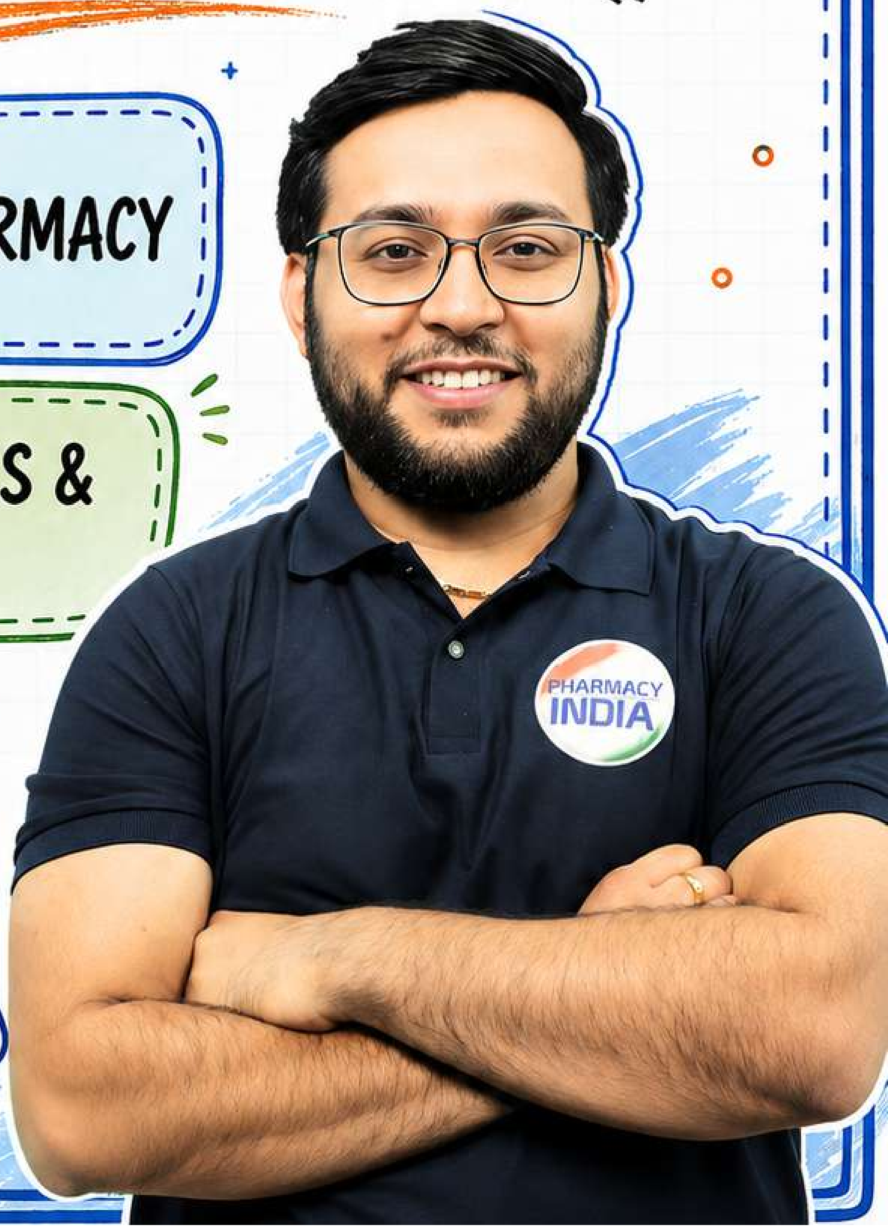
PHARMACY INDIA

PHARMACIST BOOSTER

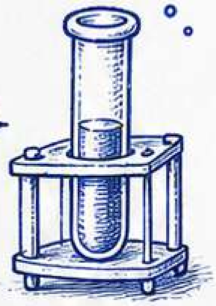
PHYSICAL PHARMACY

MICROMERITICS & RHEOLOGY



MICROMERITICS - INTRODUCTION

- Micromeritics is the science and technology of small particles.
- The term was named by Dalla Valle.
- It deals with the study of the fundamental and derived properties of individual particles and collections of particles.



