Rheology

PHA390

Pharmaceutical Technology II

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Rheology

- **It is the science related with the shape change of the material**
  - the deformation of the solids
  - the flow properties of the liquids.

- **Rheological properties are especially important in the formulation of emulsion, suspensions, semi-solid dosage forms and cosmetics for:**
  - product development,
  - determining the finished product specifications.

- **It is used in quality control and stability studies**

Applications of rheology

- **Rheological properties are also important in the selection of devices to be used in the production of a pharmaceutical system and**

- **to optimize production, processes such as mixing, transfering are related with rheology.**

  -Packaging of formulations
  -Transferring from the package
  -Flowing from bottle,
  -Draining from the tube,
  -Passing through the needle,
  -Spreading on skin..

Applications of rheology

- **is used for standardization of the properties of active and auxiliary substances**
  - To determine the structure of these materials (such as particle size),
  - the effect of production parameters and time (such as temperature, mixing)

- **Optimization of processes such as powder flow during tablet compression and capsule filling,**

- **in preparation of the tablet coating formulations and analysis of the colloidal substance used as a tablet disintegration agent,**

Viscosity

- The viscosity of a liquid can be explained with formation of internal resistance (friction) of a molecule layer against its relative motion with the other molecule layer.
- It is the measurement of rheological properties.
- The more the resistance in a fluid means the higher the measured viscosity value.

Viscosity

Viscosity can be expressed in one of the following units:

CGS * Centipoise (cP) absolute viscosity
* Centistokes (cS) kinematic viscosity

poise = dyne.sec. cm^{-2}

SI * Pascal.second (Pa.s)
(Newton / m^2 .sn^{-1})

1 Pa = 10 poise

The flow properties of the liquids are quantitatively the first time examined by Newton and expressed by the following equation.

$$F / A = \eta \, (d\nu / dr)$$

dν / dr : Two liquid layers sliding over each other (speed gradient) ***shear rate (G)***

F / A : force or shear stress per unit area, which creates the slip rate, ***shear stress (F)***

η : Dynamic viscosity coefficient

- **Suppose a water block which is made up of parallel water molecule planes.**
- **If the top surface is pushed by the force F, the bottom surface tries to stand against it.**
- **As a result, the planes between top-bottom surfaces move differently. The plane near the tangent to which the force is applied moves fast, while the plane near the base moves slower.**
- **The bottom surface resists in the opposite direction to the force F applied to stabilize it in place and with a force of the same value.**
- **As a result, there is a tension in the environment.**

$$(F/A) = \eta \, (dv/dr)$$

Shear stress

- The force per unit surface in the fluid surface A (Top surface) at which force is applied is expressed by the shear force (F/A)

Shear rate

- Displacement occurs as a result of the shear stresses of the planes over each other. In this displacement, if the distance between the top and bottom planes is R and the shear rate of the planes is V, the shear resultant strain rate (dv / dr)

Kinematic viscosity

- It is defined as the ratio between the dynamic viscosity of the liquid and the density at the same temperature
- The unit is Stokes (centistokes, cS)

$$\nu = \eta/\rho$$

ν : kinematic viscosity ($m^2.s^{-1}$)

η : dynamic viscosity (Pa.s)

ρ : density of liquid in a known temperature ($kg.\ m^{-3}$)

Kinematic viscosity

According to European Pharmacopoeia,

- viscosity is shown with (η) symbol and its unit is mPa.s
- kinematic viscosity is shown with (ν) and unit is $mm^2.s^{-1}$
- Kinematic viscosity is important when a material is pumped through pipes.

Effect of temperature

- The effect of temperature on viscosity for liquids is explained by Arrhenius equation

$$\eta = A.e^{E\upsilon/RT}$$

A = constant due to molecular weight and molar volume of liquid

$E\upsilon$ = activation energy needed to initiate intermolecular flow

R = Gas constant (cal / mol)

T = Temperature (°K)

Effect of temperature

- For liquids,

molecules become more freely with increasing temperature and the viscosity decreases.

- For gases,

the speed of the molecules increases with °C and

the viscosity increases due to the increase in kinetic energy

Fluid
is an object that continuously changes its shape with a voltage resulting in a force that is too small to be measured.

