polarimeter is +/-0.05° optical rotation, which is sufficient for some pharmacopeial purposes. In other cases an accuracy of at least +/-0.01° optical rotation is required.

The required accuracy for photoelectric polarimeters must be at least 0.01° optical rotation.

Measurement of optical rotation

The accuracy and precision of optical rotation measurements will be increased if the following is considered.

- Optical elements of the instrument must be clean and in exact alignment
- The light source should be well adjusted.
- A filter system allowing sufficient monochromatic light should be installed.
- Observations should be accurate and reproducible to the extent that differences between replicates, or between observed and true values of rotation (the latter value having been established by calibration of the polarimeter scale with suitable standards), shall not exceed one-fourth of the range given in the individual monograph for the rotation of the substance being tested.
- Polarimeter tubes should be filled in such a way that no air bubbles interfere with the beam of light.
- In polarimeter tubes with exchangeable end-plates fitted with gaskets and caps, the latter should be tightened only enough to ensure a leak-proof seal between the end-plate and the body of the tube. Excessive pressure on the end-plate may set up strains that result in interference with the measurement.
- In determining the optical rotation of a substance of low optical rotation, it is desirable to loosen the caps and tighten them again between successive readings in the measurement of both the rotation and the zero point. In this way, differences arising from end-plate strain will generally be revealed and appropriate adjustments to eliminate the cause can be made.
- The requirements for optical rotation and specific rotation apply to the dried, anhydrous, or solvent-free material in all those monographs in which standards for loss on drying, water, or solvent content are given. In calculating the result, the loss on drying, water, or solvent content determined by the method specified in the monograph should be taken into account.

Recommended procedure

If the substance is a solid, weigh a suitable portion and transfer it to a volumetric flask by means of water, or other solvent if specified in the monograph, reserving a portion of the solvent for the blank determination. Add enough solvent to bring the meniscus close to, but still below, the mark, and adjust the temperature of the flask contents by suspending the flask in a constant-temperature bath. Add solvent to the mark, and mix. Transfer the solution to the polarimeter tube, preferably within 30 minutes from the time the substance was dissolved, taking care to standardize the elapsed time in the case of substances known to undergo racemization or mutarotation. During the elapsed time interval, maintain the solution at the required temperature.

If the substance is a liquid, adjust its temperature, if necessary, and transfer it directly to the polarimeter tube.

When a polarimeter is used for visual measurement, make at least 6 readings of the observed rotation at the required temperature. Take half the readings in a clockwise and the other half in a counterclockwise direction. Substitute the reserved solvent for the solution, and make an equal number of readings on it. In the case of liquid substances, carry out blank determinations on the empty, dry tube. The zero correction is the average of the blank readings, and is subtracted from the average observed rotation if the two figures are of the same sign, or added if they are opposite in sign, to give the corrected observed rotation.

When a photoelectric polarimeter is used, a smaller number of readings is required, depending on the type of instrument.