CLASSIFICATION OF PROPERTIES

FUNDAMENTAL PROPERTIES

- Surface area
- Particle size and size distribution
- Particle number
- Particle volume
- Particle shape

DERIVED PROPERTIES

- Porosity
- Density
- Bulkiness
- Flow

FUNDAMENTAL PROPERTIES OF PARTICLES

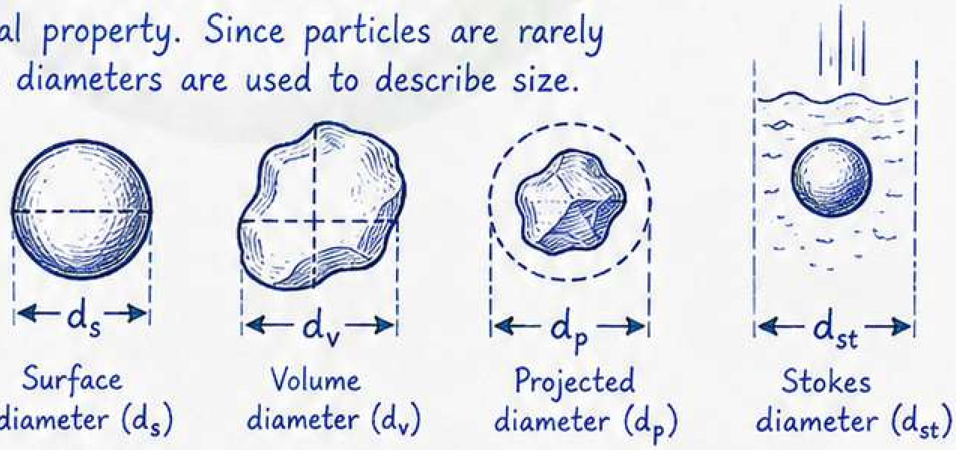
These are properties that relate to individual particles.

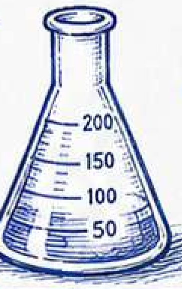
PARTICLE SIZE AND PARTICLE SIZE DISTRIBUTION

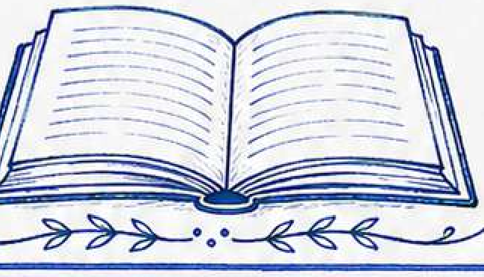
Particle size is a fundamental property. Since particles are rarely perfectly spherical, equivalent diameters are used to describe size.

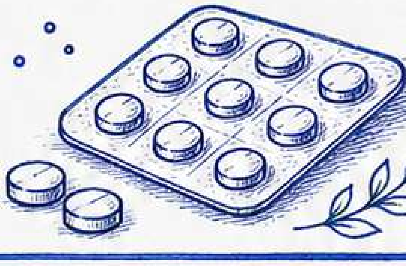
EQUIVALENT DIAMETERS

- Surface diameter (d_s)
- Volume diameter (d_v)
- Projected diameter (d_p)
- Stokes diameter (d_{st})