Fluidity
is the change in shape which continues after the external stress is removed. It is the opposite of viscosity

$$(\phi = 1/\eta)$$

Elastic deformation
The change in shape occuring with an external stress is known as deformation. If the deformation is reversibl, it is called as elastic deformation. Elastic deformation is a characteristic for solid materials.

Flow is permanent shape change which occurs in fluids.

Rheogram is flow curve

Flow types

The materials are classified according to their flow and deformation properties as:

1. Newtonian Systems

Their flow curves (rheograms) are linear

* Gases, non-colloidal fluids, true solutions are examples

2. Non-Newtonian Systems

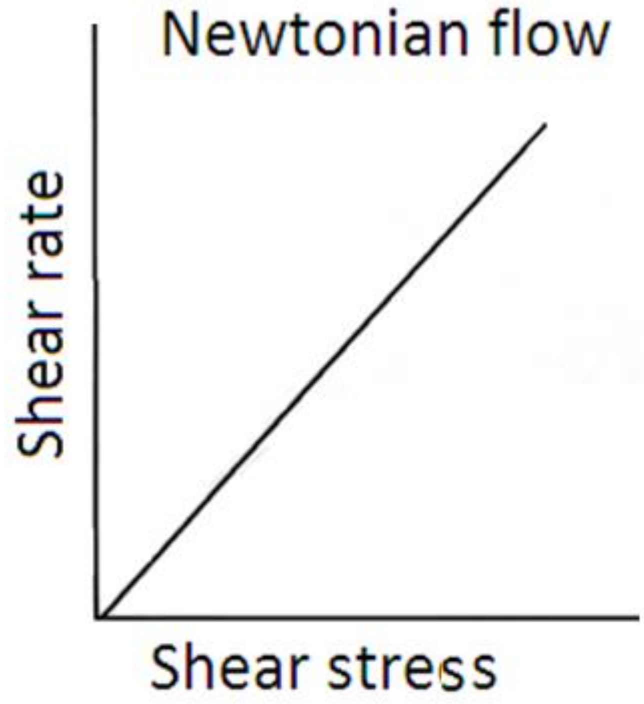
-Plastic flow
-Pseudoplastic flow
-Dilatant flow

Their flow curves are non-linear

* Emulsions, suspensions, gels and semisolids are examples.

Newtonian Systems

- In these systems shear stress increases with the increasing shear rate.
- **There is direct proportionality between shear rate and shear stress in all shear rates.**
- True solutions and non-colloidal liquids such as glycerine, alcohol, water show this type of flow.



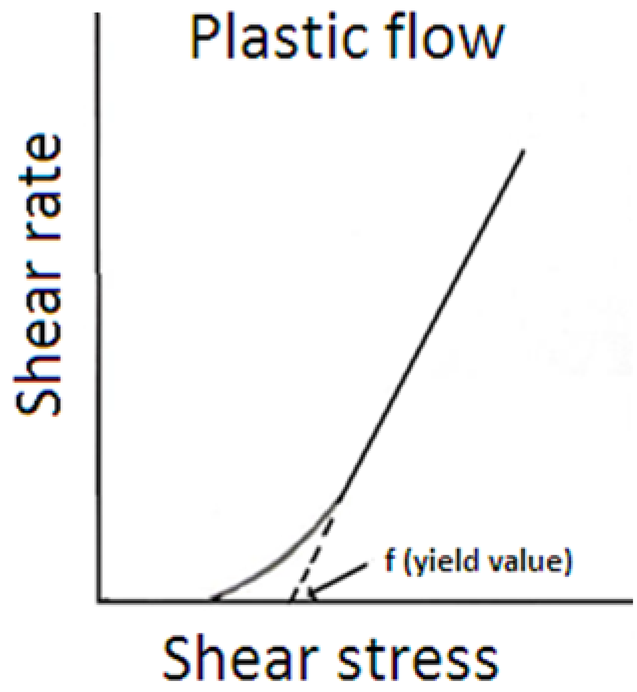
Plastic flow

- Bingham flow

- In these systems flow requires an initial stress which is called as **yield value (f).**

- Before reaching (f) value, system behaves like an elastic solid and after the yield value it begins to flow.

