Master 2: Pharmaceutical Chemistry

Module: Drug Analysis and Control

CHAPTER V. PHYSICAL ANALYSIS FOR MEDICINES QUALITY CONTROL

Optical Technique

Course.02 Optical methods for medicines quality control.

Polarimetry and Refractometry

Dr. FIZIR MERIEM

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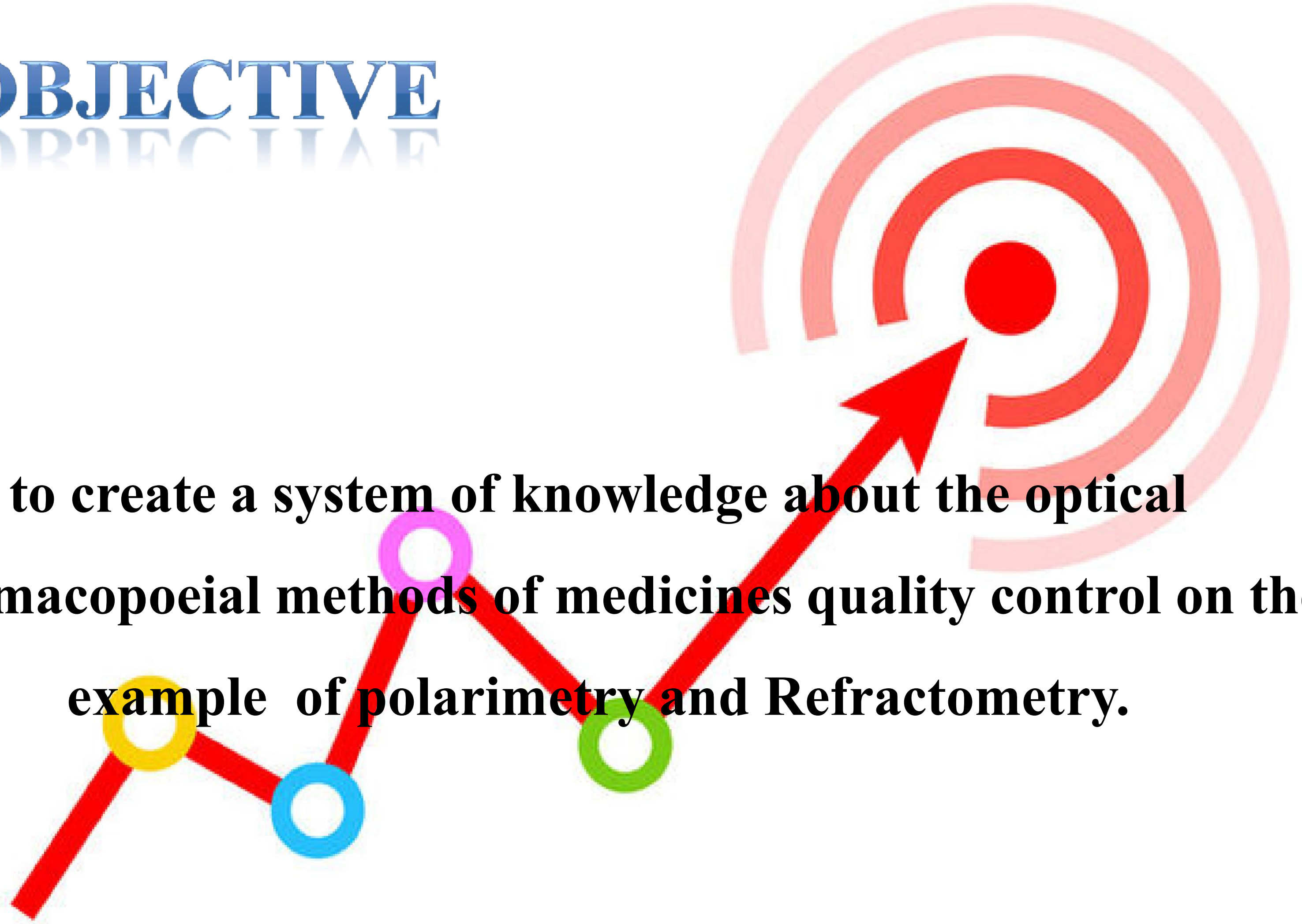
Optical methods for medicines quality control.

OBJECTIVE

to create a system of knowledge about the optical pharmacopoeial methods of medicines quality control on the example of polarimetry and Refractometry.