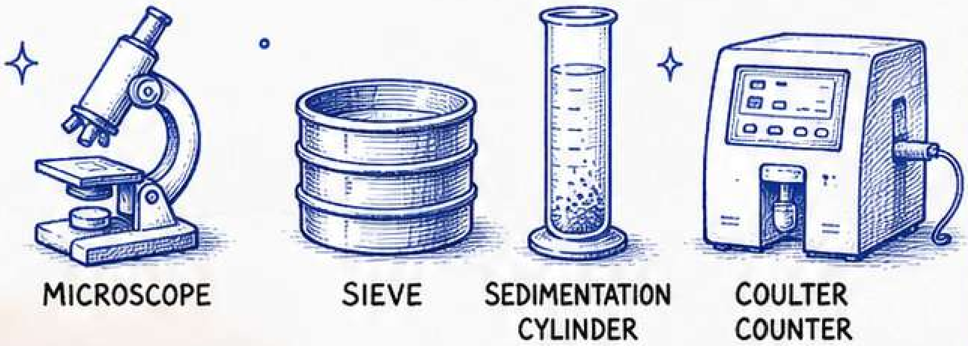




PARTICLE SIZE DETERMINATION

METHODS OF PARTICLE SIZE DETERMINATION

1. Microscopy
2. Sedimentation
3. Sieving
4. Conductivity / Electrical stream sensing zone



METHOD	SIZE RANGE (µm)	IMPORTANT POINTS
1. Optical microscope	0.2 to 100 µm	Feret, Martin, and projected diameters measured; only 2D measurements, thickness not estimated.
2. Scanning electron microscope (SEM)	0.01 to 1000 µm	Detects surface morphology and fine details.
3. Transmission electron microscope (TEM)	0.001 to 0.1 µm	Detects agglomerates and particles of more than one type.
4. Light microscope	0.1 to 1000 µm	Diameter measured only in 2D; thickness not estimated.
5. Sieving	50 to 1500 µm	Instrument: mechanical shaker; standard sieves calibrated by the National Bureau of Standards.
6. Sedimentation	1 to 200 µm	Instruments: Andreasen pipette or Andersen pipette (gravity sedimentation), balance method, hydrometer method; sedimentation rate studied by Stoke's law.
7. Conductivity / Electrical stream sensing zone	0.5 to 500 µm	Instrument: Coulter counter; also called Coulter current, Royco, HIAC, or stream sensing method; determines number of particles, particle volume, and equivalent volume diameter.

NOTE: COULTER COUNTER ALSO DETERMINES PARTICLE NUMBER AND PARTICLE VOLUME.

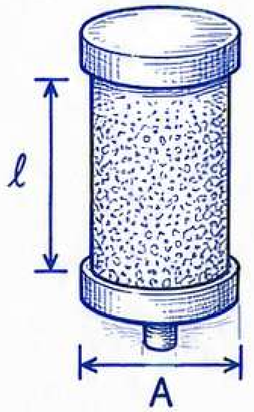
SURFACE AREA & DERIVED PROPERTIES OF POWDERS

1. SURFACE AREA

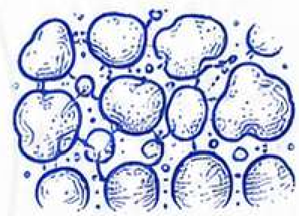
The surface area of a powder can be determined by two main methods.

Feature	Method 1: Adsorption Method	Method 2: Air Permeability Method
Principle	surface area measured by the volume of nitrogen absorbed to form a monolayer.	surface area measured by the rate at which gas or liquid permeates through a powder bed.
Equation(s) used	BET equation	Poiseuille's equation / Kozeny-Carman equation
Variables	V = volume of gas adsorbed per gram of powder at pressure P P_0 = saturated vapour pressure of liquefied nitrogen b = adsorption constant V_m = volume of gas forming a monolayer	A = cross-sectional area ΔP = pressure difference t = time of flow ℓ = length of sample holder ε = porosity S_v = surface area per gram of powder η = viscosity of air K = constant V = volume of air

POWDER BED (PACKED COLUMN)



PORE STRUCTURE IN POWDER

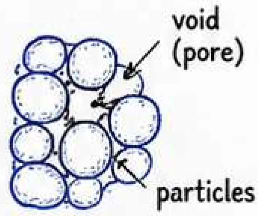


2. DERIVED PROPERTIES OF POWDERS

Bulk volume (V_b): volume occupied by the powder, including particles and void spaces.

Void volume $(v) = V_b - V_p$, where V_p = true volume.

Porosity $(\varepsilon) = \dfrac{V_b - V_p}{V_b} = 1 - \dfrac{V_p}{V_b}$.