- Suspensions, semi-solids (creams) and gels show this type of flow.



- **Yield point is a measure of flocculation degree.**

This means that;

- Flow begins after the yield value overcomes to flocculation forces.
- Therefore, yield value indicates the floculaton degree (β).
- If β value is high, then yield value will be high.

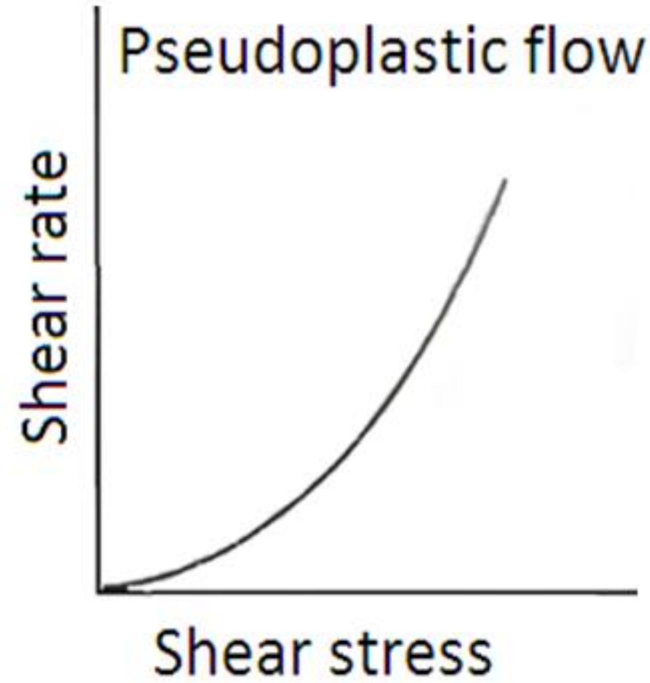
(an increase in the structure requires a greater stress to initiate motion in the system.)

Pseudoplastic flow

- **Flow curve starts from the origin, there is not any yield value.**

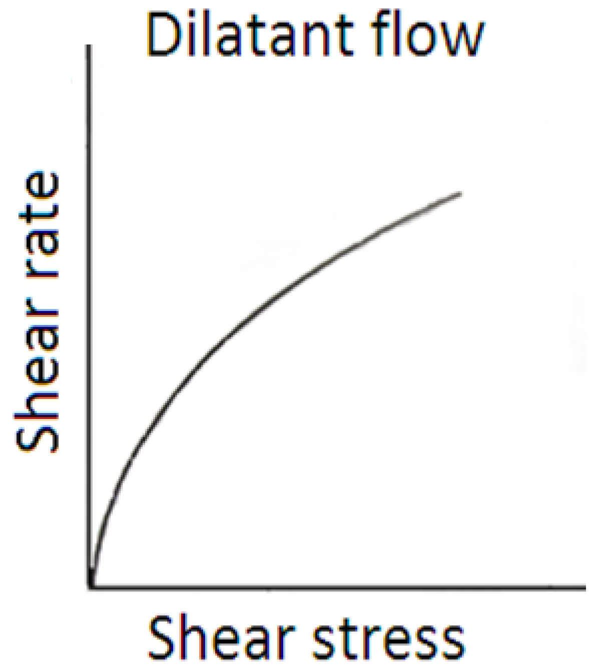
- **These systems are also called as shear-thinning, as their viscosity decreases by applying a shear stress**

- Solutions of hydrocolloids, such as methyl cellulose, sodium alginate, tragacantha etc., emulsions and suspensions show this type of flow.



Dilatant flow

- **Slope of the flow curve of dilatant system decreases by increasing shear rate, therefore the apparent viscosity increases.**
- **In these systems due to increasing shear stress a volume increase is observed (shear-thickening).**
- Deflocculated suspensions with solid particle amount over 50 % shows this flow type (concentrated starch pastes,oil paints, inks)



- Dilatant flow (dilatancy) takes place when the ratio of solid phase to the liquid phase is large.

- At rest, space between the particles will be minimum. However, when a shear stress is applied, system will expand but the liquid vehicle between the particles will stay constant.

- As the amount of vehicle will not be enough to carry particles sytem will show dilatancy.

