NEPHAR 315

Pharmaceutical Chemistry Lab II

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- *Density*
- *Melting Point*
- *Boiling Point*
- *Refractometry*
- *Polarimetry*

Density

The density, ρ, is elementary physical property of matter.

ρ = m / V (*the ratio of its* mass m to *its* volume V)

It is commonly used as

- a means of categorizing
- identifying different materials.

Density defined in a qualitative manner as the measure of the relative "heaviness" of objects with a constant volume.

For example:

- A rock is obviously denser than a crumpled piece of paper of the same size.
- A styrofoam cup is less dense than a ceramic cup.

Density may also refer to how closely "packed" or "crowded" the material appears to be - again refer to the styrofoam vs. ceramic cup.

- For a homogeneous object density is defined as *the ratio of its* mass m to *its* volume V,

$$\rho = m / V \qquad [1]$$

- Numerically it represents *the mass per unit volume of matter*.
- As it follows from equation [1], the SI unit of density is kg/m^3.
- However, g/cm^3 is another unit *commonly* used in a laboratory.

- The volume of an object increases with *increasing temperature*, because of the matter's volumetric thermal expansion.

  Therefore, according to equation [1], the density of an object depends on its temperature, *with higher temperature resulting in lower density*.

  Exception is water in temperature range 0-4 °C, for which *the density increases with increasing temperature.*

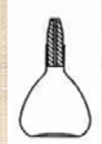
- *Relative density*, or *specific gravity*, is the *ratio* of the *density* (mass of a unit volume) of a substance to the density of a given *reference material*.
- Specific gravity usually means relative density with respect to water.
- The ratio of the density of a substance to the density of water.

  Relative density = ρ_s / ρ_{H2O}

- The term "relative density" is often preferred in modern scientific usage.
- *Specific gravity* is commonly used in industry as a simple means of obtaining information about the concentration of solutions of various materials such as brines, sugar solutions (syrups, juices, honeys etc.) and acids.

- The density of a gas further *depends on the pressure as well*.
- The relative density of gases is often measured with respect to dry air at a temperature of 20 °C and a pressure of 101.325 kPa absolute.
- The density of an gas depends on the pressure , *with higher* pressure *resulting in higher density*.
- Nevertheless, this effect is negligible in a case of liquid and/or solid matter.

- There are several experimental methods used for *density determination of liquids*.

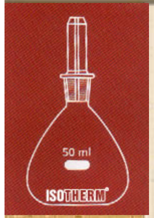


1- *Pycnometer*

-Density determination of liquids by pycnometer

-Density determination of solid matter by pycnometer

2- *Westphal Balance*



- *The pycnometer* is
  - a glass flask with
  - a close-fitting ground glass stopper with
  - a capillary hole through it, so that *air bubbles* may escape from the apparatus.
- This *fine hole* releases a spare liquid after closing a top-filled pycnometer and allows for obtaining a given volume of measured and/or working liquid with *a high accuracy*.

An empty glass pycnometer and stopper

A filled pycnometer

Density determination of liquids by pycnometer

- Density determination by pycnometer is a very *precise method*.
- *A pycnometer* is in principal just a vessel of a particular fixed internal volume V.
- It uses a working liquid with well-known density, such as water.
- The choice of liquid is distilled water for which temperature dependent values of density ρ_{H2O} are shown in Table 1.

Table 1. Temperature dependence of distilled water density ρ_{H2O}

- If you first fill it with a liquid of *unknown density weighs it* and
- *if you do the same with water you can determine the density of the liquid.*

t [°C]	ρ_{H2O} [g/cm^3]
15	0.99996
16	0.99994
17	0.99990
18	0.99985
19	0.99978
20	0.99820
21	0.99799
22	0.99777
23	0.99754
24	0.99730
25	0.99705

If the flask is

- *weighed empty,*
- *full of water, and*
- *full of a liquid whose specific gravity is desired*,

the *specific gravity* of the liquid can easily be calculated.

- First we *fill pycnometer with distilled water*. According to equation [1], the volume of water that is filling the pycnometer and the stopper is

$$V = \frac{m_{H2O}}{\rho_{H2O}} \qquad [2]$$

- where m_{H2O} is experimentally determined weight of water *(empty pycnometer weight subtracted).*
- We repeat the procedure for the liquid with unknown density ρ_L and determine its weight m_L *(measured weight minus weight of empty pycnometer).*
- Volume V obtained in this measurement is the same as the volume of water determined from equation [2].

