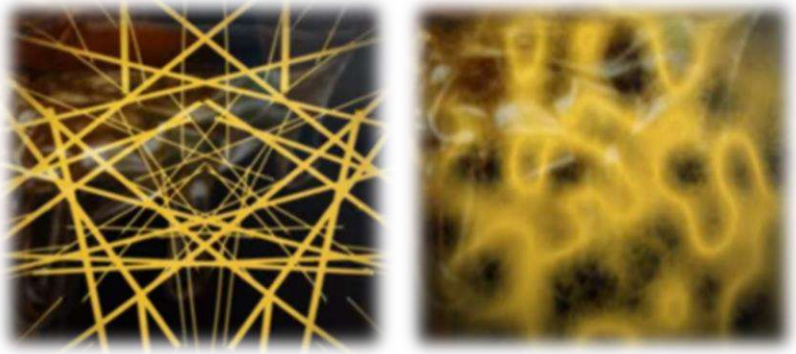
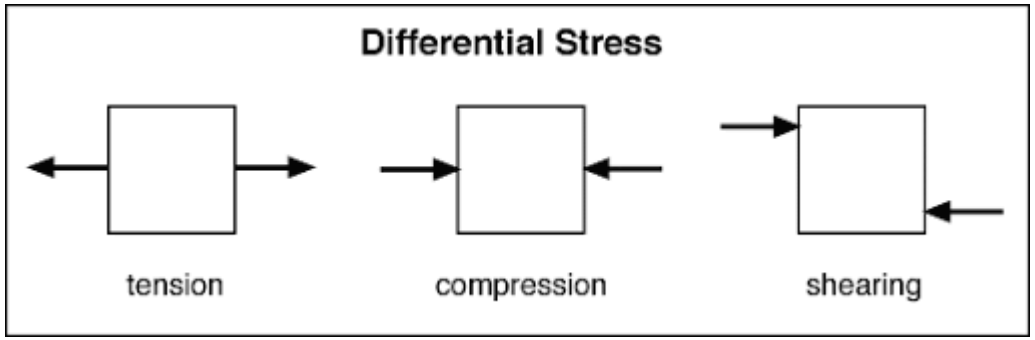
RHEOLOGY

- The term "**rheology**" from the Greek rheo ("to flow") and logos ("science"), describe the **flow of liquids** and the **deformation of solids**.
- The study of material's flow behaviour under applied deformation forces (stress).



morphology

Chemical structure



Outside forces:
Pulled/ compressed / sheared

Ambient conditions

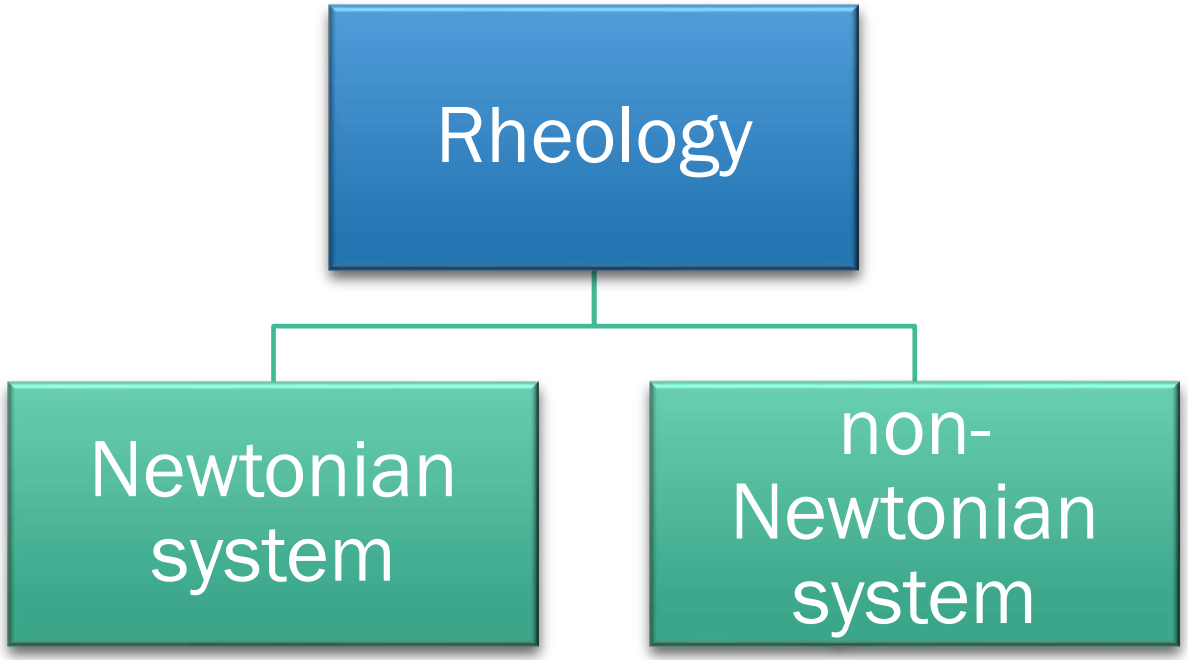
- Viscosity is an expression of the resistance of a fluid to flow; the higher the viscosity, the greater is the resistance
- simple liquids can be described in terms of absolute viscosity.
- Rheologic properties of heterogeneous dispersions are more complex, however, and cannot be expressed by a single value.
- principles of rheology are used to study paints, inks, doughs, road-building materials, cosmetics, dairy products, and other materials.

IMPORTANCE OF RHEOLOGY IN PHARMACY AND ITS APPLICATION IN THE FORMULATION AND PHARMACEUTICAL PRODUCTS

- Manufacturers of medicinal and cosmetic creams, pastes, and lotions must be capable of producing products with acceptable consistency and smoothness and reproducing these qualities each time a new batch is prepared.
- in-process material periodically during manufacture to determine its “feel” and “body” and judge proper consistency.
- The rheology of a particular product, which can range in consistency from fluid to semisolid to solid, can affect its patient acceptability, physical stability, and even biologic availability.
  - For example, viscosity has been shown to affect absorption rates of drugs from the gastrointestinal tract.

- Rheologic properties of a pharmaceutical system can influence the selection of processing equipment used in its manufacture.
- Rheology is involved in the mixing and flow of materials, their packaging into containers, and their removal prior to use, whether this is achieved by pouring from a bottle, extrusion from a tube, or passage through a syringe needle.

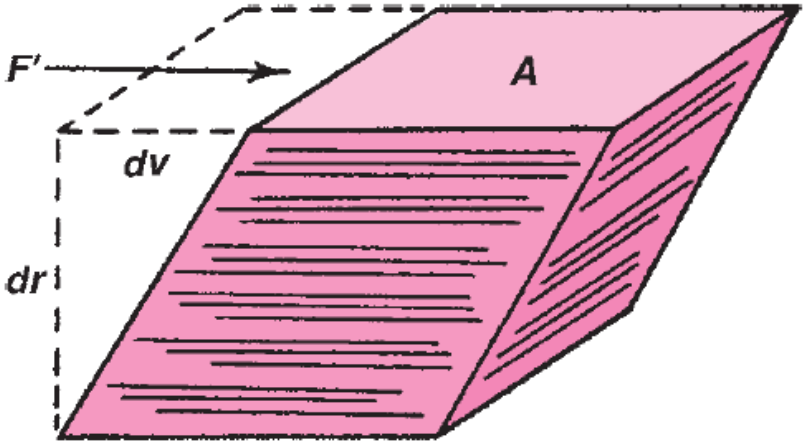
- Classification of materials according to **types of flow and deformation:**



- The choice depends on whether or not their flow properties are in accord with **Newton's law of flow.**

NEWTONIAN SYSTEMS

NEWTON'S LAW OF FLOW



- Consider a "block" of liquid consisting of parallel plates of molecules, similar to a deck of cards
- If the bottom layer is fixed in place and the top plane of liquid is moved at a constant velocity, each lower layer will move with a velocity directly proportional to its distance from the stationary bottom layer
- The difference of velocity, dv, between two planes of liquid separated by an infinitesimal distance, dr, is the velocity gradient or **rate of shear**, **dv/dr.**
- The force per unit area, **F'/A**, required to bring about flow is called the **shearing stress** and is given the symbol **F.**

- the higher the viscosity of a liquid, the greater is the force per unit area (shearing stress) required to produce a certain rate of shear.
- Hence, **rate of shear should be directly proportional to shearing stress**

$$\frac{F'}{A} = \eta \frac{dv}{dr}$$

where η is the coefficient of viscosity, usually referred to simply as viscosity.

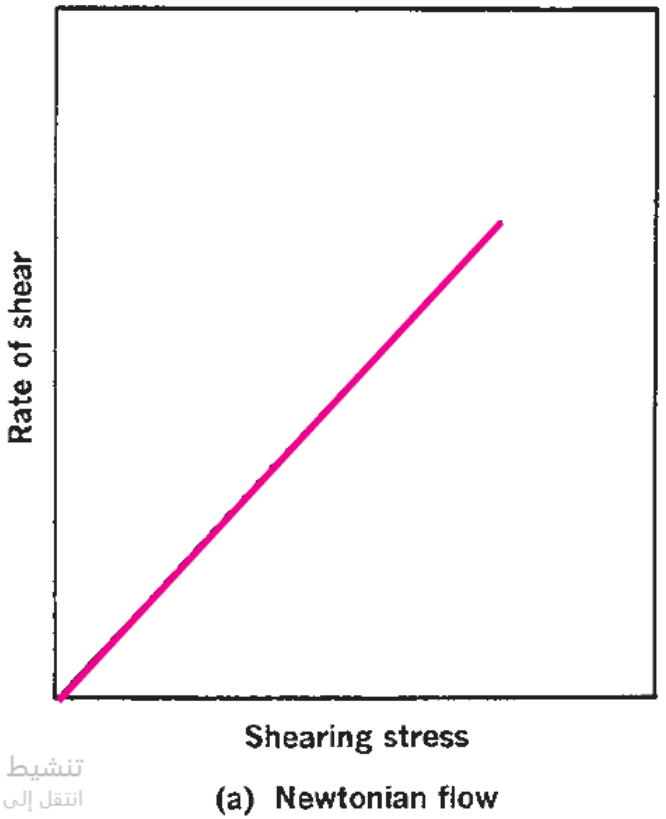
- Rate of shear is given the symbol G.