Thixotropy

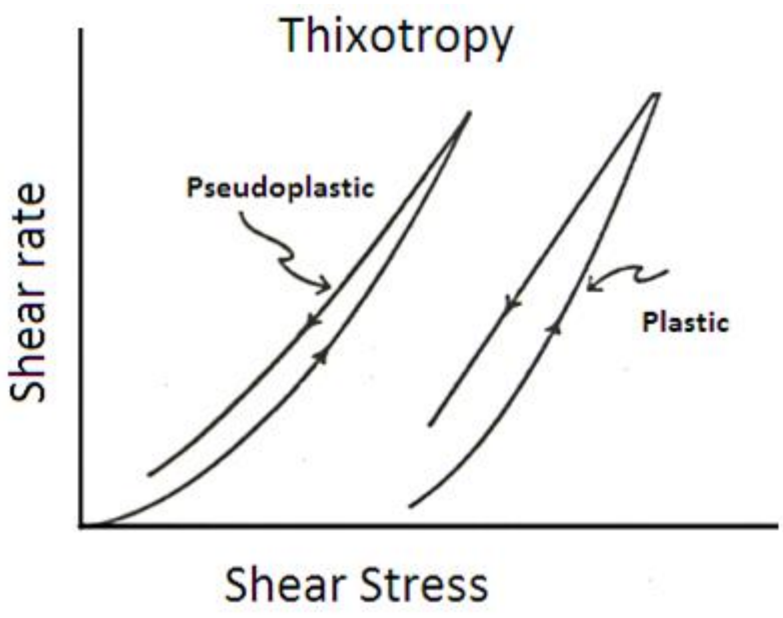
(Time dependent phenomena)

- Thixotropy is not a flow type, it is a change feature in the flow, depending on the time.
- Thixotropic systems are dispersions that enter the isothermal gel ⇔ solid transformation.
- Here, gel is a colloidal system showing a "shear limit" and solid is a colloidal system which do not show "shear limit".
- The mechanism of thixotropy can be explained as breakdown and re-forming gel-solid-gel structure.

- In these systems, the area between the up-curve and down-curve in graphics are called as **'thixotropic hysteresis loop'** and formation of this loop is an accepted criterion.

- The difference of thixotropy from pure shear thinning fluid can be explained with this loop. (shear thininnig fluids do not show loop)

Examples of common thixotropic materials are gelatin, mayonnaise, latex paint, emulsions, suspensions



- Thixotropy is desirable in liquid pharmaceutical systems as pouring from the container and spreading to the skin will be easy.

- For example, a well-formulated thixotropic suspension does not immediately collapse in the container, it becomes liquified by shaking and remains as dispersed for a sufficient period of time for dosing.
- Thixotropy is desirable for emulsions, lotions, creams, ointments and some i.m. parenterals.

- There is a relationship between the thixotropy and the sedimentation rate and this is important for the stability of the suspension:

→ **as the thixotropy grade increases, the sedimentation rate decreases**

Viscometers

Choise of criteria;

- The sensitivity of the device to measuring shear stress,
- The amount of sample in the hand is sufficient to measure,
- The temperature can be kept constant during operation,
- Easy cleaning of the device

Classification

Single point measuring instruments:

- The shear stress corresponding to a single shear rate is determined.
- These instruments are suitable for measuring Newtonian systems.

  * Capillary viscometers
  * Falling ball (sphere) viscometers

Multi-point measuring instruments:

- It is a device that can be applied at more than one shear rate.
- It is used to determine the flow properties of Newtonian and non-Newtonian systems.