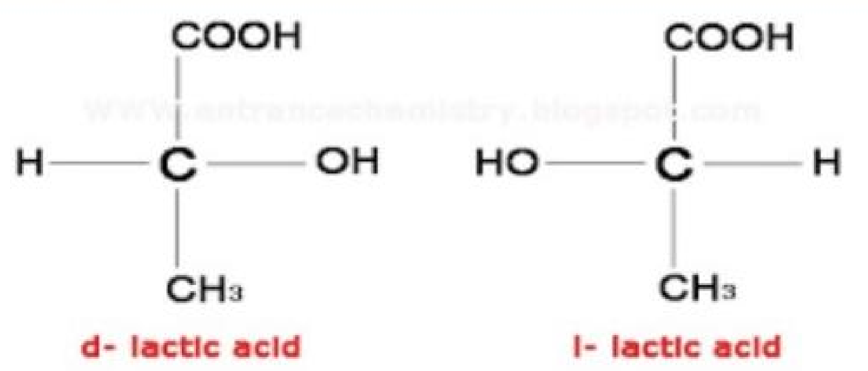


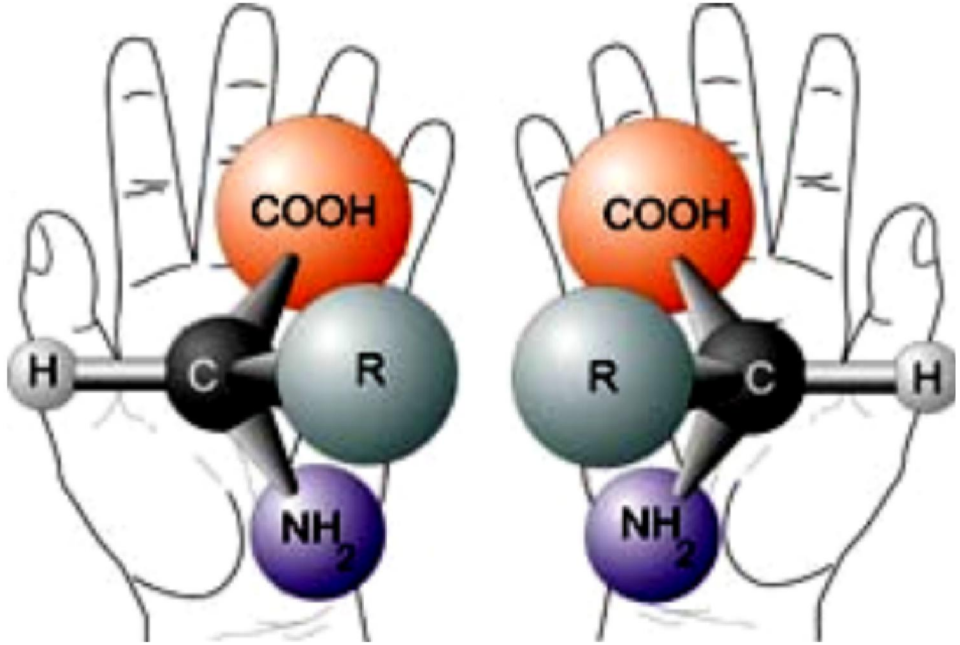
1. Polarimetry

Generality

Polarimetry is a type of qualitative and quantitative technique, used for optically active compounds.

Optical isomers, or enantiomers, have the same sequence of atoms and bonds but are different in their 3D shape. Two enantiomers are non superimposible mirror images of one another (i.e., chiral), with the most common cited example being our hands (Fig.)





Amino acids are the example of chiral molecules

1. Polarimetry

GENERALITY

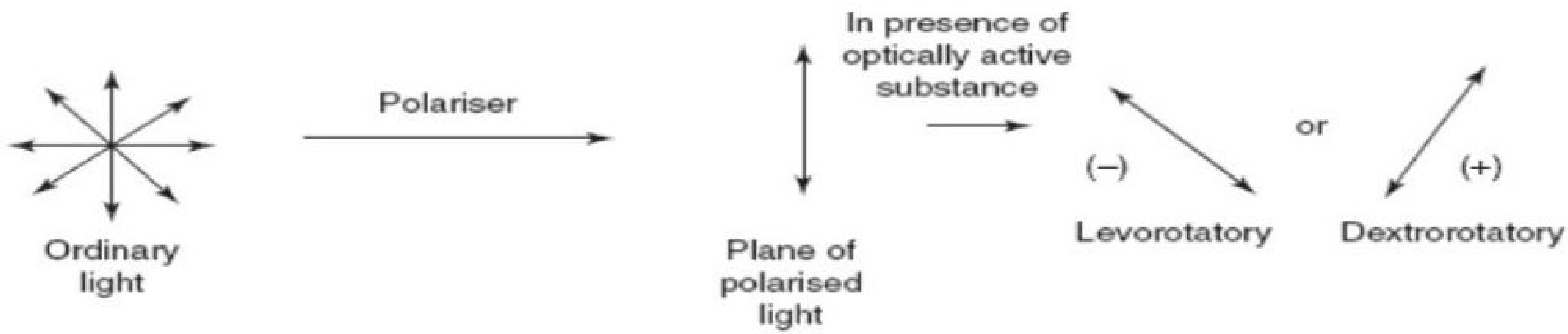
Optical isomers have basically the same properties (melting points, boiling points, etc.) but there are a few exceptions (uses in biological mechanisms and optical activity). There are drugs, called enantiopure drugs, that have different effects based on whether the drug is a racemic mixture or purely one enantiomer. For example, d-ethambutol treats tuberculosis, while l-ethambutol causes blindness.

Optical isomers differ in a property called optical activity, in which a sample rotates the plane of polarization of a polarized light beam passing through.

1. Polarimetry

DEFINITION

Polarimetry is one of the important instrumental methods employed in analysis. This measures the rotation of the polarized light as it passes through an optically active compound. This technique involves the measurement of change in the direction of vibration of polarized light when interact with an optically active compound.