- Equation is frequently written as

$$\eta = \frac{F}{G} = \frac{SS}{SR}$$

where F=F'/A and G=dv/dr

- A representative flow curve, or **rheogram**, obtained by plotting F versus G for a Newtonian system, a straight line passing through the origin is obtained.



(a) Newtonian flow

- The unit of viscosity is the **poise,** defined as the shearing force required to produce a velocity of 1 cm/sec between two parallel planes of liquid each 1 cm2 in area and separated by a distance of 1 cm.

- The cgs units for poise are dyne sec cm−2.

$$\eta = \frac{F' dr}{A\, dv} = \frac{\text{dynes} \times \text{cm}}{\text{cm}^2 \times \text{cm/sec}} = \frac{\text{dyne sec}}{\text{cm}^2}$$

$$\frac{\text{dyne sec}}{\text{cm}^2} = \frac{\text{g} \times \text{cm/sec}^2 \times \text{sec}}{\text{cm}^2} = \frac{\text{g}}{\text{cm sec}}$$

- A more convenient unit for most work is the centipoise (cp, plural cps), 1 cp being equal to 0.01 poise.
- **Fluidity**, **φ**, a term sometimes used, is defined as the reciprocal of viscosity:

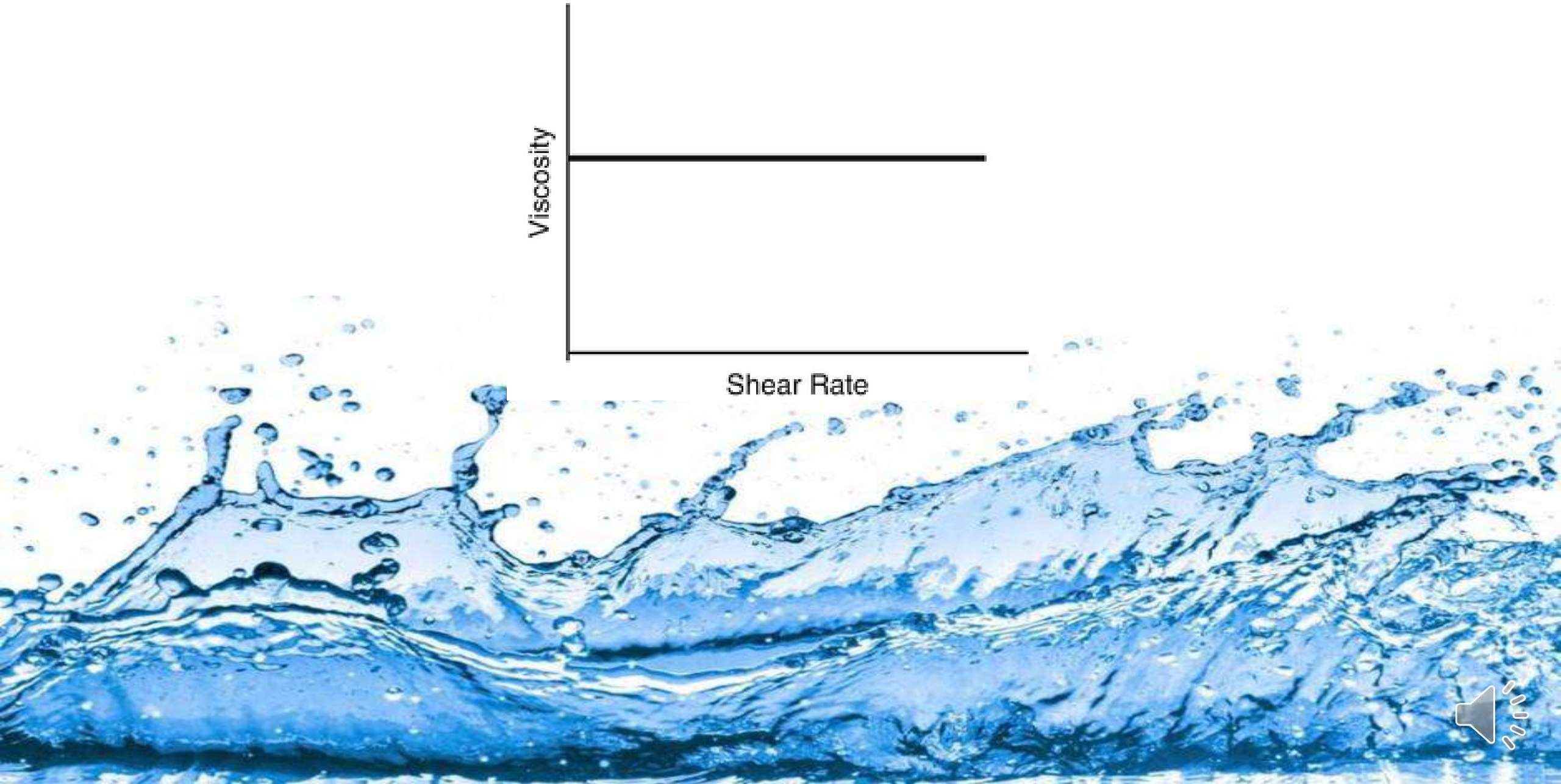
$$\phi = \frac{1}{\eta}$$

TEMPERATURE DEPENDENCE AND THE THEORY OF VISCOSITY

- Raising temperature of liquids ⟶ the viscosity decreased and the fluidity increased
- More energy is required to break bonds and permit flow in liquids composed of molecules that are associated through hydrogen bonds

VISCOSITY OF GLYCERIN AT SEVERAL TEMPERATURES*

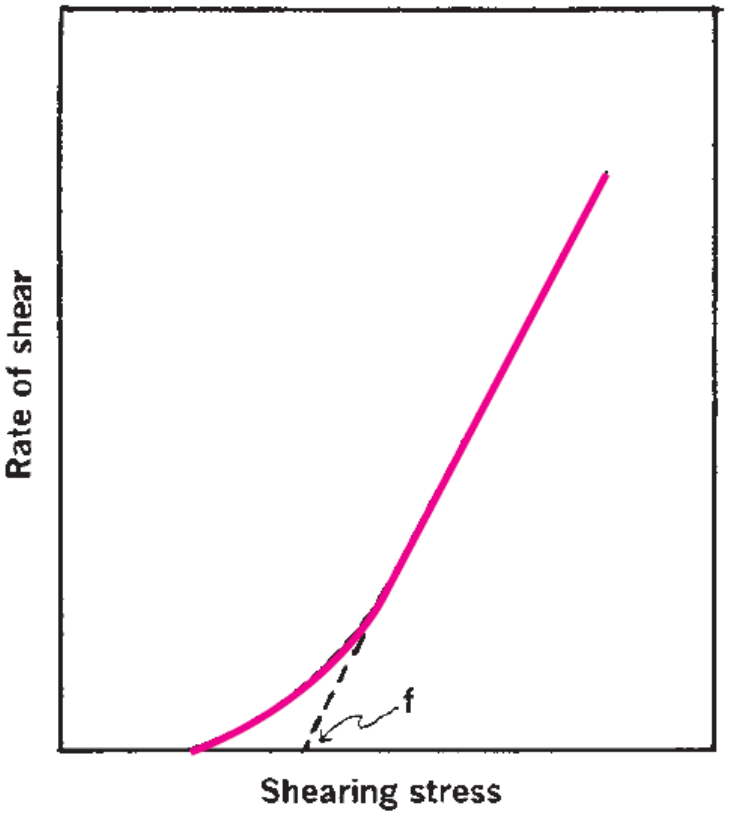
Temperature (°C)	−42	−20	0	6	15	20	25	30
Temperature (K)	231	253	273	279	288	293	298	303
$1/T(K^{-1})$	0.00432	0.00395	0.00366	0.00358	0.00347	0.00341	0.00336	0.00330
η (cp)	6.71×10^6	1.34×10^5	12110	6260	2330	1490	954	629
$\ln \eta$	15.719	11.806	9.402	8.742	7.754	7.307	6.861	6.444