3. DENSITY

Type of density	Definition / Expression	Includes	Determined by / Method
True density	weight of powder / true volume	solid material only (no pores)	gas displacement method, helium pycnometer used, gases like helium or nitrogen may be used.
Tapped density	mass of powder / volume of powder bed after tapping	powder plus interparticle void spaces	increased bulk density obtained after mechanically tapping a container.
Granule density	granule weight / granule volume	powder plus intraparticle space	determined by mercury displacement method.
Bulk density	mass of powder / bulk volume	powder plus interparticle and intraparticle spaces	determined by bulk density apparatus.

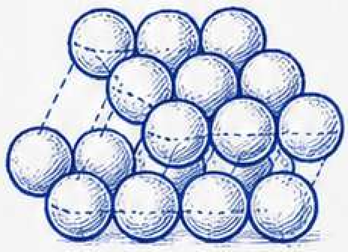
PACKING ARRANGEMENT & FLOW PROPERTIES

1. PACKAGING ARRANGEMENTS

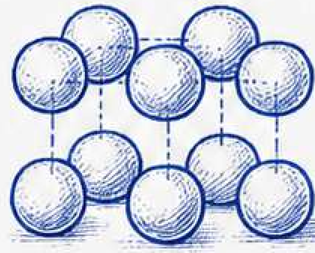
Powder beds of uniform-sized spheres can assume two ideal packing arrangements.

- Closest or rhombohedral packing – 26% porosity.
- Most open, loosest, or cubic packing – 48% porosity.

Closest packing (rhombohedral)



Cubic packing (most open)



2. FLOW PROPERTIES

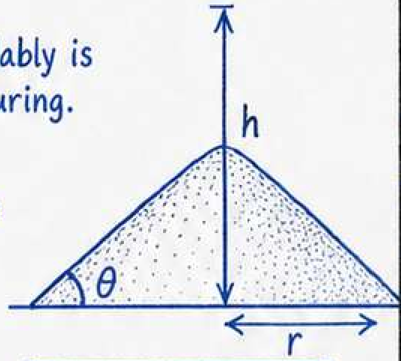
The ability of a powder to flow reliably is crucial in pharmaceutical manufacturing.

Angle of repose

The maximum angle possible between the surface of a pile of powder and the horizontal plane.

Methods to determine:

- Fixed cone method
- Rotating cylinder method
- Tilted box method



$$\boxed{\theta = \tan^{-1}\left(\frac{h}{r}\right)}$$

Angle of repose	Flow property
< 25°	Excellent
25–30°	Good
30–40°	Passable / Satisfactory
40–50°	Poor
> 50°	Very poor

Carr's index (Compressibility index) =

$$\frac{(\text{Tapped density} - \text{Bulk density})}{\text{Tapped density}} \times 100$$

Hausner's ratio =

$$\frac{\text{Tapped density}}{\text{Bulk density}}$$

Dispersibility (%) =

$$\frac{\text{Weight of powder in a watch glass}}{\text{Initial weight of sample}} \times 100$$

3. FACTORS AFFECTING FLOWABILITY

Factor	Effect
Particle size and distribution	fines increase cohesiveness and reduce flow; a mix of coarse and fine particles may fill voids and increase forces.
Particle shape and texture	spherical particles flow better, rough surfaces increase friction.
Porosity	lower density gives better flow rate.
Density	high density can reduce flow.
Hygroscopicity	increases cohesion and adhesion, decreasing flow.
Electrostatic charge	increases cohesiveness and reduces flow.

NOTE

Brownian motion is the random movement of particles in a fluid and is observed when particle size is reduced to about 2 μm or less.