Dextro= right designated by ‘d’, (+), clockwise
Levo= left designated by ‘l’, (-), counterclockwise

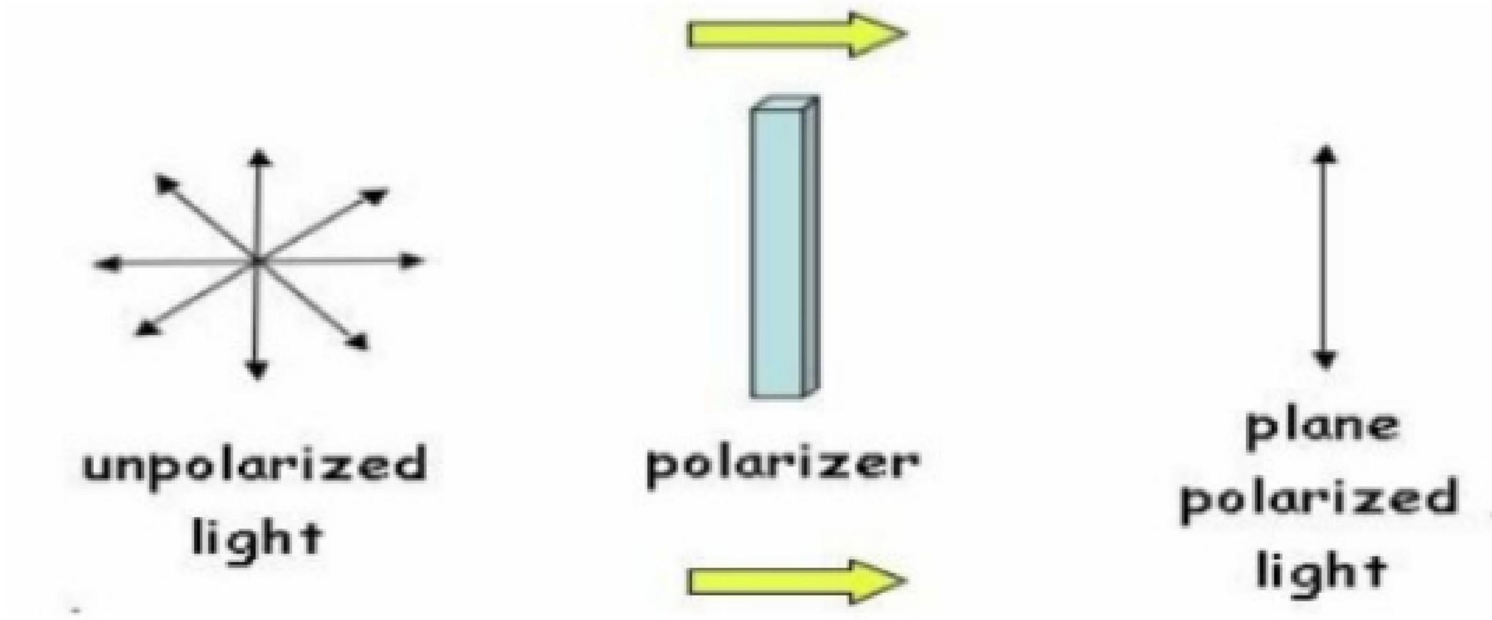
1. Polarimetry

PLANE POLARIZED LIGHT

According to wave theory of light, an ordinary ray light is considered to be vibrating in all planes at right angle to the direction of propagation. If this ordinary ray of light is passed through a Nicol prism, the emergent ray has its vibration only in one plane.

This light having wave motion in only one plane is known as Plane Polarised Light.

- **NICOL Prism –**
- **Iceland Spar**
- **Calcite (CaCO3 form)**
- **(or) Polaroid**