Viscosity
Shear Rate

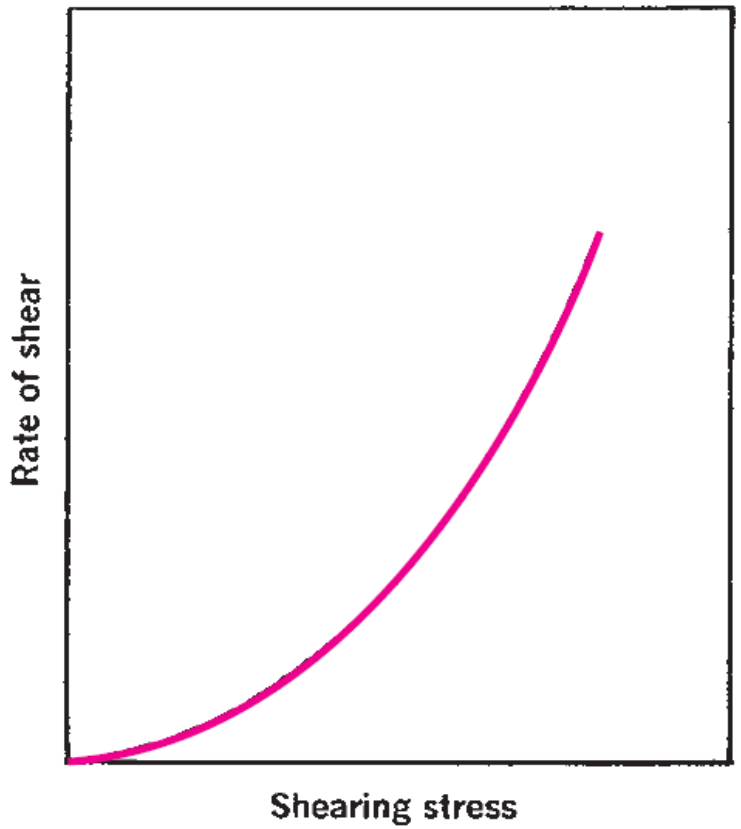
NON-NEWTONIAN SYSTEMS

- The majority of fluid pharmaceutical products are not simple liquids and do not follow Newton's law of flow.
- These systems are referred to as **non-Newtonian.**
- Non-Newtonian behavior is generally exhibited by liquid and solid heterogeneous dispersions such as colloidal solutions, emulsions, liquid suspensions, and ointments.
- When non-Newtonian materials are analyzed in a rotational viscometer and results are plotted, various consistency curves, representing three classes of flow, are recognized:

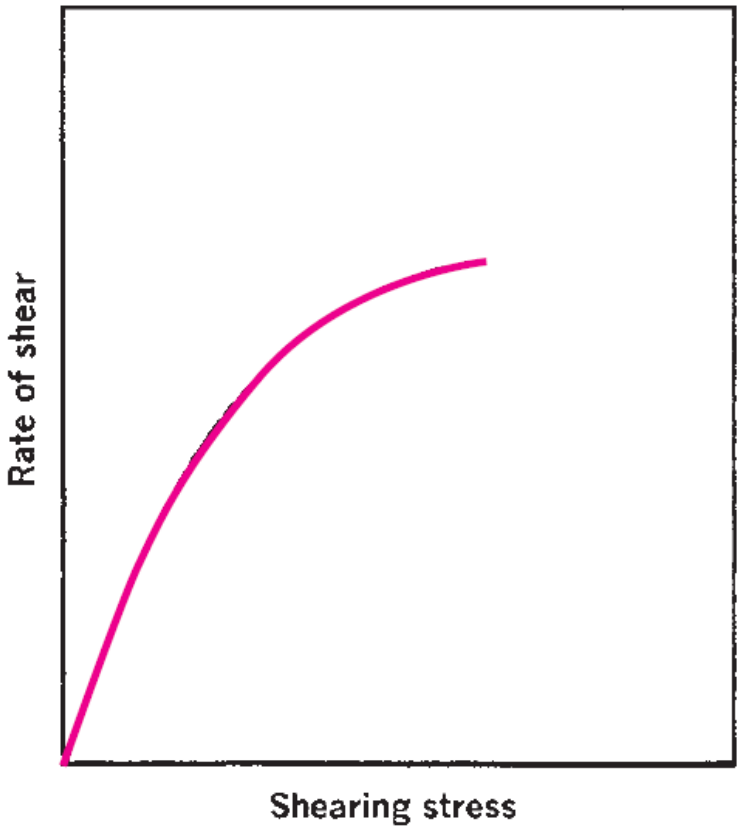
    1) Plastic
    2) Pseudoplastic
    3) dilatant



(b) Simple plastic flow



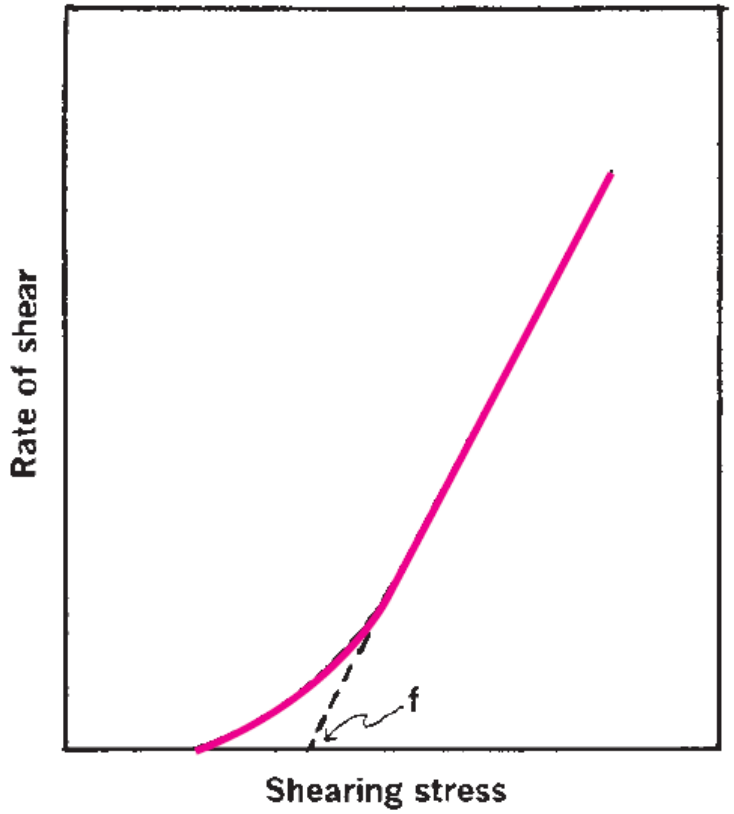
(c) Simple pseudoplastic flow



(d) Dilatant flow

PLASTIC FLOW

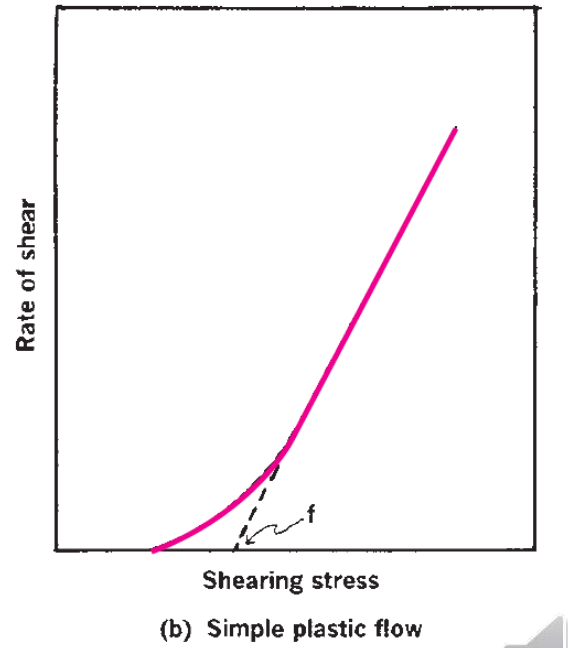
- materials that exhibit plastic flow are known as **Bingham bodies**
- Plastic flow curves do not pass through the origin but rather intersect the shearing stress axis (or will if the straight part of the curve is extrapolated to the axis) at a particular point referred to as the **yield value**
- A Bingham body does not begin to flow until a shearing stress corresponding to the yield value is exceeded.
- At stresses below the yield value, the substance acts as an elastic material.



(b) Simple plastic flow

- The rheologist classifies Bingham bodies, that is, those substances that exhibit a yield value, as solids, whereas substances that begin to flow at the smallest shearing stress and show no yield value are defined as liquids.
- The slope of the rheogram in Figure b is termed the **mobility**, analogous to fluidity in Newtonian systems, and its reciprocal is known as the plastic viscosity, U.
- The equation describing plastic flow is

$$U = \frac{F - f}{G}$$



(b) Simple plastic flow

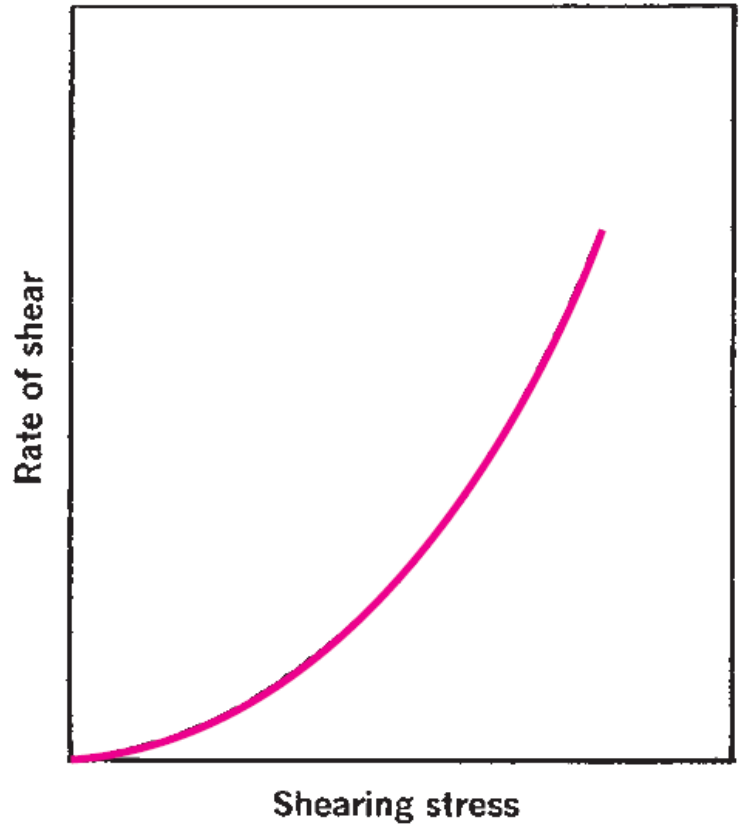
where f is the yield value, or intercept, on the shear stress axis in dynes/cm2,

- Plastic flow is associated with the presence of flocculated particles in concentrated suspensions.
- A yield value exists because of the contacts between adjacent particles (brought about by van derWaals forces), which must be broken down before flow can occur.
- Consequently, the yield value is an indication of force of flocculation: **The more flocculated the suspension, the higher will be the yield value.**

- Frictional forces between moving particles can also contribute to yield value.
- a plastic system resembles a Newtonian system at shear stresses above the yield value.

