Rheology علم الجريان

It is the study of flow, includes the viscosity characteristics of powders, fluids, and semi solids.
Materials are divided into two general categories

1- Newtonian السوائل النيوتونية

2- Non Newtonian السوائل اللانيوتونية

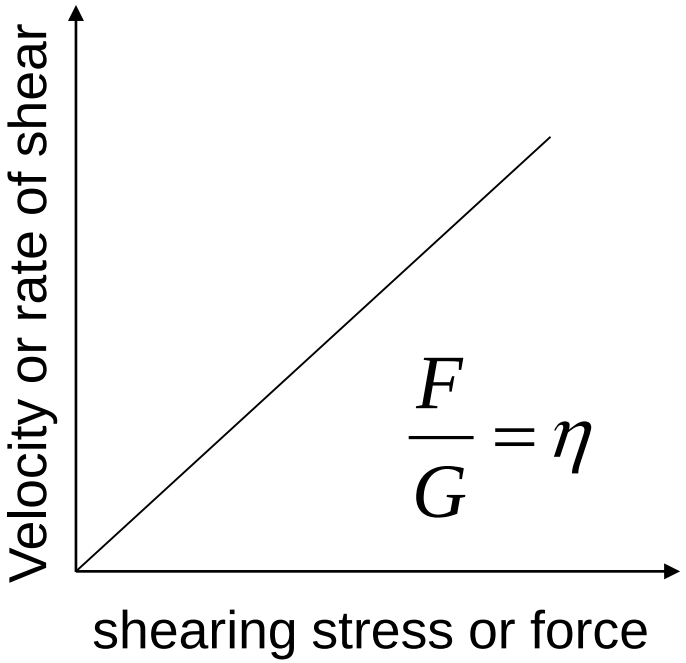
depending on their flow characteristics.
Newtonian flow is characterized by constant viscosity, regardless of the shear rates applied.
Non Newtonian flow includes:

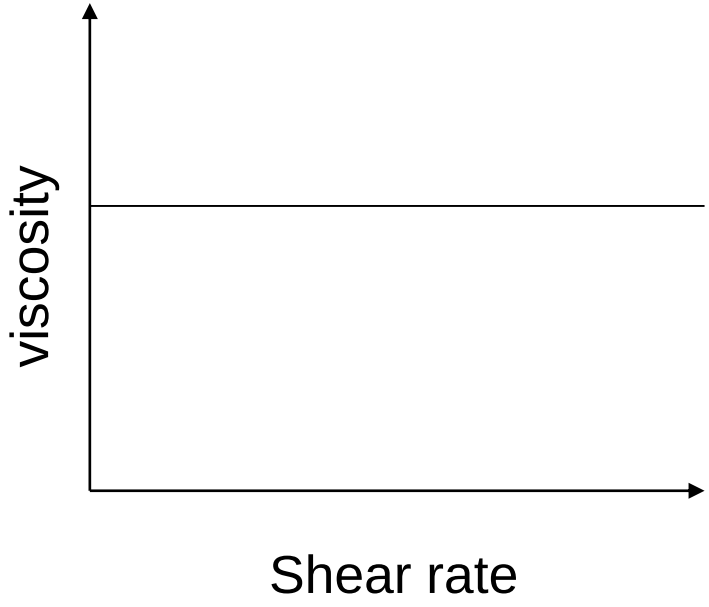
a- plastic البلاستيكي

b- pseudo plastic الشبه بلاستيكي

c- dilatants flow

The Newtonian flow rheogram





Newtonian liquids their viscosity is additive:

$$\frac{1}{\eta} = \frac{1}{\eta} V_1 + \frac{1}{\eta} V2$$

η is the viscosity of the solution

V_1 and V_2 are the volume fraction of pure liquids

Example:

What is the viscosity of the liquid resulting from mixing 300 ml of liquid A (η = 1.0 cp) and 200 ml of liquid B (η = 3.4cp)?