  * Rotational type viscometers (Rotating cylinder)

Capillary viscometers

TYPE	MODEL
Glass capillary types	Ostwald Cannon-Fenske Ubbelohde
Cylinder-piston type	Instron Rheometer
Orifice type	Engler Saybolt Redwood

Capillary viscometers

- In these devices the liquid flow down from a tube and the viscosity is determined by measuring the time for the liquid to flow between two points on the capillary.
- During operation, it is important to keep the temperature and fluid volume constant and to keep the tool upright.
- Its principle depends on the following equation derived from the «**Poiseuille equation**».
-
- The type of viscosity measured with this method is **kinematic viscosity**

Poiseuille equation

$$\eta = \frac{\Pi \, . r^4 . \, P. \, t}{8. \, v. \, l}$$

η = viscosity
Π = 3.14
r = capillary tube diameter (cm)
P = pressure (dyn/cm^2)
t = time (sn)
l = capillary tube lenght (cm)
v = volume of the liquid flow in t time (cm^3)

- ✓ The fluid is added to the bulb on the right side and is pulled by a suction to the upper mark on the bulk in the reservoir. The fluid is then allowed to flow back down through the capillary. The time for liquid to pass between 2 timing marks is measured.

- ✓ The following equation is simpified form of poiseuille equation and it is used for calculating the kinematic viscosity.

$$\eta = t \times C$$

η: kinematic viscosity, cS
t : flow time, s
C: constant

Falling ball viscometer

- The device consists of a cylindrical tube having a graduated section and a stainless steel ball which falls in the liquid. The time required for the ball travel between the marks is measured.

- The most important disadvantage of this method is the necessity of measuring large volumes and clear liquids.

- Viscosity is calculated from the following equation which is derived from the «**STOKES equation**».

$$\eta = F\,(Sk - Sf)\,K$$

η : viscosity coefficient, cP
F : falling time, s
Sk : density for ball (factory-supplied)
Sf : density of the liquid at the same temperature
K : constant for ball (supplied by the factory).

Rotational viscometers

1. **Rotating spindle viscometer**
   *Brookfield

2. **Coaxial cylinder viscometers**
(Cup and bob, couette viscometers)
   *Haake rotovisko
   *Stormer
   *Searle

3. **Cone and Plate viscometers**
   *Ferranti Shirley

Brookfield viscometer

- These viscometers have a rotating spindle connected to the motor of the device by a spring and capable of rotating at different speeds.
- There is a difference between the rotation speed of motor and the rotary shaft. This difference is expressed as the rotation momentum or torque (S)
- in synchro-lectic models viscosity is calculated as:

$$F = \eta / U . S$$

η : viscosity coefficient, cP
F : viscosity measurement factor (factory)
U : revolutions per minute (speed factor)
S : rotational momentum (from scale)

- In digital models, viscosity is directly read (cP or Pa.s)from monitor of the apparatus,

Coaxial cylinder viscometer (Cup and Bob type)

Test material is placed between the cylinders called as Bob and Cup

- Cup is the stationery part (outer) and bob is the cylinder in contact with the liquid inside the fluid.
- As bob rotates, the liquid drifts around itself, which causes a torque (rotational momentum).
- This torque is proportional to the shear stress of the liquid.

Haake Rotovisco

- **Coaxial cylindric viscometer**
- It consists of two interlocked cylinders with a small opening between them.
- Materials for testing are applied between these cylinders.

Stormer

- **Couette type**
- (Also Cup and bob)

- Fluid to be tested is filled between the cylinders and balanced with a mass. Systems is let to turn 100 times and the mass changed with a higher one

- These weighs help the bob to rotate inside the cup.

Cone and plate type

- Consists of a cone with an angle less than 5°, and a flat plate.
- The fluid sample fills the narrow space between these two.
- The cone speed (rotation) can be adjusted by a motor

Advantages

- ease of measurement due to constant shear rate
- uses very small sample sizes
- wide range of viscosity can be measured

Penetrometer

- It is a tool that is used to measure consistency in petri dishes like petroleum jelly, a pin pointed needle and a funnel.
- It is used to measure the penetration rate of the semi-solid.
- They are in semi-rigid controls on pharmacopoeias.

Viscoelasticity

Elastic materials strain when stretched and immediately return to their original state once the stress is removed.

- Viscoelastic materials show both viscous and elastic characteristics when undergoing deformation.
- Viscoelasticity of materials can be measured with

  *** Oscillation tests**

  *** Creep tests**

- These tests are suitable for semisolids, creams, gels, foods, cosmetics which can show viscoelastic properties.
- The analysis depends on mechanical properties of materials. In these analysis, the deformation or stress is measured as a function of time.
- If the system is a elastic solid, the deformation is reversibl while in viscous liquids deformation (flow) is irreversibl.