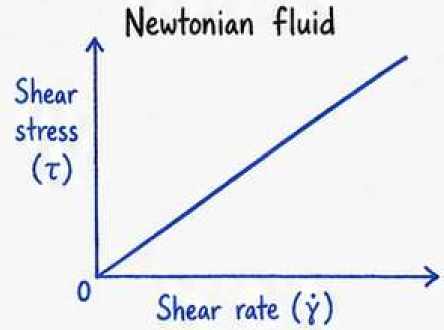
RHEOLOGY – INTRODUCTION & BASIC TERMS

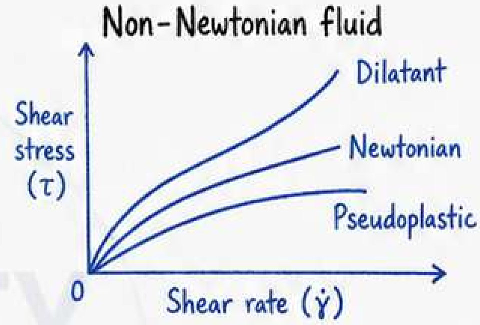
- The term rheology was suggested by Bingham and Crawford from the Greek words rheo (to flow) and logos (science).
- Rheology is the science that deals with the flow of liquids and the deformation of solids.

NEWTONIAN AND NON-NEWTONIAN SYSTEMS

Newtonian flow	Non-Newtonian flow
• follows Newton's law of viscosity • shearing stress is directly proportional to shear rate • viscosity remains constant irrespective of applied stress • examples: water, glycerine, chloroform, castor oil, olive oil, ethanol, syrup solution, very dilute colloidal solutions.	• does not follow Newton's law • viscosity changes with applied stress or shear rate • rheology often determined with Brookfield viscometer • examples: concentrated colloidal solutions, emulsions, suspensions, ointments.

RHEOGRAMS

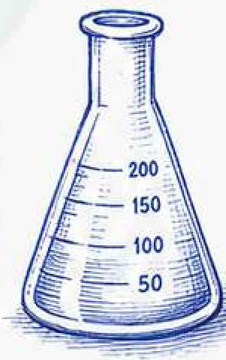




$$\text{Viscosity } \eta = \frac{\text{Shearing stress}}{\text{Rate of shear}} = \frac{F}{G} = \frac{F'/A}{dv/dr}$$

VISCOSITY AND ITS MEASUREMENT

Term	Definition
Viscosity (η)	resistance of a fluid to flow; CGS unit: poise.
Coefficient of viscosity	force per unit area required to maintain unit difference in velocity between two parallel layers of liquid one unit distance apart; SI unit: pascal-second (Pa·s).
Fluidity (ϕ)	$1/\eta$.
Kinematic viscosity	η/ρ, where ρ is density of the liquid; unit: stokes or centistokes.

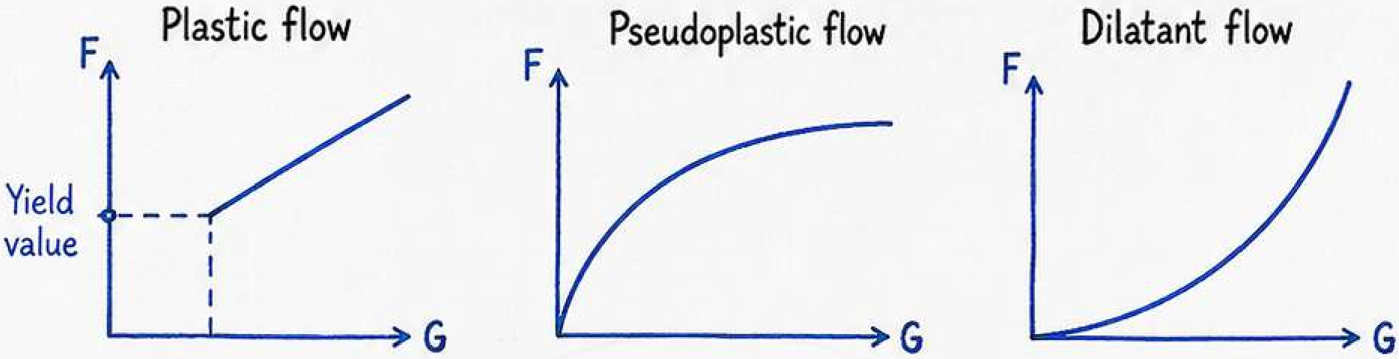


CLASSIFICATION OF FLOW BEHAVIOUR

- Flow of fluid
  - Newtonian flow
  - Non-Newtonian flow
    - Time independent
      - Plastic
      - Pseudoplastic
      - Dilatant
    - Time dependent
      - Thixotropy
      - Rheopexy