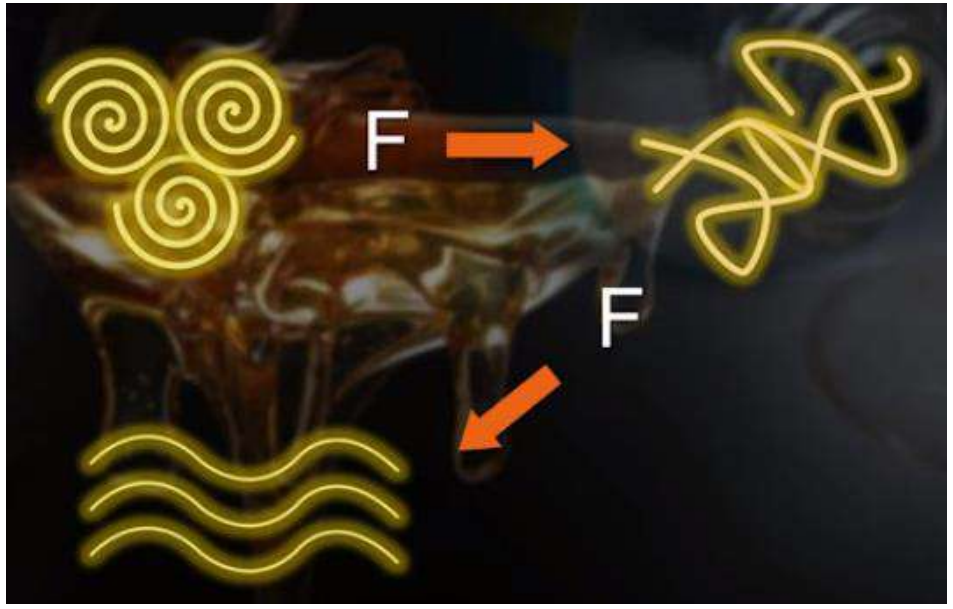
PSEUDOPLASTIC FLOW (SHEAR THINNING)

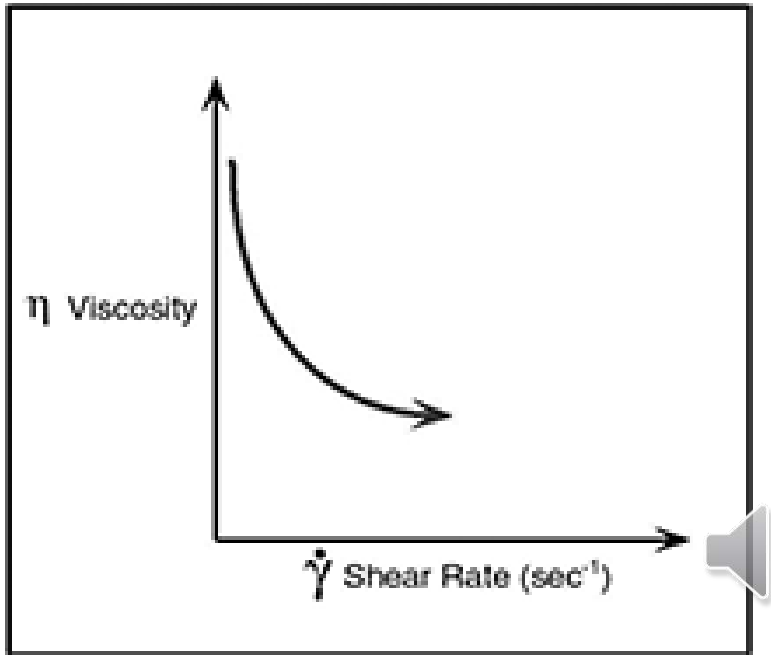
- Many pharmaceutical products, including liquid dispersions of natural and synthetic gums exhibit pseudoplastic flow.
- Pseudoplastic flow is typically exhibited by **polymers in solution**
- As seen in Figure c, the consistency curve for a pseudoplastic material begins at the origin (or at least approaches it at low rates of shear).
- Therefore, there is no yield value as there is in a plastic system.



(c) Simple pseudoplastic flow

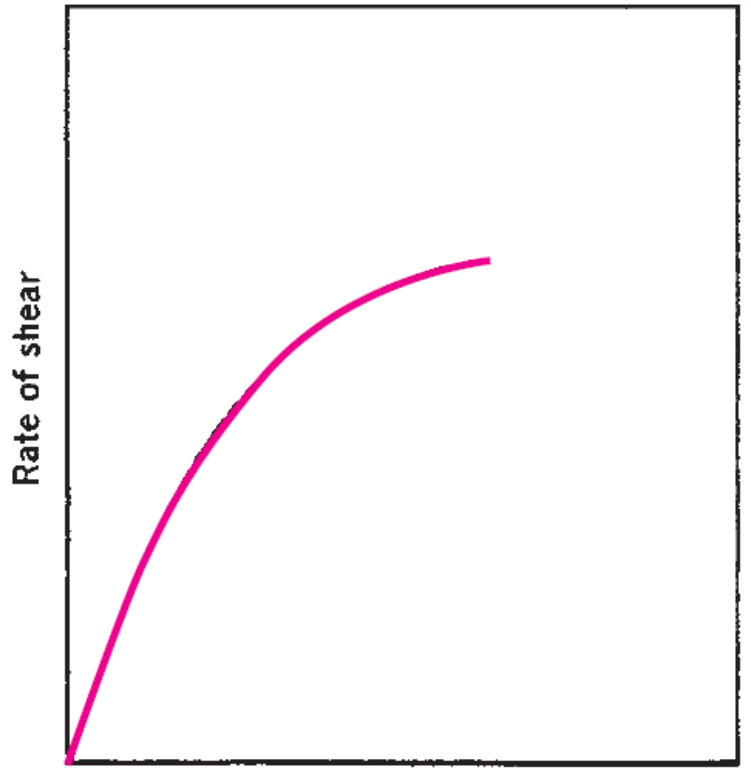
- The curved rheogram for pseudoplastic materials results from a shearing action on long-chain molecules of materials such as linear polymers.
- As shearing stress is increased, normally disarranged molecules begin to align their long axes in the direction of flow.
- This orientation reduces internal resistance of the material and allows a greater rate of shear at each successive shearing stress.



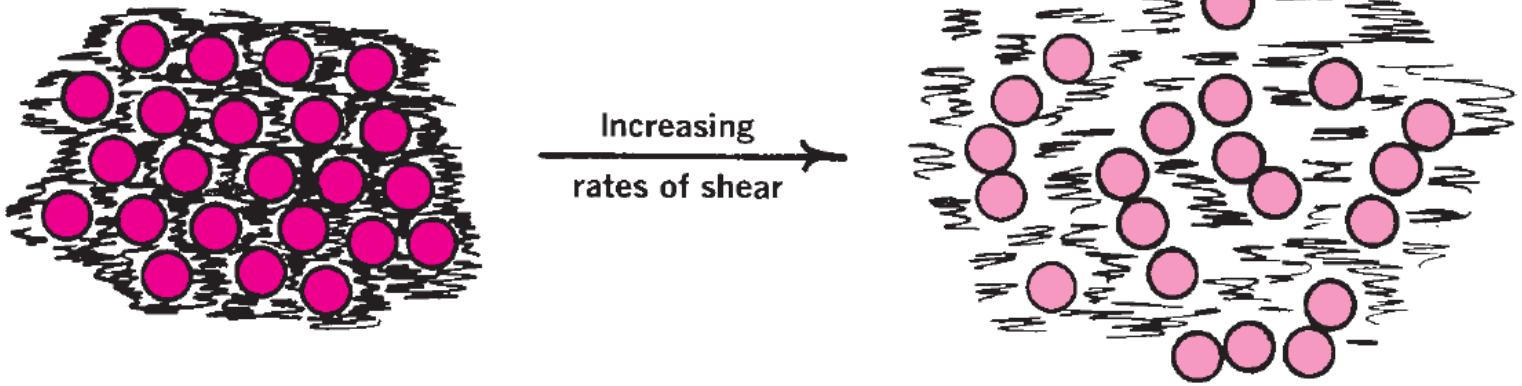


DILATANT FLOW (SHEAR THICKENING)

- Certain suspensions with a high percentage of dispersed solids exhibit an increase in resistance to flow with increasing rates of shear.
- Such systems actually increase in volume when sheared and are hence termed dilatant