unpolarized
light
polarizer
plane
polarized
light

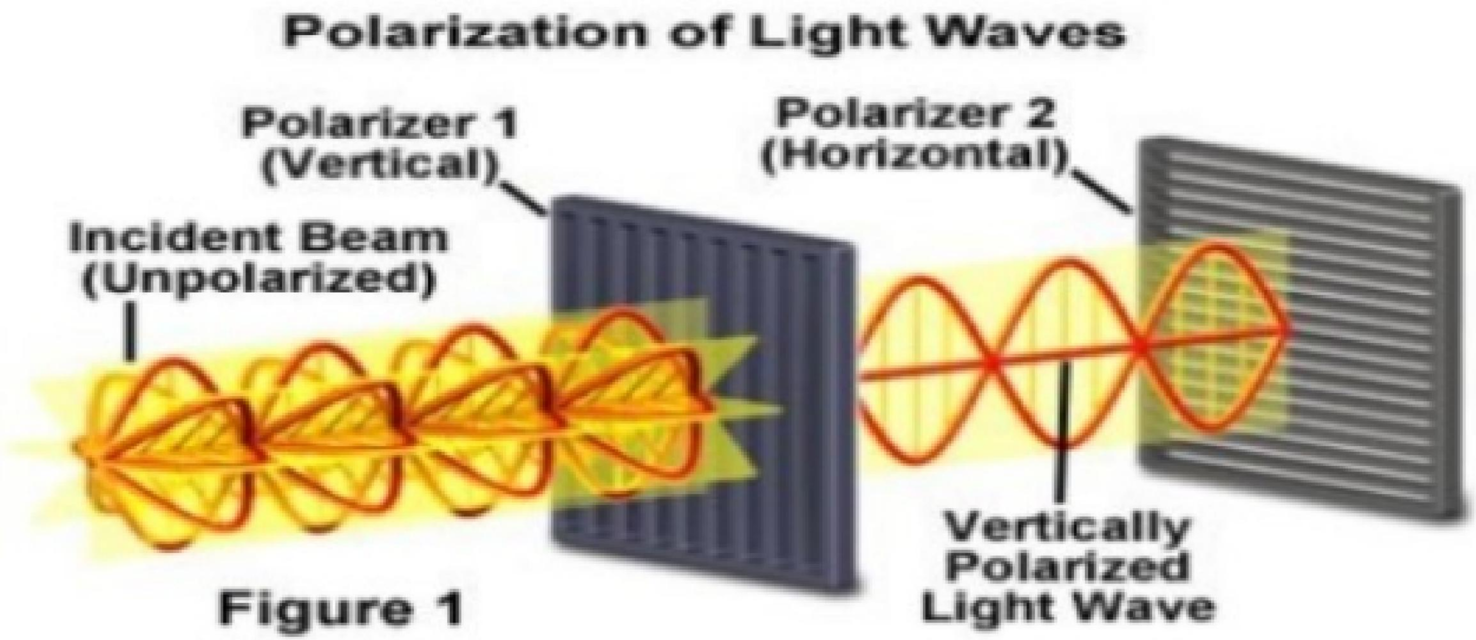

Polarization of Light Waves
Polarizer 1
(Vertical)
Polarizer 2
(Horizontal)
Incident Beam
(Unpolarized)
Vertically
Polarized
Light Wave

Figure 1

1. Polarimetry

OPTICAL ACTIVITY

- Displayed by solutions of some compounds, notably many sugars.
- The magnitude of rotation depend upon the following factors:

1. Nature of Substance
2. Length of liquid column (l) through which light passes.
3. Concentration of the solution.
4. Nature of the solvent.
5. Temperature of the solution (t)
6. Wavelength of the light used

1. Polarimetry

SPECIFIC ROTATION

•The Rotatory Power of a given solution is generally expressed as specific rotation.

 It is the number of degrees of rotation of plane polarized light produced by one gram of the substance per ml. The measurements is carried out at temp (T) using sodium light (D line). The Specific rotation can be Calculated by the following relation:

[α] = specific rotation, T = temperature, λ = wavelength, θ= optical rotation, c = concentration in g/100ml, l = optical path length in dm

$$[\alpha]_D^t = \frac{100 \times \text{observed angle of rotation}}{\text{length in decimeters} \times \text{Grams of substance in 100 ml of solution}}$$

$$[\alpha]_D^t = \frac{100 \times \theta}{l \times c}$$

1. Polarimetry

INSTRUMENTATION:POLARIMETER

•The Polarimeter is a device used to measure the effect of plane-polarized light on optically active compounds.

•The components of polarimeter are:

• A light source : usually a sodium lamp

• A polarizer: Nicol Prism

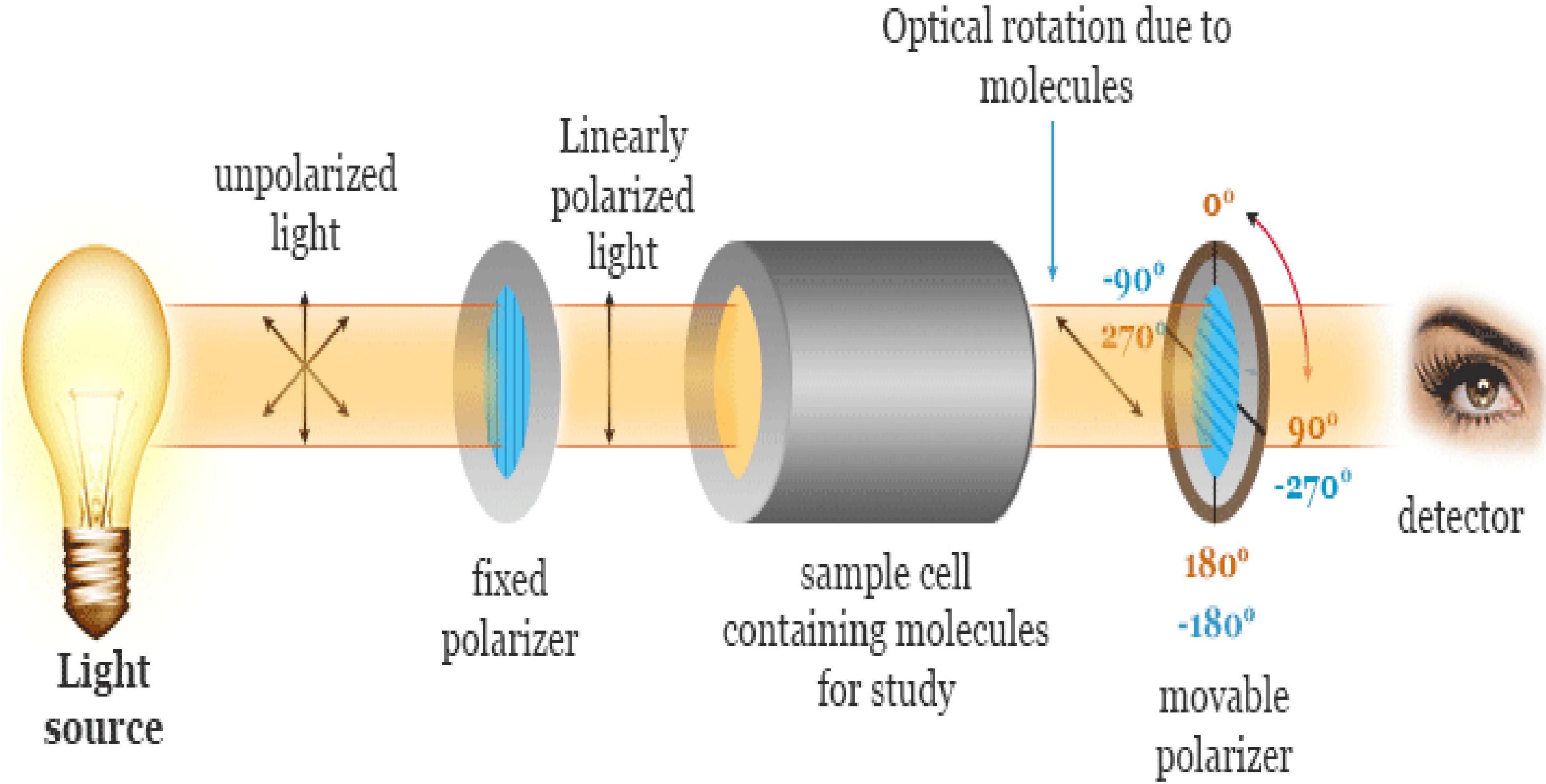
• A tube for holding sample in the light beam: sample cell