TIME-INDEPENDENT NON-NEWTONIAN FLOW

RHEOGRAMS (F vs G)



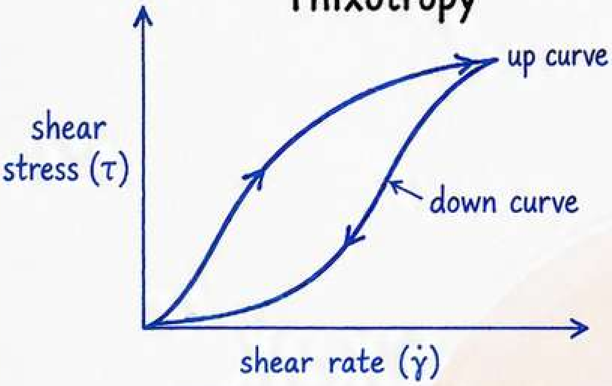
F = shearing stress   G = rate of shear

Feature	Plastic flow	Pseudoplastic flow	Dilatant flow
Definition / Description	curve does not pass through origin; material behaves like an elastic solid until yield value is reached; beyond yield value it flows linearly like a Newtonian fluid; term used for plastic fluids is mobility.	curve starts at origin; no yield value; viscosity decreases as shear rate increases because polymer chains align in the direction of flow.	curve starts at origin; no yield value; viscosity increases as shear rate increases because particles pack more closely and interparticle friction increases.
Also known as	Bingham bodies	Shear-thinning system	Shear-thickening system
Yield value	Present	Absent	Absent
Viscosity behavior	Constant after yield point	Decreases with increase in shear rate	Increases with increase in shear rate
Notes / Examples	exhibited by flocculated suspensions; examples zinc oxide suspension in mineral oil, certain paints, ointments, concentrated flocculated suspensions.	seen with natural and synthetic gums; examples tragacanth, sodium alginate, methyl cellulose, sodium CMC, polymer dispersions.	seen with high concentration suspensions; examples corn starch suspension, kaolin in water, zinc oxide in water, inorganic pigment suspensions.

TIME-DEPENDENT NON-NEWTONIAN FLOW

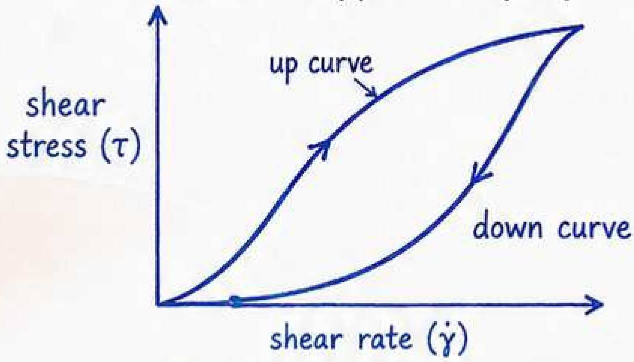
RHEOGRAMS (TYPICAL HYSTERESIS LOOPS)