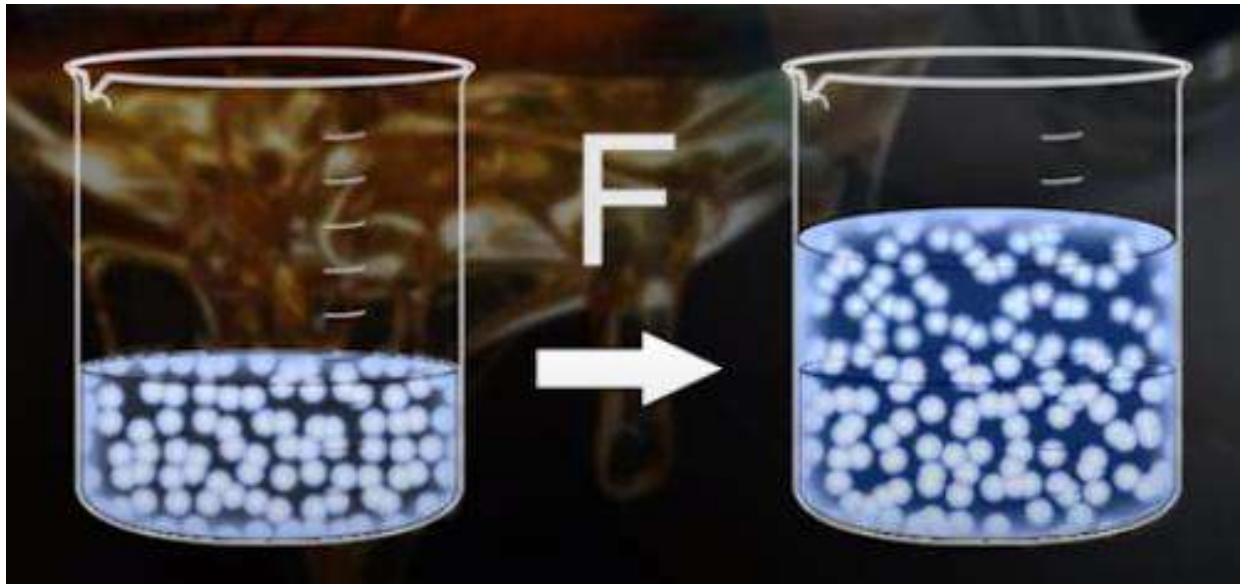


(d) Dilatant flow



Close-packed particles;
minimum void volume;
sufficient vehicle;
relatively low consistency

Open-packed (dilated) particles;
increased void volume;
insufficient vehicle;
relatively high consistency



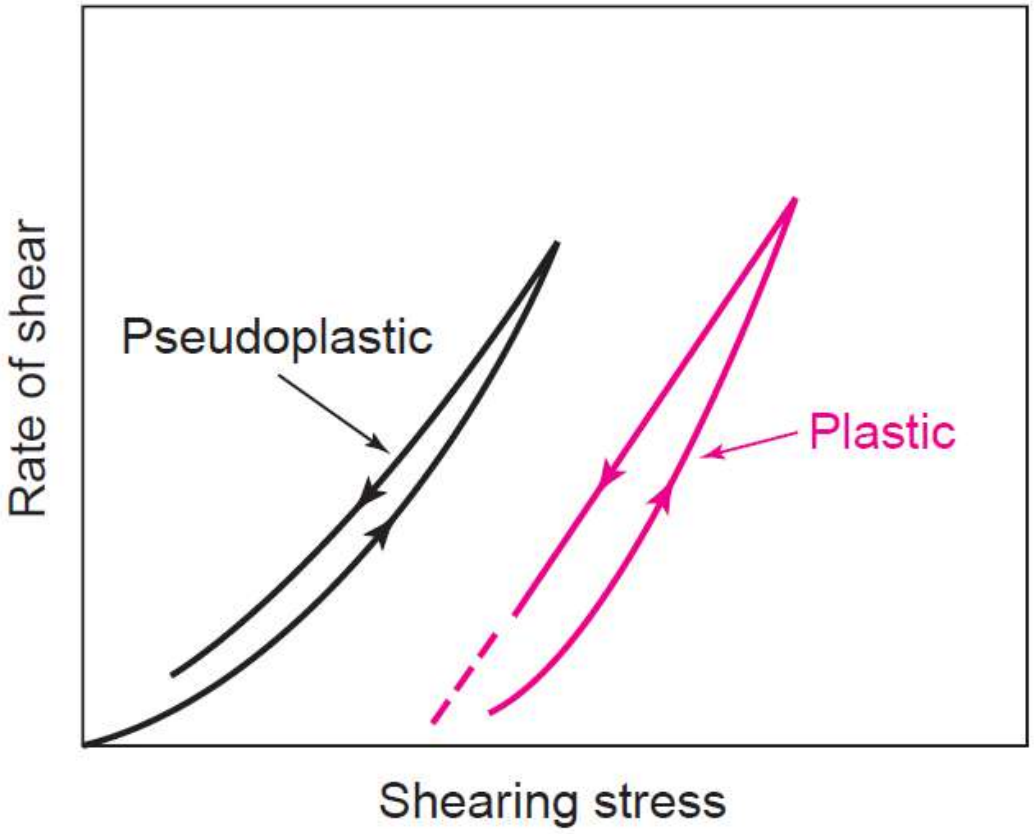
THIXOTROPY

- for Newtonian systems:

  → if the rate of shear were reduced once the desired maximum had been reached, the downcurve would be identical with, and superimposable on, the upcurve.

- for non-Newtonian systems

  → the downcurve can be displaced relative to the upcurve. showing that the material has a lower consistency at any one rate of shear on the downcurve than it had on the upcurve



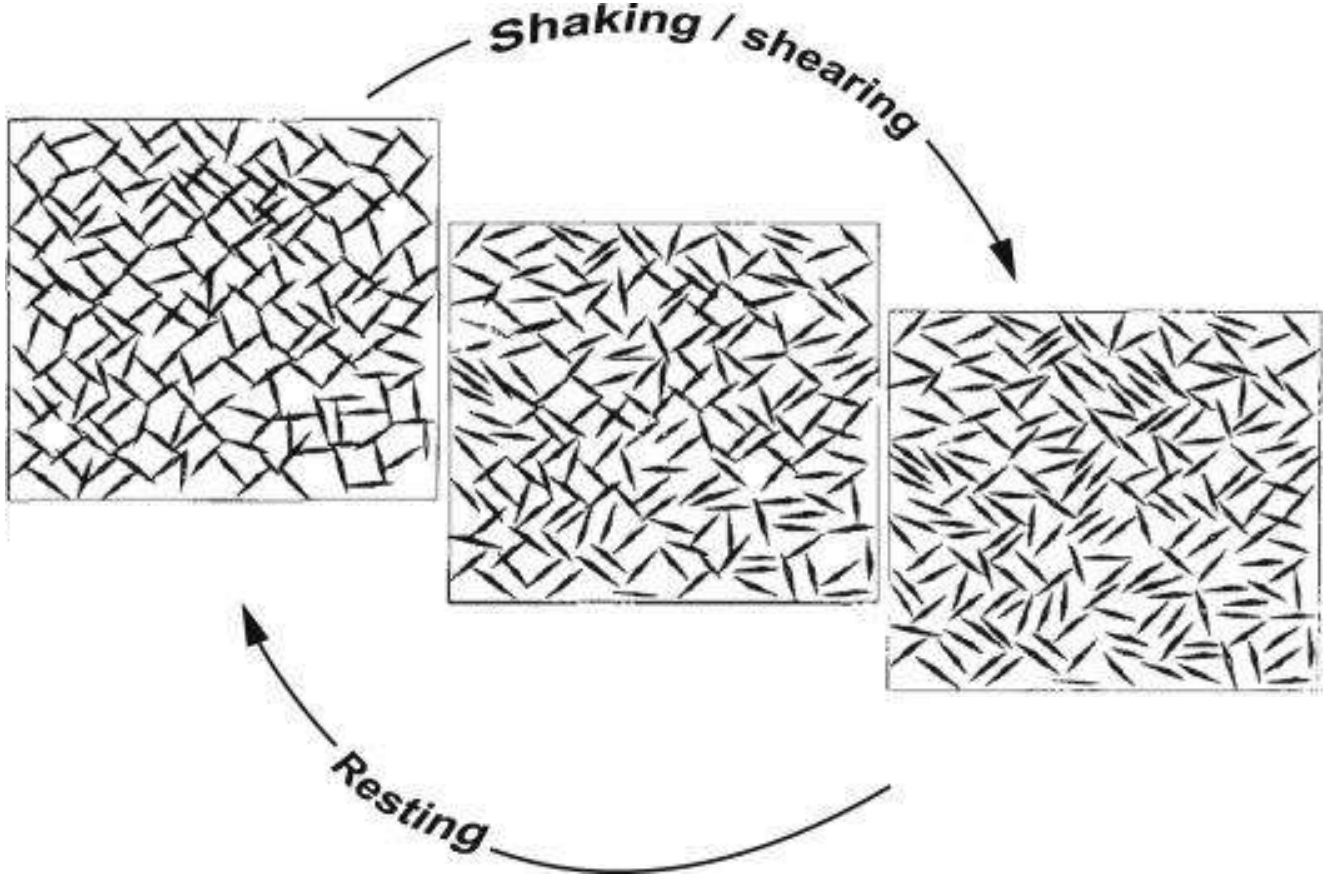
- This indicates a breakdown of structure (and hence shear thinning) that does not reform immediately when stress is removed or reduced.
- This phenomenon, known as **thixotropy**, can be defined as "slow recovery, on standing of a material, of a consistency lost through shearing."
- thixotropy can be applied **only** to shear-thinning systems.

Ketchup is a good example of a thixotropic substance. It does not flow even when the bottle is held upside down.