• An analyzer: Nicol prism aligned to intercept the linearly

•polarized ray as it emerges from the sample solution , and

• A scale: to measure the rotation of plane polarized light

INSTRUMENTATION:POLARIMETER



An automatic digital polarimeter

1. Polarimetry

POLARIMETER: Working

•if no or optically inactive sample is present in the tube and the instrument is reading zero (0o), the axes of plane polarized light and the analyzer is exactly parallel the observer will detect maximum amount (100 % transmittance) of light passing through.

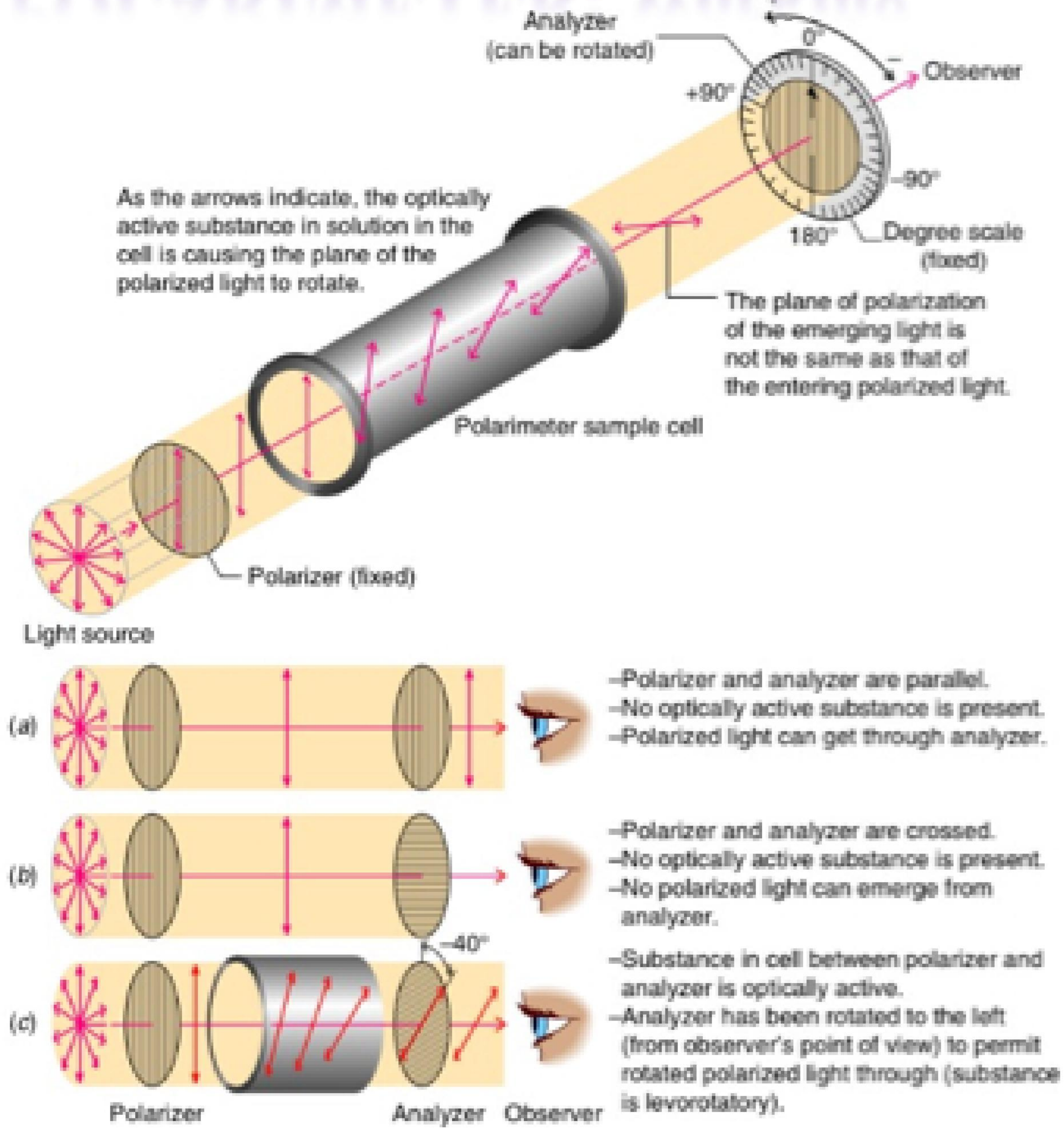
• if the sample is optically active the plane of PPL will be rotated as it pass through the tube