- It follows alternated equation

$$V = \frac{m_L}{\rho_L} \qquad [3]$$

Combining equations [2] and [3]

$$\frac{m_{H2O}}{\rho_{H2O}} = \frac{m_L}{\rho_L} \qquad [4]$$

yields a relation that provides *the density of measured liquid*

$$\rho_L = \frac{m_L}{m_{H2O}} \cdot \rho_{H2O} \qquad [5]$$

m_p	mass of empty pycnometer
$m_p + m_{H2O}$	mass of water filled pycnometer
$m_p + m_L$	mass of liquid filled pycnometer
ρ_{H2O}	density of water
ρ_L	Unknown density of liquid

$$\rho_L = \frac{m_L}{m_{H2O}} \cdot \rho_{H2O}$$

Example

- A student collected the following data in attempting to determine *the density of an unknown liquid* by the pycnometer method. Determine the density of the unknown liquid. (ρ_{H2O} at 23°C is 0.9975 g/mL)

Temperature of the water = 23.0 °C

Mass of dry pycnometer = 32.4345 g

Mass of pycnometer + water = 58.0558 g

Mass of the pycnometer + unknown liquid = 52.8734 g

Solution:

m_L = (mass of the pycnometer + unknown liquid) – (mass of pycnometer)

= 52.8734 g – 32.4345 g = 20.4389 g

m_{H2O} = (mass of pycnometer + water) – (mass of pycnometer)

= 58.0558 g – 32.4345 g = 25.6213 g

ρ_L = 25.6213 g:20.4389 g x 0.9975 g/mL

= 0.7957 g/mL

$$\rho_L = \frac{(mp + mL) - mp}{(mp + mH_2O) - mp} \times \rho H_2O$$

$$\rho_L = \frac{m_L}{m_{H2O}} \cdot \rho_{H2O}$$

Density determination of solid matter by pycnometer

Pycnometer can be also used to determine the density of the solid phase in porous solids.

To determine the density of a porous solid, a sample must first be crushed, ground, or powdered to the point that all pores are opened. Pycnometers can then be used.

The density of homogeneous solid object does not dissolve in working liquid or immersion liquid (for example; water, ethanol).

- The powder is added to the pycnometer, which is then weighed, giving the weight of the powder sample.
- The pycnometer is then filled with a liquid of known density, in which the powder is completely insoluble ***(immersion liquid).***
- The weight of the displaced liquid can then be determined, and hence *the specific gravity of the powder*.

- First, we need to measure

  the weight of pycnometer together with inserted object
- m_0+m_S (m_0 = mass of empty pycnometer;

  m_S = mass of unknown solid).
- We add water and determine the weight m'_{H2O} (measured weight minus m_0+m_S).
- The volume of added water V'_{H2O} can be obtained as [6]

$$V'_{H2O} = \frac{m'_{H2O}}{\rho_{H2O}}$$

- The volume of measured solid object V_S is the difference between the volume of water that fills *the empty pycnometer* V and volume V'_{H2O}

[7]
$$V_S = V - V'_{H2O} = \frac{m_{H2O} - m'_{H2O}}{\rho_{H2O}}$$

- Density of measured object ρ_S can be then calculated as [8]

$$\rho_S = \frac{m_S}{V_S}$$

$\mathbf{m_p}$	mass of empty pycnometer (with stopper)
$\mathbf{m_p + m_{imm.lq}}$	mass of immersion liquid filled pycnometer
$\mathbf{m_p + m_S}$	mass of solid filled pycnometer
$\mathbf{m_p + m_{imm.lq} + m_S}$	mass of immersion liquid and solid filled pycnometer
$\rho_{imm.lq}$	density of immersion liquid
ρ_S	Unknown density of solid

$$\rho_s = \frac{(m_p + m_s) - m_p}{[(m_p + m_{imm.lq}) - m_p] - [(m_p + m_{imm.lq} + m_S) - (m_p + m_S)]} \times \rho_{imm.lq}$$

Example

- A student collected the following data in attempting to determine *the density of an unknown solid* by the pycnometer method which used immersion liquid as EtOH ($\rho = 0.802$ g/cm^3). Determine the density of the unknown solid.

- $m_p = 10.8542$ g
- $m_p + m_S = 11.0402$ g
- $m_p + m_{imm.lq} = 18.8746$ g
- $m_p + m_{imm.lq} + m_S = 18.9551$ g

Solution:

$$\rho_s = \frac{(m_p + m_s) - m_p}{[(m_p + m_{imm.lq}) - m_p] - [(m_p + m_{imm.lq} + m_S) - (m_p + m_S)]} \times \rho_{imm.lq}$$

$$\rho_s = \frac{(11.0402 - 10.8542)}{(18.8746 - 10.8542) - (18.9551 - 11.0402)} \times 0.802$$

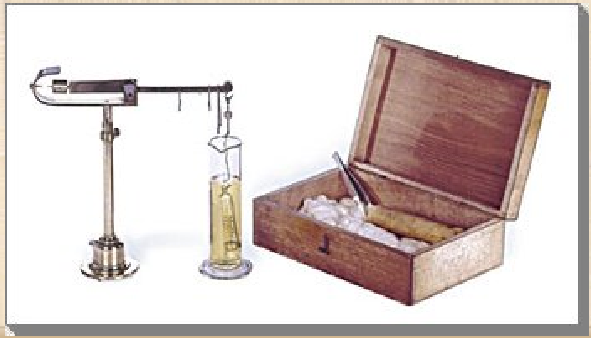
$$= \frac{0.186}{0.1055} \times 0.802 = 1.4139 \text{ g/cm}^3$$

Westphal Balance

- *Westphal Balance* is an older type of specific gravity balance.

This Westphal Balance is shown in its box, along with the characteristic U-shaped balancing masses and the plummet in the upper right-hand corner. The sliding top of the box has the decorative molding attached to it.