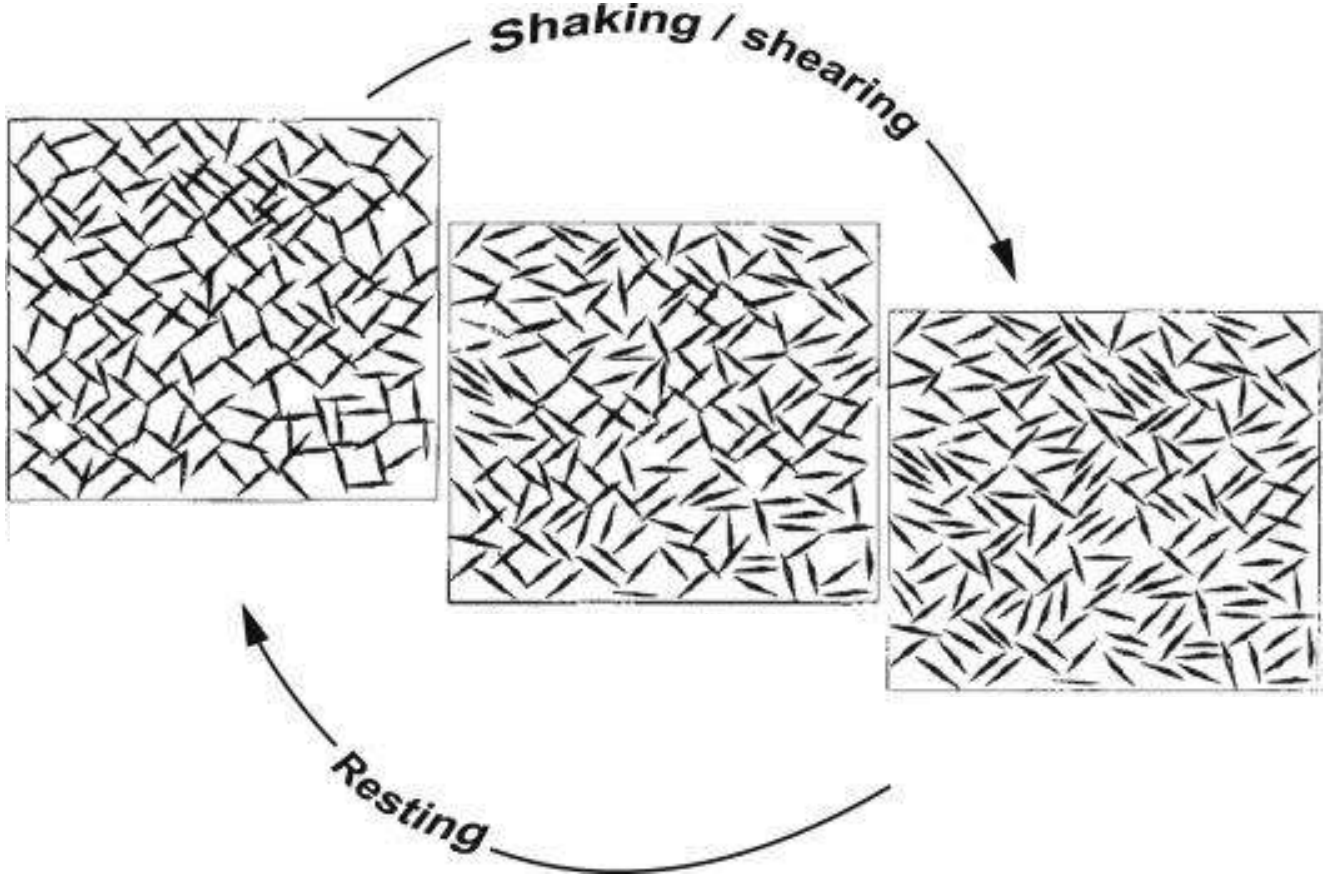
However, when the bottle is struck (vibrated), the ketchup temporarily liquefies and flows.

Once the vibration stops, the ketchup returns to its original viscous state.

- Thixotropic systems usually contain **asymmetric particles** that, through numerous points of contact, set up a loose three dimensional network throughout the sample.
- At rest, this structure confers some degree of rigidity on the system, and it resembles a gel.
- As shear is applied and flow starts, this structure begins to break down as points of contact are disrupted and particles become aligned.

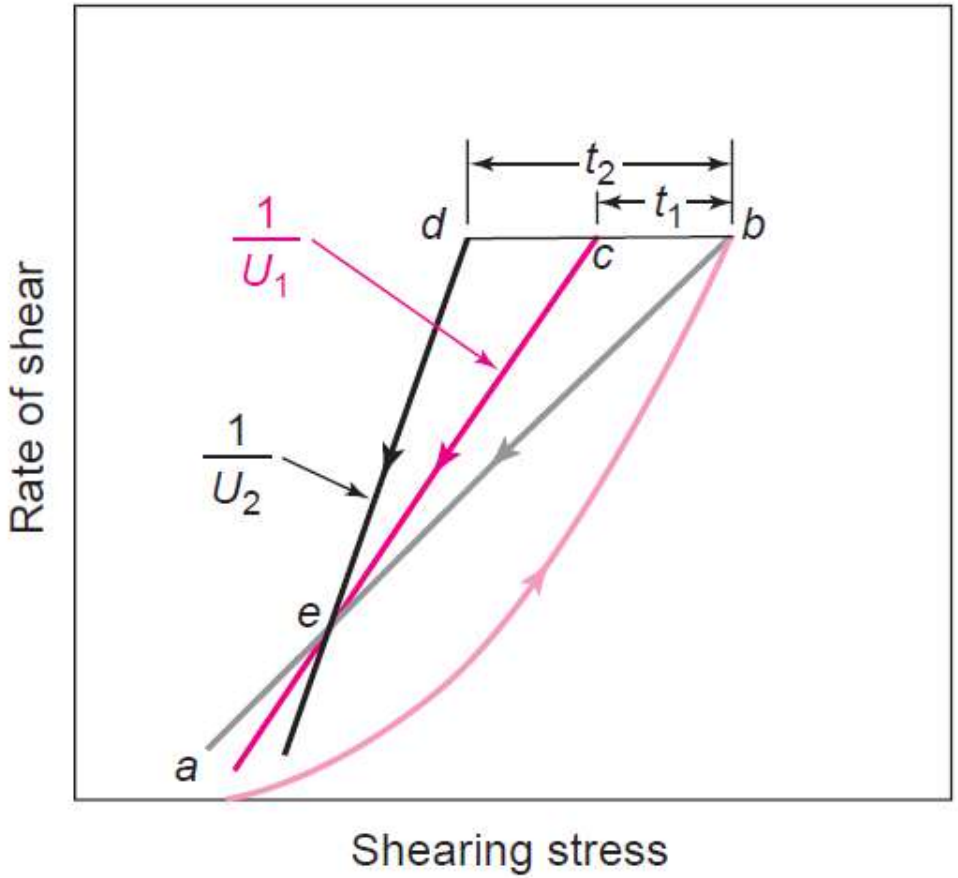


- The material undergoes a **gel-to-sol** transformation and exhibits shear thinning.
- On removal of stress, the structure starts to reform.
- This process is not instantaneous; rather, it is a progressive restoration of consistency as asymmetric particles come into contact with one another by undergoing **random Brownian movement.**



- Rheograms obtained with thixotropic materials are therefore highly dependent on:
  a) the **rate** at which shear is increased or decreased
  b) the length of **time** a sample is subjected to any one rate of shear.
     ✓ (the previous history of the sample has a significant effect on the rheologic properties of a thixotropic system)

- suppose that in Figure the shear rate of a thixotropic material is increased in a constant manner from point a to point b and is then decreased at the same rate back to e.
- Typically, this would result in the so-called **hysteresis loop** abe.
- If, however, the sample was taken to point b and the shear rate held constant for a certain period of time (say, t1 seconds), shearing stress, and hence consistency, would decrease to an extent depending on time of shear, rate of shear, and degree of structure in the sample.



- Decreasing the shear rate would then result in the hysteresis loop abce.
- If the sample had been held at the same rate of shear for t2 seconds, the loop abcde would have been observed.

MEASUREMENT OF THIXOTROPY

A- The most apparent characteristic of a thixotropic system is the hysteresis loop formed by the upcurves and downcurves of the rheogram.

- This area of hysteresis has been proposed as a measure of thixotropic breakdown; it can be obtained readily by means of a planimeter

B- thixotropic coefficient, B, the rate of breakdown with time at constant shear rate, is calculated as follows:

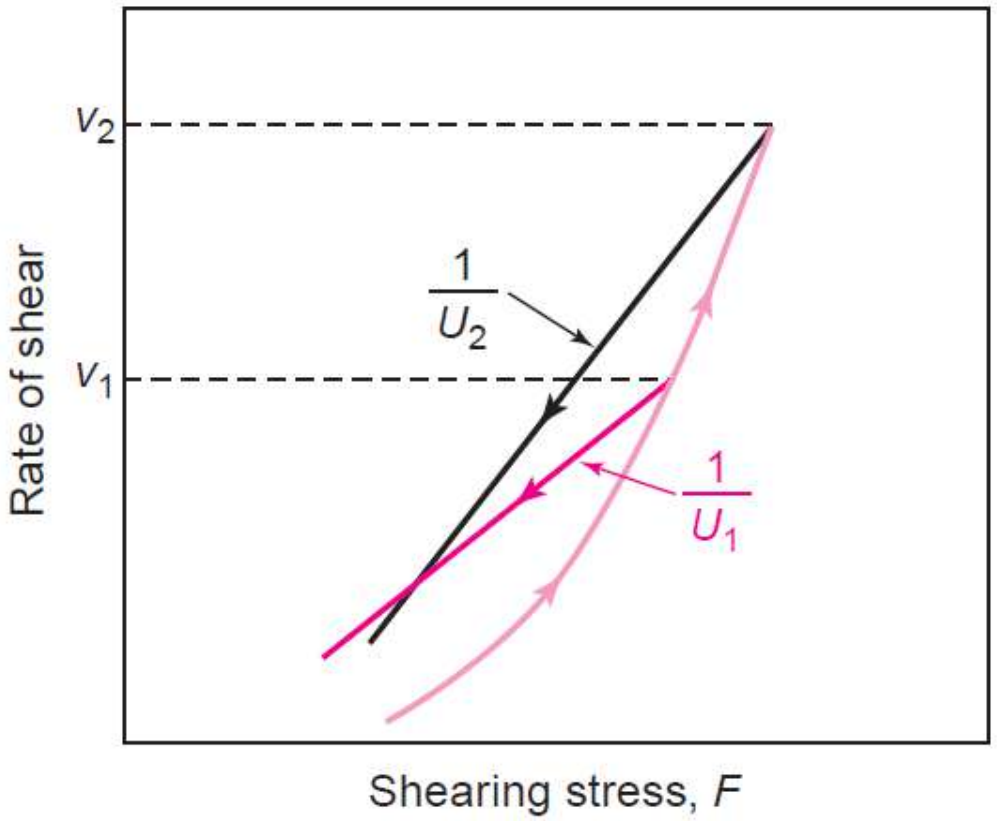
$$B = \frac{U_1 - U_2}{\ln \frac{t_2}{t_1}}$$