•in order to detect the maximum brightness of the light (ie. 100% transmittance) observer will have to rotate the axis of the analyzer in either clockwise or counterclockwise direction

• if the analyzer is rotated in a clockwise direction, the rotation (αin degree) is said to be positive (+), and such substance are dextrorotatory

• if the rotation is counterclockwise, the α is –ve, and such substances are c/a levorotatory

POLARIMETER: Working



Circuit to explain the rotation
of polarized light plane
as it passes through the optically
active sample

POLARIMETER: Calibration

Polarimeters can be calibrated – or at least verified – by measuring a quartz plate, which is constructed to always read at a certain angle of rotation (usually +34°, but +17° and +8,5° are also popular depending on the sample).

Quartz plates are preferred by many users because solid samples are much less affected by variations in temperature, and do not need to be mixed on-demand like sucrose solutions

1. Polarimetry

APPLICATIONS

•polarimeter can also be usedto measure the ratio of enantiomers in solutions.

•Polarimeters can identify unknown samples based on this if other variables such as concentration and length of sample cell length are controlled or at least known.

•measure blood sugar concentration in diabetic people.

•polarimetric method is a simple and accurate means for determination of structure in micro analysis of expensive and non-duplicable samples.

•it is employed in quality control, process control and research in the pharmaceutical, chemical, essential oil, flavor and food industries.

• it is so well established that the United States Pharmacopoeia and the Food & Drug Administration include polarimetric specifications for numerous substances.

1. Polarimetry

RESEARCH APPLICATIONS

•Research applications for polarimetry are found in industry, research institutes and universities as a means of:

❖isolating and identifying unknowns, crystallized from various solvents or separated by HPLC.

❖evaluating and characterizing optically active compounds by measuring their specific rotation and comparing this value with the theoretical values found in literature.

❖investigating kinetic reactions by measuring optical rotation as a function of time.

❖monitoring changes in concentration of an optically active component in a reaction mixture, as in enzymatic cleavage.

❖distinguishing between optical isomers.

1. Polarimetry

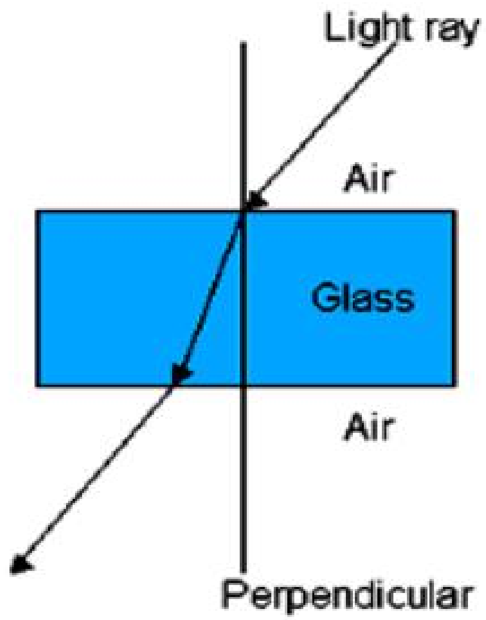
PHARMACEUTICAL APPLICATIONS

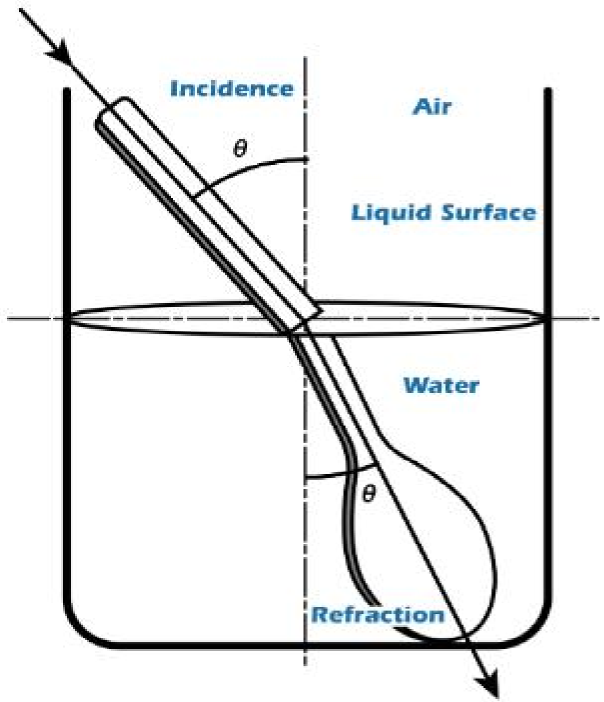
- **To determine product purity by measuring specific rotation and optical rotation of: Amino acids, Amino sugars, Analgesics, Antibiotics Cocaine, Dextrose, Diuretics, Serums, Steroids, Tranquilizers, Vitamins etc.**
- **For raw materials inspection of: Camphors, Citric acid, Glyceric acid Gums Lavender oil, Lemon oil Orange oil Spearmint oil.**