- The Westphal Balance was first described by German chemist *Carl Friedrich Mohr* in 1832.
- Modifications were made by the good *Dr. Westphal* who replaced a tray method with an adjustable arm counterweight.



For extremely accurate density readings one may prefer to use a pycnometer although for speed and ease of use a Westphal can quickly provide a very close approximation to the true density of any liquid solution.

- The Westphal Balance operates by suspending a glass tube (with a mercury thermometer contained within it) into a sample of a solution of unknown density via a thin platinum wire.

- The scale is balanced by an array of horseshoe shaped counterweights which come in 5 g, 0.5 g, 0.05 g, and 0.005 g masses.

- These counterweights (sometimes called riders) respectively signify the ones place of the specific gravity of the sample solution,
- the tenths place,
- the hundredths place, and
- the thousandths place.

- The numerical value each rider represents is equal to the numbered notch of the arm which it sits in when the scale is balanced.

Melting Point

- The melting point is *a characteristic property* of a substance.
- It is the temperature at which the *crystalline phase* of a substance changes to the *liquid state*.
- The normal melting point of a solid is defined as the temperature at which the solid and liquid are in equilibrium at a total pressure of 1 atmosphere.

- Since the melting point of a solid can be easily and *accurately determined* with *small amounts of material*, it is the *physical property* that has most often been used for the identification and characterization of solids.
- A pure substance normally has *a sharp melting point*,
- whereas an impure substance melts over a temperature range that is *lower than* the melting point of the *pure substance* (melting point depression).

- Some organic compounds will however melt irreproducible due to *decomposition*. During the melting process, all of the energy added to a substance is consumed as heat of fusion, and the temperature remains constant.

Melting point determination is used in research and development as well as in

- quality control to identify
- check the purity of a wide range of substances.

- *Automated melting point apparatus* which is simple and fast is used for determination of melting points nowadays.
- The theory behind the melting point instrument is that; if a sample is heated at a constant rate in a capillary, the transmission of light through the sample and hence the light intensity measured by a sensor (the camera) changes with increasing temperature.
- The sample is considered to have melted when a predefined level of light transmission is reached.

Capillary Melting Points

Capillary melting points, either in an oil bath or a melting-point apparatus, are most often used for the determination of the melting point of a solid.

A few crystals of the compound are placed in a thin walled capillary tube 10-15 cm long, about 1 mm in inside diameter, and closed at one end.

The capillary, which contains the sample, and a thermometer are then suspended so they can be heated slowly and evenly. The temperature range over which the sample is observed to melt is taken as the melting point.

Filling a Capillary Tube

Usually, the melting point capillary can be filled by

- pressing the open end into a small heap of the crystals of the substance,

- turning the capillary open end up, and

- vibrating it by drawing a file across the side to rattle the crystals down into the bottom.

If filling does not work, drop the tube, open end up, down a length of glass tubing about 1 cm in diameter (or a long condenser) onto a hard surface such as

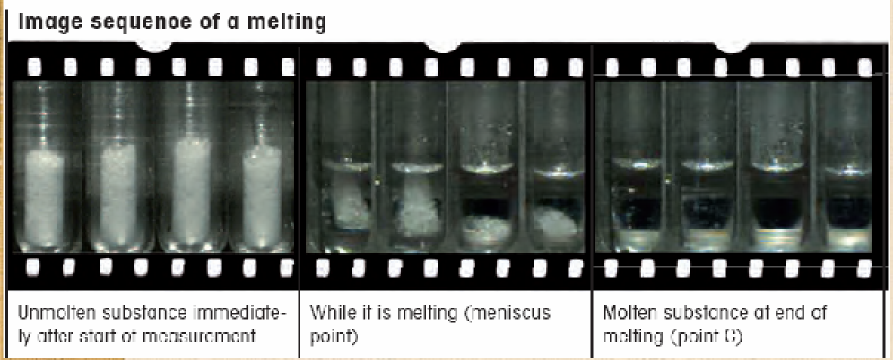
a porcelain sink,

stone desktop,

or the iron base of a ring stand.

The solid should be tightly packed to a depth of 2-3 mm.

Functional Definition of Melting Point



Strictly speaking, *the melting point is never a "point".* It is invariably a narrow range, about 1° for most compounds, but 0.5° for some, 1.5 – 2.0° for others. Part of the range is an experimental artifact.

- Since heat transfer is often uneven, all parts of a solid sample are unlikely to be at the same temperature simultaneously.
- While *some regions* of the sample may be at the melting point (solid and liquid in equilibrium), *other regions* may be at slightly higher or lower temperatures.
- Thus, visible melting will occur over a range of temperatures.

- Therefore, the proper report of a melting point is the temperature range from the *first visible appearance of liquid* (distinguished from "softening" of the crystal)

  to the disappearance of the *last visible crystal of solid*.

  The end is the most important point, but the whole range is needed for full interpretation.

  (e.g. benzoic acid, m.p. = 120 – 121.5°C).

Effects of an “Impurity”

If two different compounds, A and B, are intimately mixed, the melting point behavior of the mixture differs from that of either pure compound.

When a small portion of B is mixed with A, the upper limit of the melting point range of A is lowered.