where U1 and U2 are the plastic viscosities of the two downcurves

- thixotropic coefficient, M(the structural breakdown due to increasing shear rate): two hysteresis loops are obtained having different maximum rates of shear, v1 and v2
- the loss in shearing stress per unit increase in shear rate, is obtained from

$$M = \frac{U_1 - U_2}{\ln(v_2/v_1)}$$

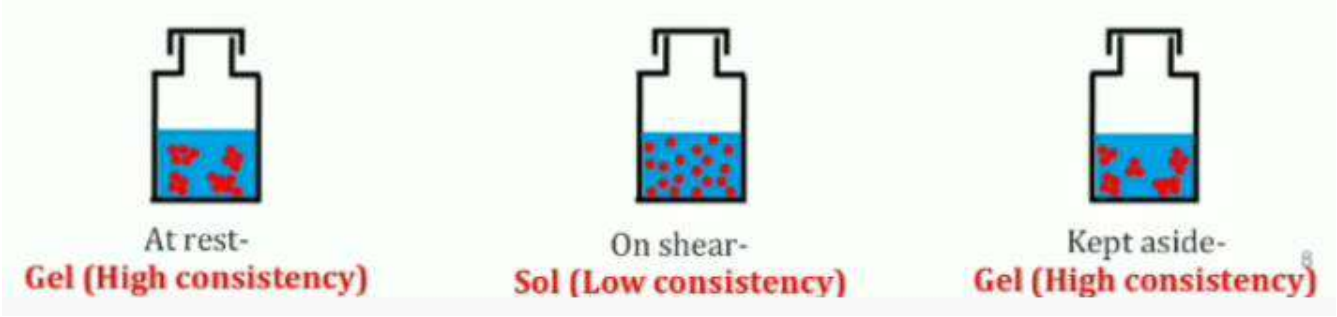
where M is in dynes sec/cm2 and U1 and U2 are the plastic viscosities for two separate downcurves having maximum shearing rates of v1 and v2, respectively



THIXOTROPY IN FORMULATION

1- Thixotropy is a desirable property in liquid pharmaceutical systems that ideally should have a high consistency in the container, yet pour or spread easily.

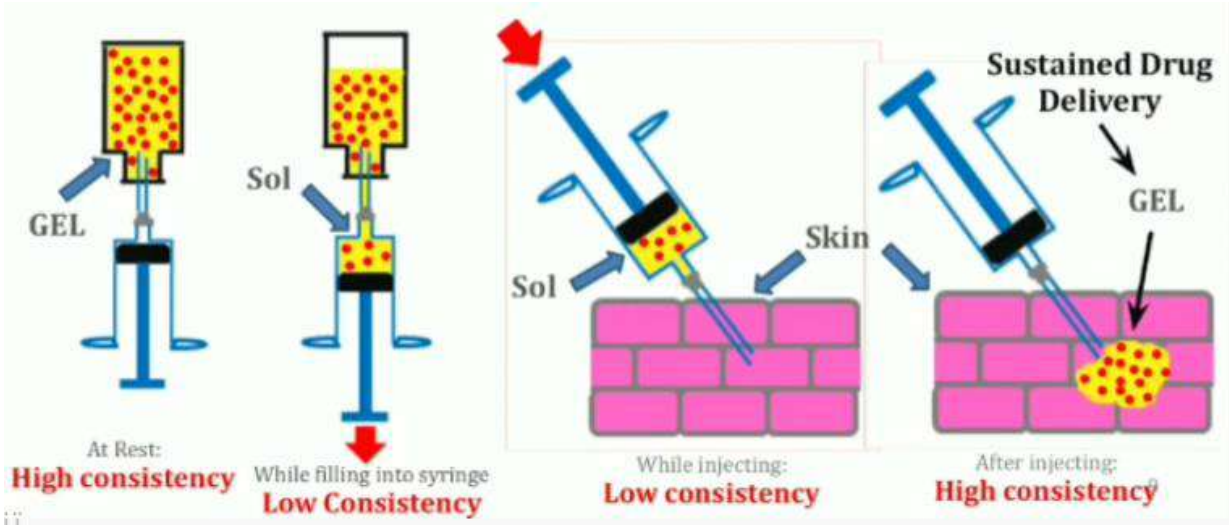
- For example, a well formulated thixotropic suspension will not settle out readily in the container (↓sedimentation rate), will become fluid on shaking, and will remain long enough for a dose to be dispensed.
- Finally, it will regain consistency rapidly enough so as to maintain the particles in a suspended state.



- With regard to suspension stability, there is a relationship between degree of thixotropy and rate of sedimentation; the greater the thixotropy, the lower the rate of settling.

2- Concentrated parenteral suspensions containing from 40% to 70% w/v of **procaine penicillin G** in water were found to have a high inherent thixotropy and were shear thinning.

- Consequently, breakdown of the structure occurred when the suspension was caused to pass through the hypodermic needle.
- Consistency was then recovered as rheologic structure reformed.
- This led to formation of a depot of drug at the site of intramuscular injection where drug was slowly removed and made available to the body

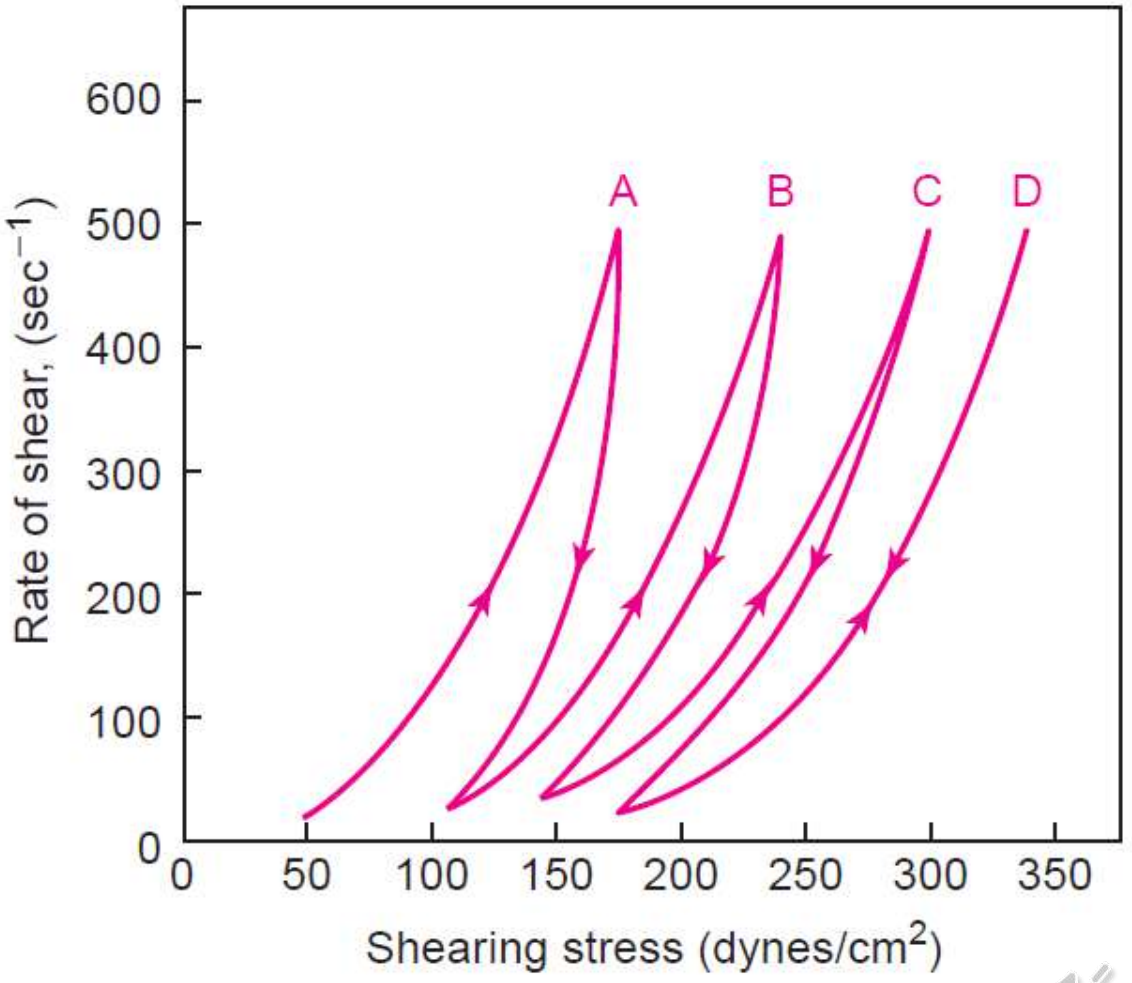


- A similar pattern of behaviour is desirable with emulsions, lotions, creams, ointments, and parenteral suspensions to be used for intramuscular depot therapy.