2. Refractometry

GENERALITY

Refraction of light is the bending of light rays at the interface of dissimilar substances. When light is passing from a lower refractive substance into a higher refractive substance the light rays bend toward the perpendicular to the surface. Refraction can be easily demonstrated by placing a spoon in a glass of water (Fig). As the light passes from the air into the water it is bent and the utensil appears bent.





2. Refractometry

Refractive index

In optics the refractive index or index of refraction n of a substance (optical medium) is a dimensionless number that describes how light, or any other radiation, propagates through that medium. It is defined as

$n = c/\upsilon$

where c is the speed of light in vacuum and υ is the phase velocity in the substance. For example, the refractive index of water is 1,33, meaning that light travels 1,33 times as fast in vacuum as it does in water (Table).

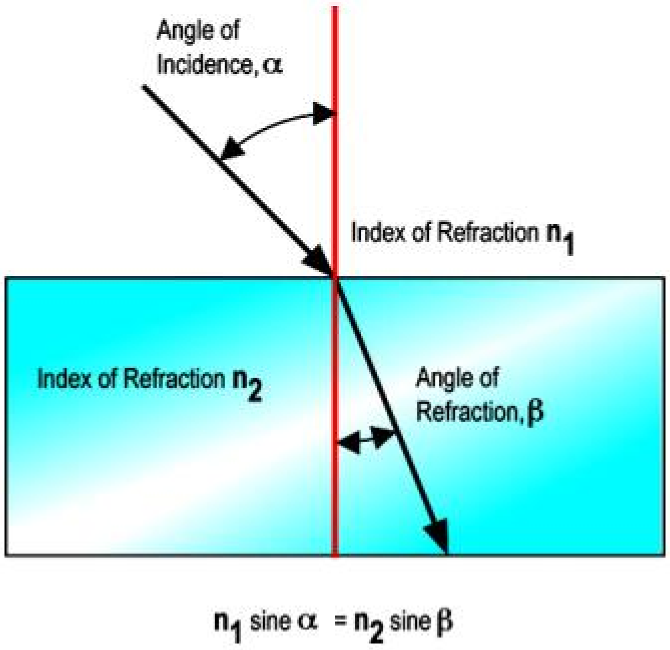
2. Refractometry

Refractive index

The historically first occurrence of the refractive index was in Snell's law of refraction:

$$n1 \cdot \sin\theta 1 = n2 \cdot \sin\theta 2,$$

where θ1 and θ2 are the angles of incidence of a ray crossing the interface between two media with refractive indices n1and n2



Graphical representation of the refractive index

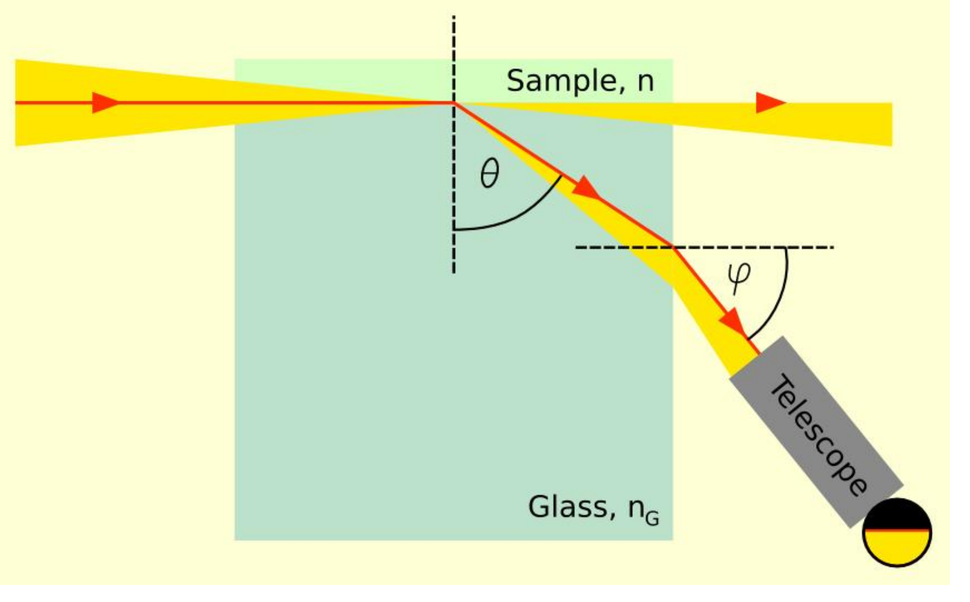
Selected refractive indices at λ = 589 nm