Increasing the amount of B in A continuously decreases the upper limit of the melting range of the resultant mixture until such point that B ceases to be the impurity in A, and A then becomes the impurity in B.

The point at which this occurs is called the eutectic; the eutectic temperature and composition of a mixture varies with the nature of the components A and B.

The upper limit of the melting range of a compound containing an impurity is always lower than that of the *pure compound*.

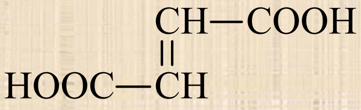
Molecular Weight

- Although melting points do generally increase with *increasing molecular weight*, the first members of homologous series often have melting points that are considerably different from what would be expected on the basis of the behavior of the higher homology.
- Sometimes, as with the normal alkanes, the melting points of successive members of the series always increase, but by a larger or smaller amount, depending upon whether the number of carbons is even or odd.

Polarity

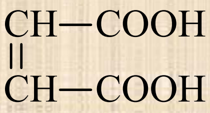
- As with boiling points, compounds with *polar functional groups* generally have *higher melting points* than compounds with nonpolar functional groups.
- In contrast to the case with boiling points, highly branched or cyclic molecules (relatively symmetrical molecules) tend to have *higher melting points* than their straight-chain isomers.
- In extreme cases, a liquid range does not exist at a vapor pressure of less than 760 Torr; at atmospheric pressure, the substance will *sublime* without melting.

  Hexachloroethane and perfluoro-cyclohexane behave in this way.



$$\begin{array}{l} \qquad CH-COOH \\ \qquad \| \\ HOOC-CH \end{array}$$

Fumaric acid (200 °C)
trans



$$\begin{array}{l} CH-COOH \\ \| \\ CH-COOH \end{array}$$

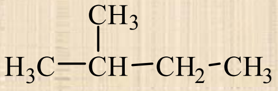
Maleic acid (138°C)
cis

For isomeric compounds, trans-compounds generally have higher melting points than cis-compounds.

Carnelley's Rule

- In organic chemistry Carnelley's Rule established in 1882 by Thomas Carnelley, states that *high molecular symmetry is associated with high melting point.*
- Carnelley based his rule on examination of 15,000 chemical compounds.
- Pyridine has a lower symmetry than benzene hence its lower melting point but the melting point again increases with diazine and triazines.

For example for three structural isomers with molecular formula C_5H_{12} the melting point increases in the series

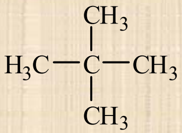


$$H_3C-\overset{CH_3}{\overset{|}{CH}}-CH_2-CH_3$$

- isopentane -160 °C (113 K)

$H_3C-CH_2-CH_2-CH_2-CH_3$

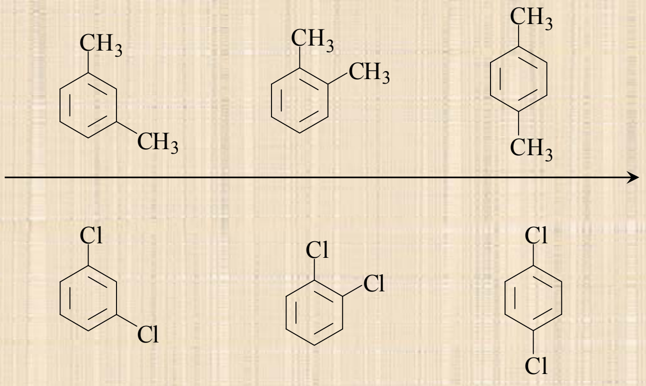
- n-pentane -129.8 °C (143 K)



$$H_3C-\underset{CH_3}{\underset{|}{\overset{CH_3}{\overset{|}{C}}}}-CH_3$$

- neopentane -18 °C (255 K).

- Likewise in xylenes and also dichlorobenzenes the melting point increases in the order *meta, ortho* and then *para*.



Boiling Point

- *The boiling point of a compound* is the temperature at which it changes from a liquid to a gas.

This is a physical property often used

- to identify substances or
- to check the purity

of the compound.

- *The boiling point of a liquid* is an important *physical property*.

- While the boiling point is *a characteristic physical property of a compound*, many compounds may have the same boiling point.
- *A liquid boiling point* is the temperature when its vapor pressure is equal to the atmospheric pressure.
- Like melting points, boiling points are *characteristic properties of pure materials*.
- Boiling points are approximately related to their molecular weight, *the higher the molecular weight, the higher the boiling point*.

Factors Influencing Boiling Point

- *Structural features of a compound influence the boiling point* by

increasing or

decreasing the molecules' ability

to establish and maintain non-covalent interactions that hold the molecules close together in the liquid state.

- The structural features of a compound that influence boiling point are:

a)* *Polarity –

-Increased H-bonds,

-polar covalent bonds or

-formal charges

in a molecule tend to *increase the boiling point*.

More polar elements in a molecule increase the total number of dipole-dipole, ion-dipole and/or H-bonding interactions.

More energy is necessary to break these interactions and allow the molecules to move away from each other into a gaseous state.

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b) *Molecular Weight:* Increased molecular weight increases boiling point.