Thixotropy



DOWN CURVE SHIFTS LEFT OF THE UP CURVE

Antithixotropy / Rheopexy



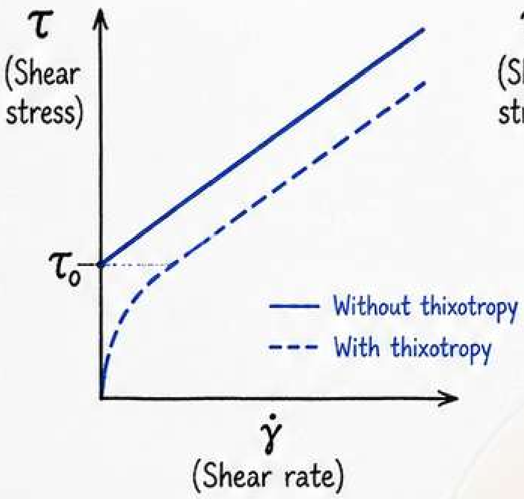
DOWN CURVE SHIFTS RIGHT OF THE UP CURVE

Parameter	Thixotropy	Negative Rheopexy / Antithixotropy
Definition / description	a phenomenon in which a system undergoes a reversible Gel → Sol → Gel transformation; viscosity decreases as a function of time under shear and recovers on standing.	a Sol → Gel → Sol type behavior in which viscosity increases on the down curve; also called rheopexy in this comparison context.
System type	Gel – Sol – Gel	Sol – Gel – Sol
Shear behavior	shear-thinning system; down curve shifts left of the up curve	shear-thickening type behavior; down curve shifts right of the up curve
Time dependence	at rest the system behaves like a gel; under shear the structure breaks and gel changes to sol; on standing, sol changes to gel again.	on repeated shear cycling, the consistency increases until eventually the up and down curves coincide.
Examples	procaine penicillin G (40–70% w/v in water), bentonite gel, petrolatum, Manuka honey is a thixotropic material.	low solid content flocculating systems, magnesia magma at equilibrium forms solution.

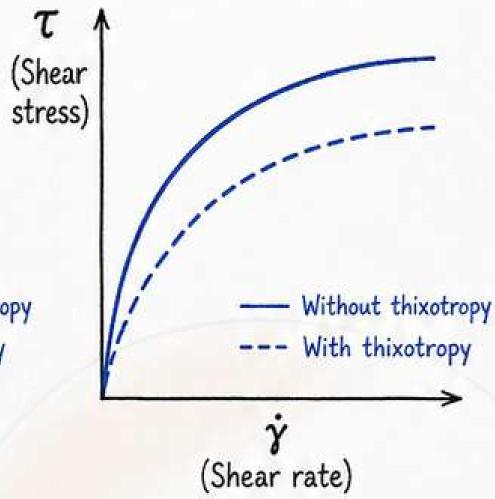
NOTE: Rheopexy is a phenomenon in which a sol transforms to a gel state more readily rather than remaining a sol at rest.

THIXOTROPIC EFFECTS ON FLOW SYSTEMS

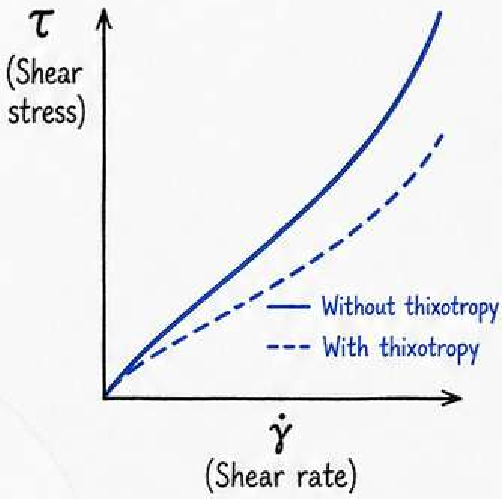
1. PLASTIC FLOW (BINGHAM BODIES)



2. PSEUDOPLASTIC FLOW (SHEAR-THINNING)



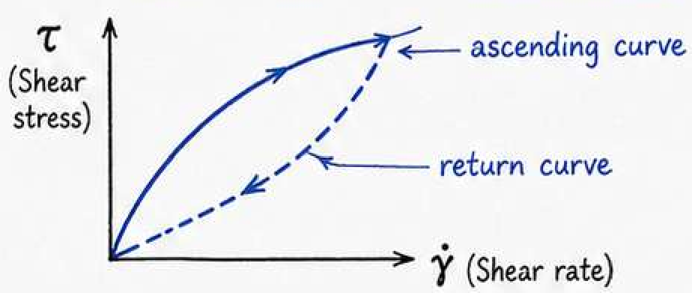
3. DILATANT FLOW (SHEAR-THICKENING)