Material	*N*
Gases at 0 °C and 1 atm	
Air	1,000293
Helium	1,000036
Hydrogen	1,000132
Carbondioxide	1,00045
Liquids at 20 °C	
Water	1,333
Ethanol	1,36
Benzene	1,501
Solids	
Ice	1,309
Fusedsilica	1,46
PMMA (Plexiglas)	1,49
Crownglass (typical)	1,52
Flintglass (typical)	1,62
Diamond	2,42

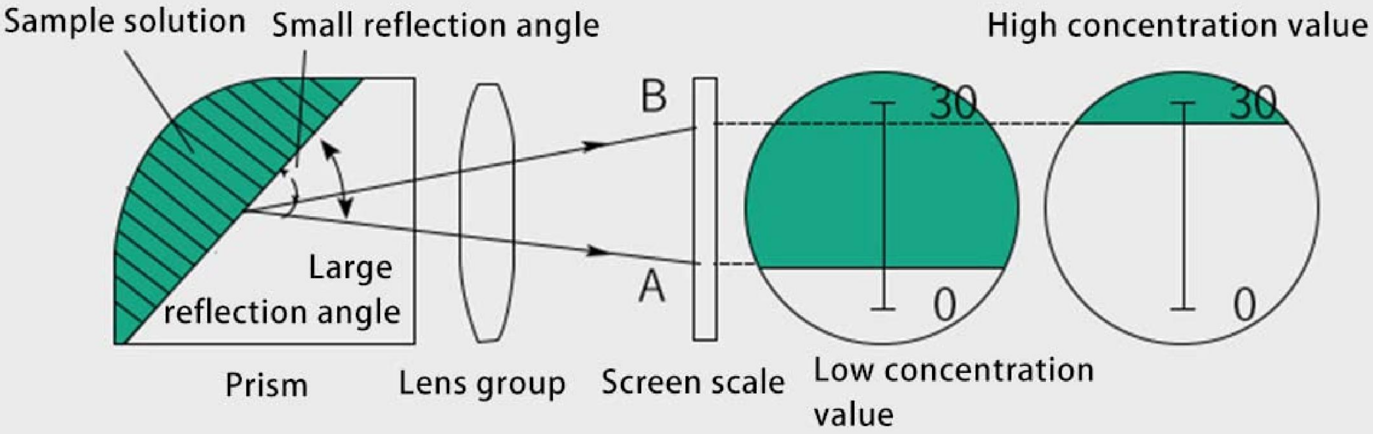
2. Refractometry

Refractometer

Refractometers are instruments that measure the bending of light as it crosses an interface between dissimilar substances and converts the bending light rays into a useful scale. A refractometer is a laboratory or field device for the measurement of an index of refraction.



Measurement Principle



2. Refractometry

Application

Finding Refractive Indices

One of the most common uses of the refractive index is to compare the value you obtain with values listed in the literature. This comparison is used to help confirm the identity of the compound and/or assess its purity.

There are also many computer-based chemical databases that contain refractive indexes.

These can be particularly useful if your sample is an unknown and you want to search for compounds with similar indexes of refraction.

2. Refractometry

Application

Comparing Refractive Indices

Since the refractive index of a substance depends on the wavelength it is important that the refractive index you are comparing to was obtained at the same wavelength as the one you determined. This is usually not an issue since the vast majority of refractive indexes are obtained using the sodium D line at 589.3 nm. Even refractometers that use white light are normally constructed so that the refractive index obtained corresponds to that for light at 589.3 nm.

The refractive index also depends on the temperature. Thus, it is best to obtain the refractive index of your sample at the same temperature as the value you plan to compare with; in most cases this will be 20 °C.

A typical laboratory refractometer can determine the refractive index of a sample to a precision of ± 0.0002. However, small amounts of impurities can cause significant changes in the refractive index of a substance. Thus, unless you have rigorously purified your compound, a good rule of thumb is that anything within ± 0.002 of the literature value is a satisfactory match.

Another possible source of error is miscalibration of the refractometer. This is readily checked by using a sample of known refractive index. Distilled water is a particularly convenient standard since it is nontoxic, readily available in pure form, and its refractive index varies only slightly with temperature. Probably the most common source of error in analog refractometers is misreading of the scale. If the index of refraction you determined seems inconsistent with other data, try repeating the measurement.

2. Refractometry

Application

Determining Concentrations of solutions

Determining the concentration of a solute in a solution is probably the most popular use of refractometry. For example, refractometer-based methods have been developed for determining the percentage of sugar in fruits, juices, and syrups, the percentage of alcohol in beer or wine, the salinity of water, and the concentration of antifreeze in radiator fluid. Many industries use refractometer-based methods in quality control applications.

2. Refractometry

Application

In medicine, a refractometer is used to measure the total plasma protein in a blood sample and urine specific gravity.

In drug diagnostics, a refractometer is used to measure the specific gravity in human urine. Refractometers are often used in pharmaceutical applications for quality control of raw intermediate and final products.

Refractometer users in pharmaceutical research, toxicology testing, compounding, and drug monitoring may require instru-ments with reliable temperature control, compliance tracking, and specific measurement ranges. For example, refractometers can be used for total parenteral nutrition (TPN) control, toxicology testing (Urine SG), pharmacy compounding and drug diversion.