A higher molecular weight compound has more atoms that can be involved in non-covalent interactions.

The greater the number of non-covalent interactions, the more energy (higher boiling point temperature) that is necessary to break the non-covalent interactions to transform the compound from the liquid phase to the gas phase.

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c) *Branching:* Branching *decreases boiling point*. Branching blocks molecules from packing together too closely. The closer molecules are, the stronger the *non-covalent interactions*.

Thus, molecules that are forced to be farther away from each other due to branching have weaker non-covalent interactions.

Less energy (lower temperatures) is needed to induce a phase change from the liquid phase to the gas for branched compounds relative to straight chain compounds.

Refractometry

- *Refractometry* is the method of measuring substances′ refractive index in order to, for example, assess their composition or purity.
- It is important from both the scientific and technological point of views owing to its numerous applications.

- The *refractive index* is a unitless number, between 1.3000 and 1.7000 for most compounds, and is normally determined to five digit precision.
- A refractometer measures the extent to which light is bent (i.e. refracted) when it moves from air into a sample and is typically used to determine *the refractive index* (n) of a liquid sample.

- Since the index of refraction depends on both the temperature of the sample and the wavelength of light used these are both indicated when reporting the *refractive index*:

$$n_{\mathrm{D}}^{20} \;\; 1.3742$$

- The italicized n denotes refractive index,
- the superscript indicates the temperature in degrees Celsius, and
- the subscript denotes the wavelength of light (in this case the D indicates the *sodium D line* at 589 nm).

- The *refractive index* is commonly determined as part of the characterization of liquid samples.

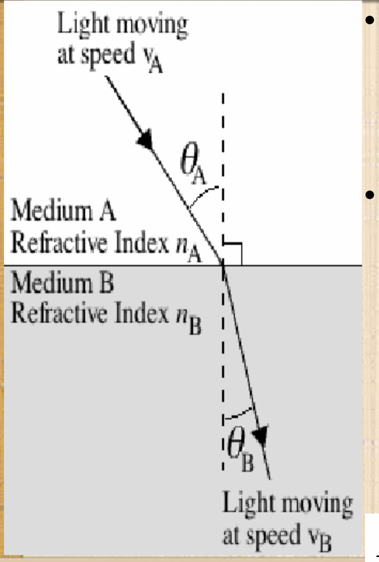
  It is also commonly used to:
- Help identify or confirm the identity of a sample by comparing its refractive index to known values.
- Assess the purity of a sample by comparing its refractive index to the value for the pure substance.
- Determine the concentration of a solute in a solution by comparing the solution's refractive index to a standard curve.

Theory

- The speed of light in a vacuum is always the same, but when light moves through any other medium it travels more slowly since it is constantly being absorbed and reemitted by the atoms in the material.

- The ratio of the speed of light in a vacuum to the speed of light in another substance is defined as the *refractive index* for the substance.

$$\text{refractive index } (n) \text{ of substance} = \frac{\text{speed of light in a vacuum}}{\text{speed of light in substance}} \quad \text{(Eqn 1)}$$



- In the case shown, the speed of light in medium A is ***greater than*** the speed of light in medium B.
- The relationship between ***light's speed*** in the two mediums (**v_A** and **v_B**), the ***angles of incidence*** (θ_A) and refraction (θ_B) and the ***refractive indexes*** of the two mediums (***n_A*** and ***n_B***) is shown below:

$$\frac{v_A}{v_B} = \frac{\sin\theta_A}{\sin\theta_B} = \frac{n_B}{n_A} \quad \text{(Eqn 2)}$$

- *Samples with different refractive indexes* will produce different angles of refraction and this will be reflected in a change in the position of the *borderline between the light and dark regions*.

- By appropriately calibrating the scale, the position of the borderline can be used to determine the *refractive index* of any sample.

- In an actual Abbé refractometer there is not a detector on the back of the refracting prism, and there are additional optics, but this is the essential principle.

Abbé refractometer

- *The most common* and *universal* refractometer for laboratory use is the *Abbé refractometer* and its variations.
- *The Abbe' refractometer* provides a quick and easy means for

  determining refractive index and

  dispersion for liquids and solids.

- In most *liquids* and *solids* the speed of light, and hence the index of refraction, varies significantly with wavelength.

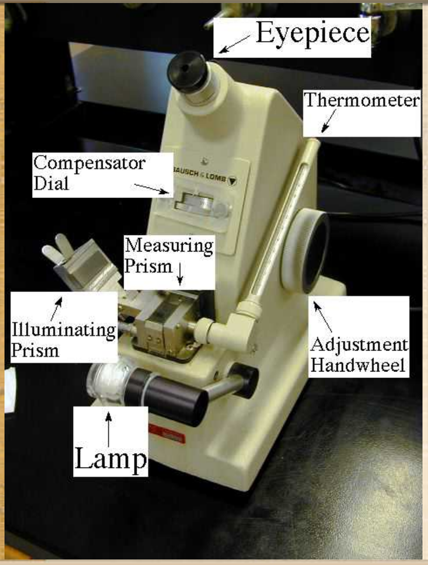
Refractometers are very important in industry. It is used in the examination of organic compounds (oils, solvents, etc.),

- solutions,
- food products,
- serum protein concentration.
- *In veterinary medicine*, a refractometer is used to measure the total plasma protein in a blood sample and urine specific gravity.
- *In gemmology*, a refractometer is used to help identify gem materials by measuring their refractive index.