NEGATIVE THIXOTROPY (ANTI-THIXOTROPY)

- represents an increase rather than a decrease in consistency on the down-curve.
- Characterised by increase in thickness or resistance to flow with increased time of shear
- when magnesia magma was alternately sheared at increasing and then at decreasing rates of shear, the magma continuously thickened (an increase in shearing stress per unit shear rate) but at a decreasing rate, and it finally reached an equilibrium state in which further cycles of increasing–decreasing shear rates no longer increased the consistency of the material.

- Rheogram of magnesia magma showing antithixotropic behavior.
- The material is sheared at repeated increasing and then decreasing rates of shear.
- At stage D, further cycling no longer increased the consistency, and the upcurves and down-curves coincided.



RHEOPEXY

- It is a phenomenon in which a solid forms a gel more readily when gently shaken or otherwise sheared than when allowed to form the gel while the material is kept at rest

https://youtu.be/S8gP3yWsloc

DETERMINATION OF RHEOLOGIC PROPERTIES

CHOICE OF VISCOMETER

- **Newtonian system** is directly proportional to shearing stress, instruments that operate at a single shear rate can be used.
- These "single-point" instruments provide a single point on the rheogram; extrapolation of a line through this point to the origin will result in a complete rheogram.

- With **non-Newtonian systems**, the instrument can operate at a variety of shear rates. Such multipoint instruments are capable of producing a complete rheogram for non-Newtonian systems.

- For example, multipoint evaluation of pseudoplastic materials would allow assessment of viscosity of a suspending agent at rest (negligible shear rate), while being agitated, poured from a bottle, or applied to the skin (moderately high shear rate).

- Single-point instruments are unable to describe these changes.
- although all viscometers can be used to determine viscosity of Newtonian systems, only those with variable–shear-rate controls can be used for non-Newtonian materials

- single–shear-rate instruments suitable for use only with Newtonian materials,
  a) Capillary viscometer
  b) falling-sphere viscometer

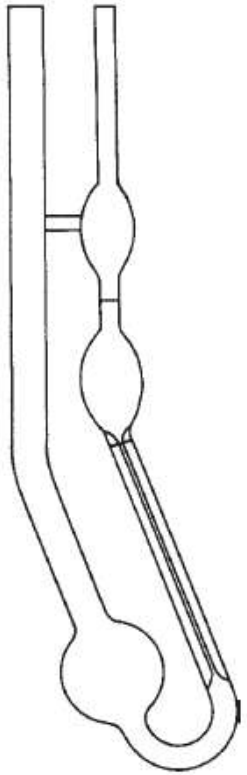


Fig. 19–11. Ostwald–Cannon–Fenske viscometer.

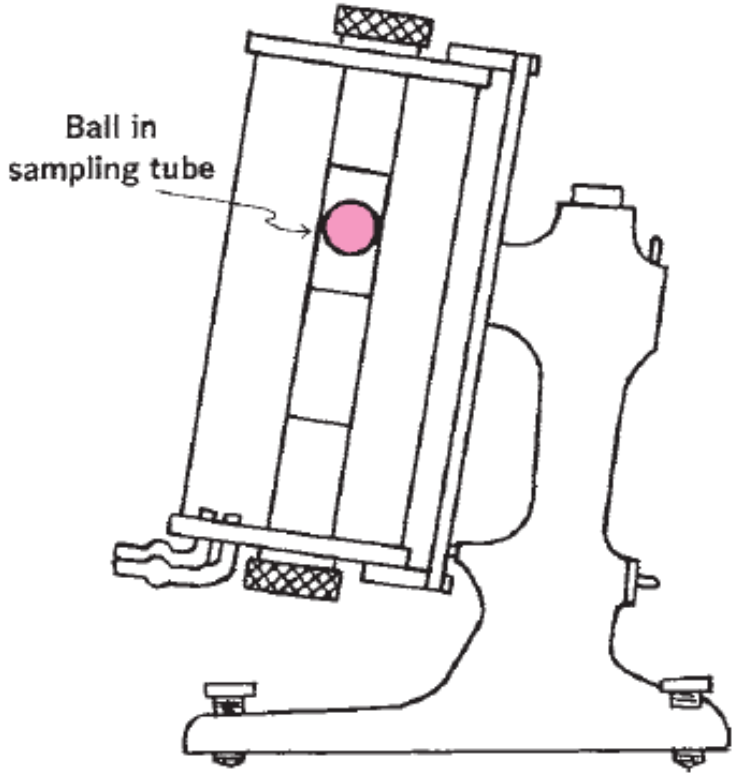


Fig. 19–13. Hoeppler falling-ball viscometer.

- multipoint, rotational instruments used with both Newtonian and non-Newtonian systems:
  a) cup-and-bob viscometer
  b) cone-and-plate viscometer

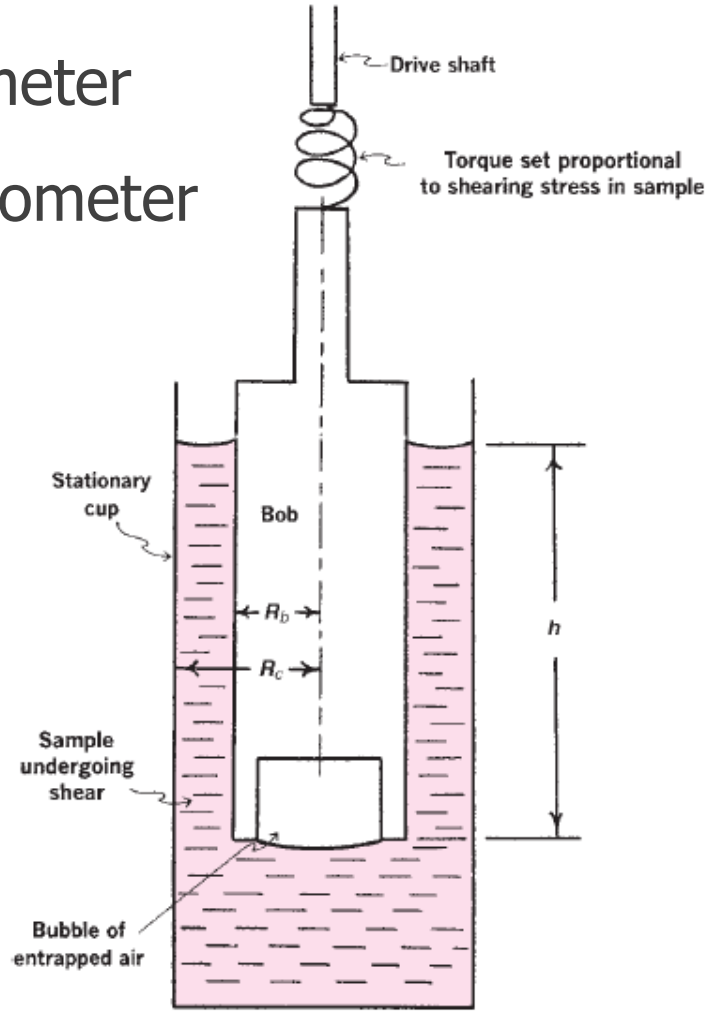


Fig. 19–14. Principle of rotational cup-and-bob viscometer (Searle type). See text for explanation.

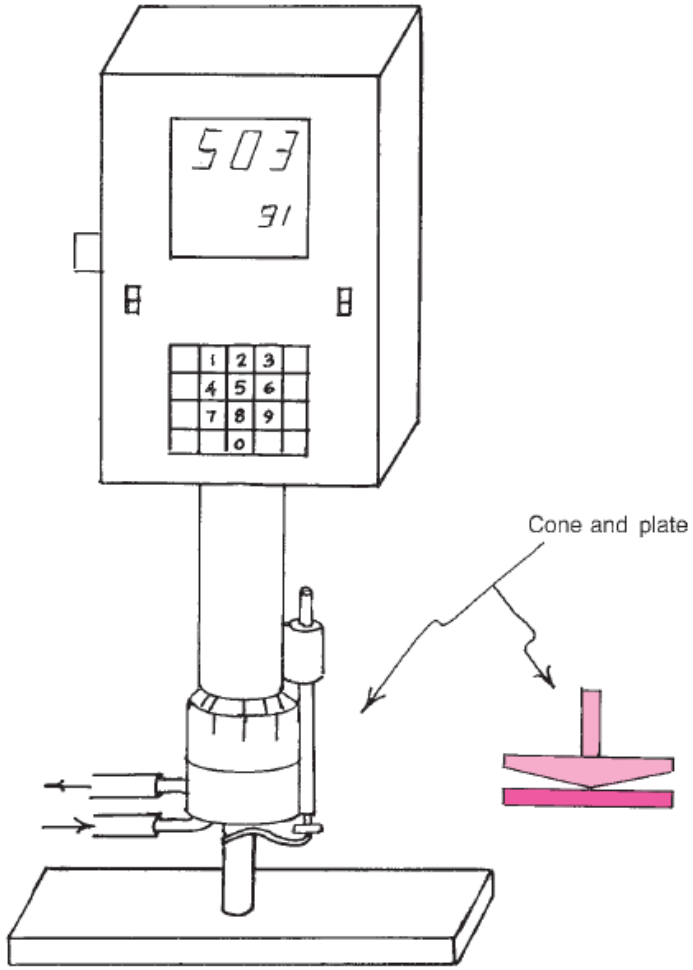


Fig. 19–17. A digital-type cone-and-plate Brookfield viscometer.