FLOW TYPE	WITHOUT THIXOTROPY	WITH THIXOTROPY	EXAMPLES
PLASTIC FLOW (BINGHAM BODIES)	• curve does not pass origin; requires a yield value before flow starts; then becomes linear.	• shows a hysteresis loop; down curve shifted left; viscosity decreases under shear and recovers slowly.	• Bentonite gel • Petrolatum
PSEUDOPLASTIC FLOW (SHEAR-THINNING)	• viscosity decreases with increase in shear; no yield value.	• additional viscosity loss occurs over time under shear; hysteresis loop forms.	• Tragacanth • Sodium alginate • Methylcellulose dispersions
DILATANT FLOW (SHEAR-THICKENING)	• viscosity increases with increase in shear; common in high solid suspensions.	• after shear removal, viscosity recovers slowly; gel-sol related reversible behavior may be shown diagrammatically.	• Quicksand • Corn starch suspension

NOTE:

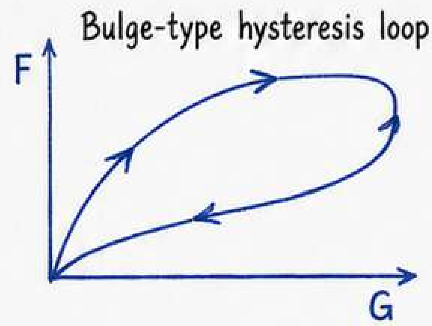
In thixotropy, a hysteresis loop is formed because the return curve lies to the left of the ascending curve.

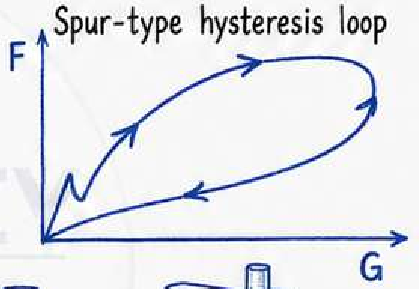


MEASUREMENT OF THIXOTROPY & VISCOMETERS

MEASUREMENT OF THIXOTROPY

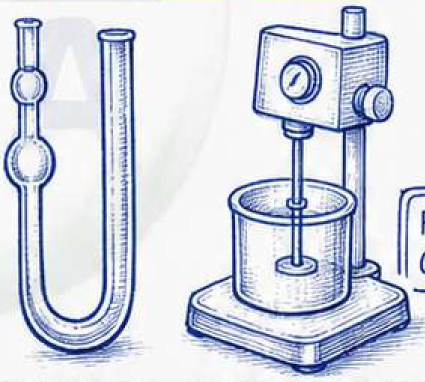
Type	Rheogram / Description	Example
Bulges	Rheogram of a thixotropic material showing a bulge in the hysteresis loop.	bentonite 10–15%
Spurs	Rheogram showing a spur value (γ) in the hysteresis loop; γ is a sharp point of structural breakdown in the viscometer at low shear rate.	procaine penicillin gel





DETERMINATION OF RHEOLOGICAL PROPERTIES (VISCOMETERS)

Type of viscometer	Used for	Examples
Single point viscometer	used for Newtonian flow	falling sphere viscometer, capillary viscometer
Multi point viscometer	used for non-Newtonian flow	cup and bob, cone and plate



F = shearing stress
G = rate of shear

Viscometer	Principle / method	Application / used for
1. Capillary viscometer = Ostwald viscometer	time of flow through a capillary under gravity is compared with a liquid of known viscosity; based on Poiseuille's law.	used for relative viscosity and measurement of Newtonian fluids.
2. Falling sphere viscometer = Hoeppler viscometer	time taken for a ball to fall between two marks is measured; usable over about 0.5 to 200,000 poise.	used for Newtonian fluids.
3. Rotational viscometer = cup and bob viscometer	torque required to rotate the bob in the liquid-filled cup is measured; torque is proportional to viscosity.	used for Newtonian and non-Newtonian fluids; determines viscosity, yield value, and thixotropy.
4. Cone and plate viscometer	sample is sheared between a stationary plate and a rotating cone.	used for rheological evaluation of pharmaceutical semisolids.
5. Brookfield viscometer = spindle type	torque required to rotate a spindle in a fluid indicates viscosity.	used to study rheological properties of suspensions.

$$\frac{\eta_1}{\eta_2} = \frac{\rho_1 t_1}{\rho_2 t_2}$$

Poiseuille's law relates viscosity to capillary flow.