- Thus, for the most accurate measurements it is necessary to *use monochromatic light*.
- The most widely used wavelength of light for refractometry is the sodium D line at 589 nm.
- If white light were used in the simple *Abbé refractometer* optics shown in Figure 2, dispersion would result in the light and dark borderline being in different places for different wavelengths of light.
- The resulting "fuzziness" of the borderline would make precise work impossible.

- However, many Abbé refractometers are able to operate satisfactorily with white light by introducing a set of "compensating prisms" into the optical path after the refracting prism.
- These compensating prisms are designed so that they can be adjusted to correct (i.e., compensate for) the dispersion of the sample in such a way that they reproduce the refractive index that would be obtained with monochromatic light of 589 nm, the sodium D line.

Abbé refractometer



Many refractometers are equipped with a thermometer and a means of circulating water through the refractometer to maintain a given temperature.

Most of the refractive index measurements reported in the literature are determined at 20 or 25 °C.

- Operation consists of placing 1 or 2 drops of the water sample on the prism, closing a glass plate over the sample, then looking through the eyepiece for the reading.

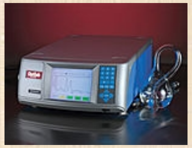
Types of refractometers

There are four main types of refractometers:

- *traditional handheld refractometers,*
- *digital handheld refractometers,*
- *laboratory refractometers (Abbé ref.),*
- *inline process refractometers.*

Hand-Held Digital Refractometer

Digital Refractometer



Digital Abbé refractometer

- As mentioned earlier, the speed of light in a substance is *slower than* in a vacuum since the light is being absorbed and reemitted by the atoms in the sample.
- Since the density of a liquid *usually decreases with temperature*,
- it is not surprising that the *speed of light in a liquid* will normally increase as the *temperature increases*.

- Thus, *the index of refraction normally decreases as the temperature increases* for a liquid.
- For many organic liquids *the index of refraction decreases* by approximately 0.0005 for every 1 °C increase in temperature.
- However, for water the variation is only about -0.0001/°C.

n_{D}^{25}

Temperature dependence of refractive index for selected substances.

Substance			
Isopropanol	1.3802	1.3772	1.3749
Acetone	1.3616	1.3588	1.3560
Ethyl Acetate	1.3747	1.3742	1.3700
Water	1.3334	1.3330	1.3325

Structural Information

- The refractive index *does not provide detailed information about a molecule's structure*,

  and it is not usually used for this purpose since spectroscopic techniques are much more powerful at revealing details of molecular structure.

One structural factor that influences the refractive index of a sample is its *polarizability*.

- Substances containing *more polarizable* ("soft") groups (e.g., iodine atoms or aromatic rings)

  will normally have *higher refractive indexes* than substances containing *less polarizable* ("hard") groups (e.g., oxygen atoms or alkyl groups).

Table 2. Effect of polarizable groups on refractive index.

Substance	2-Iodoethanol	2-Fluoroethanol	Benzene	Cyclohexane
n_{D}^{20}	1.5720	1.3670	1.5010	1.4260

Different types of refractometers are used for measuring *gases*, *liquids* such as oils or water-based, and even certain transparent or translucent *solids* such as gemstones.

- *Abbé refractometer*
- *Immersion or dipping refractometer*
- *Pulfrich refractometer*
- *Interference refractometer*

- The *immersion or dipping refractometer* is basically an Abbé type refractometer of *short range* and *without an illuminating prism*.
- The dipping refractometer is used primarily for determining solution concentrations, such as in *the sugar industry, pharmaceuticals, and milk*. It is particularly useful for acids since only the inert prism dips into the solution.

- The *Pulfrich refractometer* is actually only as accurate as a standard Abbé (one unit in the fourth decimal place) in absolute determinations.
- However, it can give measurements to 2-3 units in the fifth-place for differential measurements and for *dispersion determinations*.

- The *Rayleigh interference refractometer*, still widely used for determining the refractive indices of gases and liquids.

- The *Lorentz–Lorenz equation*, also known as the Clausius–Mossotti relation and Maxwell's formula, relates the *refractive index*.
- The most general form of the Lorentz-Lorenz equation is

$$r = \frac{n^2-1}{n^2+2} \times \frac{1}{\rho}$$

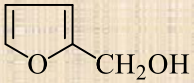
- *n* is the *refractive index*, ρ is *density*
- molar refractive index

$$R = \frac{n^2-1}{n^2+2} \times \frac{MW}{\rho}$$

Tablo 1: Atom refractive index

Group	**Rm**	**Group**	**Rm**
H	1.100	**Br**	8.865
C	2.418	**I**	13.900
C=C	1.733	**N (primary aliphatic amine)**	2.322
C≡C	2.398	**N (secondary aliphatic amine)**	2.499
O(carbonyl) C=O	2.211	**N (tertiary aliphatic amine)**	2.840
O(hydroxyl) (O-H)	1.525	**N (primary aromatic amine)**	3.21
O(ether, ester) (C-O-)	1.643	**N (secondary aromatic amine)**	3.59
S(thiocarbonyl) (C=S)	7.97	**N (tertiary aromatic amine)**	4.36
S (thiol) (S-H)	7.69	**N (amide)**	2.65
F	1.0	**-NO_2 group (aromatic)**	7.30
Cl	5.967	**-C≡ group**	5.459

Molar refractive index of Furfuryl alcohol ($n_D^{20} = 1.4850$) can be calculated in two different ways;



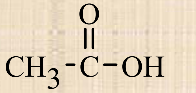
5C = 5 (2.42) = 12.10
6H = 6 (1.10) = 6.60
O = 1 (1.52) = 1.52
O = 1 (1.64) = 1.64
C=C = 2 (1.73) = 3.46

R = 25.32 ml/mol

or **Lorentz-Lorenz** equation;

$$R = \frac{(1.4850)^2-1}{(1.4850)^2+2} \cdot \frac{98}{1.1296} = 24.78 \text{ ml /mol}$$

Which compound has molar refractive index of 12.98?

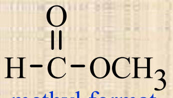


$$CH_3-\overset{\overset{O}{\|}}{C}-OH$$

acetic acid

2C = 2x 2.42 = 4.84
4H = 4 x 1.1 = 4.40
C=O = 1x 2.21 = 2.21
O-H = 1x 1.53 = 1.53

12.98



$$H-\overset{\overset{O}{\|}}{C}-OCH_3$$

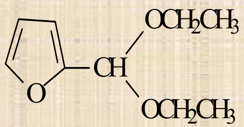
methyl format

2C = 2 x 2.42 = 4.84
4H = 4 x 1.1 = 4.40
C=O = 1x 2.21 = 2.21
C-O = 1x 1.64 = 1.64

13.09

Molar refractive index of acetic acid is 12.98.

Question: Calculate the density of 2-Furaldehyde diethylacetal (refractive index n_D^{20}= 1.4440) (C= 12, H= 1, O=16).



$C_9H_{14}O_3$ (MW: 170)
R= 45.557 ml/mol

$$R = \frac{n^2 - 1}{n^2 + 2} \times \frac{MW}{\rho}$$

Group	Rm	
H	1.100	→ x 14 = 15.4
C	2.418	→ x 9 = 21.762
C=C	1.733	→ x 2 = 3.466
O(ether, ester) **(C-O-)**	1.643	→ x 3 = 4.929
		45.557

$$45.557 = \frac{(1.4440)^2 - 1}{(1.4440)^2 + 2} \times \frac{170}{\rho}$$

$$\rho = 0.9912 \text{ g/ml}$$

Polarimeter

- *Polarimetry* measures the extent to which a substance interacts with plane polarized light; whether it rotates plane polarized light to the left, to the right, or not at all.
- The measuring instrument is called *a polarimeter*.
- If the substance rotates plane polarized light to the *left* or to the *right*, it is called *optically active*.
- Typical optically active substances contain at least one asymmetric atom in their molecule structure.

Such atoms are C(carbon), S(sulfur), P(phosphor), Si(silica) and few others.

- This asymmetry leads to the formation of two isomers (+;-) which both cause an optical rotation, but in different directions.
- Some well known optical substances are *tartaric acid, lactic acid, benzoic acid and derivates, amino acids, proteins and of course sugars*.
- If an optically *active substance* (f.i. sugar) is dissolved in an optically *inactive liquid* (as water for instance), the degrees of angle rotation, depend - amongst others - on the concentration of the solution.
- This angle of rotation is absolutely determined by a polarimeter with highest precision.

- If a compound does not have a chiral center, it will not rotate light at all.
- The number of degrees and the direction of rotation are measured to give the observed rotation. The observed rotation must be corrected for the length of the cell used and the solution concentration.
- Comparing the corrected observed rotation to literature values can aid in *the identification of an unknown compound*.

- These measurements are useful for studying the structure of anisotropic materials, and for *checking the purity of chiral mixtures*.
- A sample that contains only one enantiomer of a chiral molecule is said to be optically pure.

- *The enantiomer* that rotates light to the right, or clockwise when viewing in the direction of light propagation,

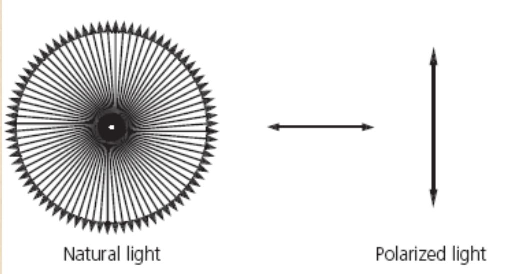
  is called the *dextrorotatory* (d) or (+) enantiomer,

- *the enantiomer* that rotates light to the left, or counterclockwise,

  is called the *levorotatory* (l) or (-) enantiomer.

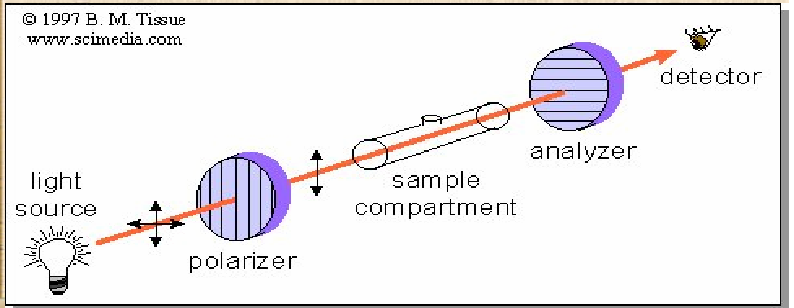
- Optical rotation occurs because optically active samples have different refractive indices for left- and right-circularly polarized light.
- Another way to make this statement is that left- and right-circularly polarized light travel through an optically active sample at different velocities.
- This condition occurs because a chiral center has a specific geometric arrangement of *four different substituents*, each of which has a different electronic polarizability.

- Light travels through matter by interacting with the electron clouds that are present.
- Left-circularly polarized light therefore interacts with an anisotropic medium differently than does right-circularly polarized light.



Instrumentation

- The simplest polarimeter consists of a monochromatic light source, a polarizer, a sample cell, a second polarizer, which is called the analyzer, and a light detector. The analyzer is oriented 90° to the polarizer so that no light reaches the detector.



Optical rotation depends on the following:

1. Nature of the sample
2. Concentration of the optical active components
3. Wavelength of the light
4. Temperature of the sample
5. Optical path length (length of the measuring tube)

$$[\alpha]_{\lambda}^{T} = \frac{\alpha}{L \times c}$$

α = measured rotation in degrees
c = concentration in g/cm^3
L = tube length in decimeters (dm)
[α] = specific rotation in degrees. mL/dm.g

Weeks	Dates	Experiment
1	4 March 2010	Demo
2	11 March 2010	Demo
3	18 March 2010	Demo
4	25 March 2010	Separation of Solid-Solid mixture
5	1 April 2010	Solid density - Liquid density
6	8 April 2010	Boiling point determination- Melting point determination
7	15 April 2010	Separation of Liquid-Liquid mixture
8	22 April 2010	Refractometer – Polarimeter
9	29 April 2010	**Intermediate Exam**
10	6 May 2010	Pharmacopeia analysis (Urea, water purified)
11	13 May 2010	HPLC experiment
12	20 May 2010	Separation of aminoacids by TLC
13	27 May 2010	Column chromatography
14	3 June 2010	**Compensation week- presentation**

SEPARATION OF SOLID MIXTURES

1- Paracetamol- Chlorpheniramine maleate- Phenylpropanolamine hydrochloride (Corsal capsule) mixture is separated with soxhlet extraction using chloroform. Chloroform phase is checked by thin layer chromatography.

Thin Layer Chromatography:

Stationary Phase: Silica gel GF 254

Mobile Phase: Benzene-Diethyl ether-Acetic acid (60:30:15)

Detection of spots: Under UV lamp at 254 nm

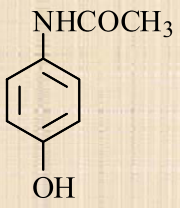
2- Phenacetin-Aspirin sample is solved in 10 ml chloroform and extracted three times with 10 ml 4% sodium bicarbonate solution. Chloroform and sodium bicarbonate phases are checked by thin layer chromatography.

Thin Layer Chromatography:

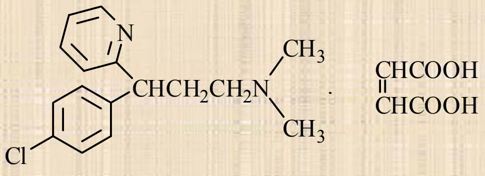
Stationary Phase: Silica gel GF 254

Mobile Phase: Benzene-Diethyl ether-Acetic acid (60:30:15)

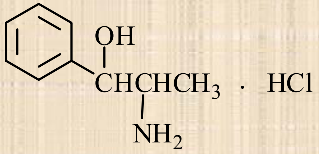
Detection of spots: Under UV lamp at 254 nm



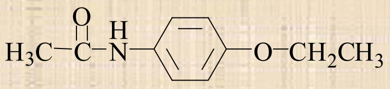
Paracetamol



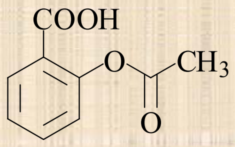
Chlorpheniramine maleate



Phenylpropanolamine hydrochloride



Phenacetin



Aspirin

SEPARATION OF SOLID- SOLID MIXTURES
(EXPERIMENT No: 1A)

Date:

- **Students’ Name, Surname:**
- **Number:**
- **Group No:**
- **Scope of the Experiment:**
- **Principle of the Experiment:**
- **Formulas of the Active Substances:**
- **Required Materials:** Detergant, cleaning towel, ruler, calculator
- **Chromatogram Data:**
- **Stationary Phase:**
- **Mobile Phase:**
- **Development Time:**
- **Development Temperature:**
- **Detection of Spots:**
- **Calculation of R_f:**
- **Scheme of Soxhilet Apparatus:**
- **Results:**