$$\frac{1}{\eta} = \frac{1}{1} \times 0.6 + \frac{1}{3.4} \times 0.4$$

η = 1.4 cps

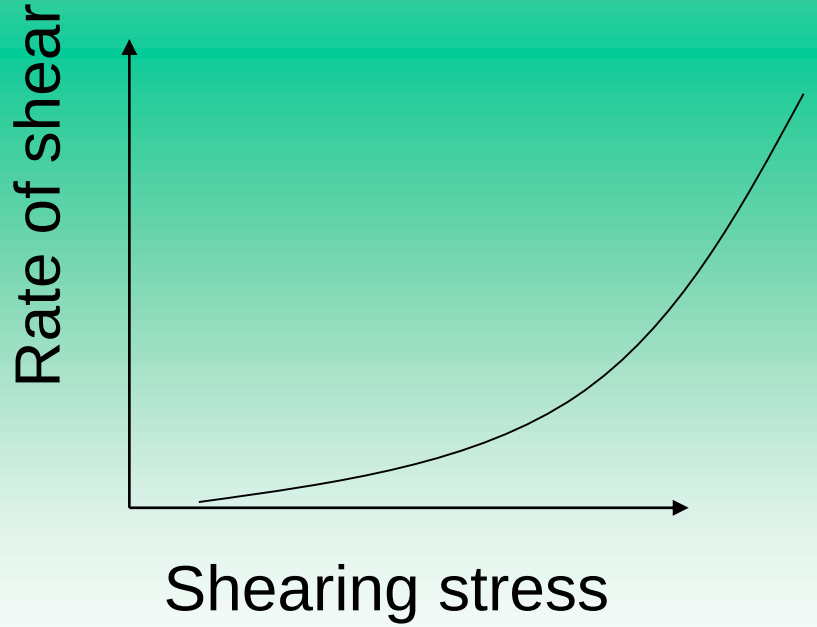
Non-newtonian Materials

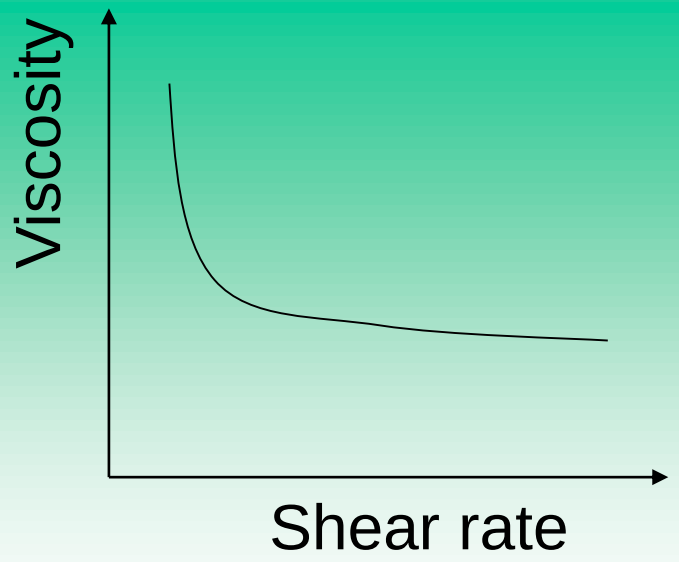
Colloidal solutions **المحاليل الغرويدية**

Emulsions **المستحلبات**

Suspension **المعلقات**

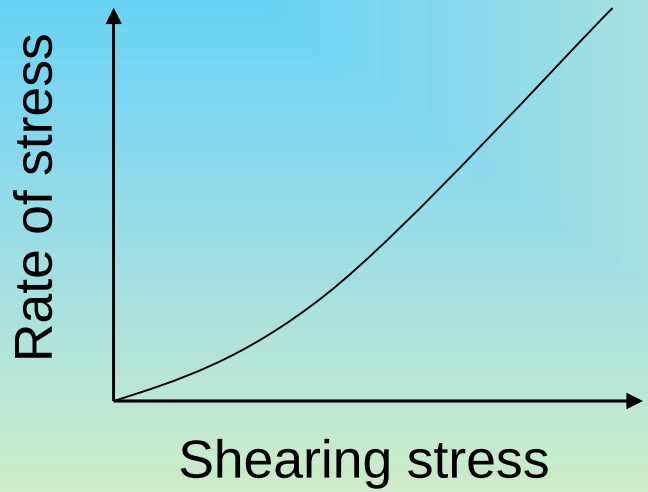
Ointments **المراهم**

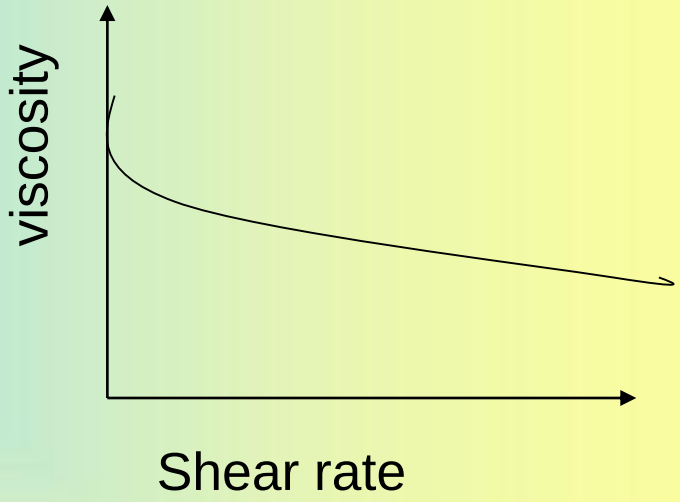




Pseudo plastic flow الانسياب الشبه البلاستيكي

The rheogram is like this:





The viscosity is not constant.

It decreases while the shearing stress increases.

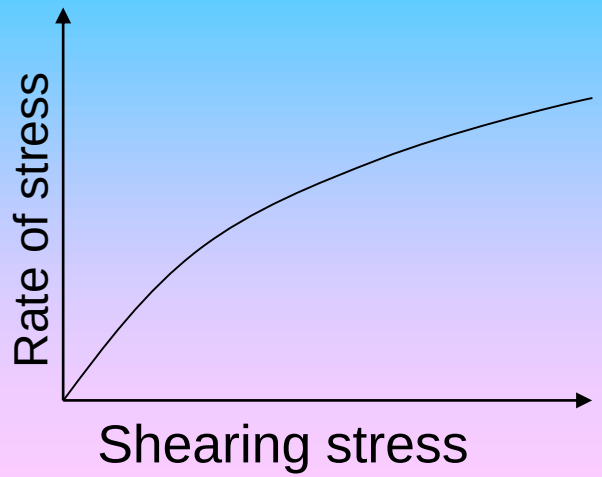
The relation between rate of stress and shearing stress is not linear

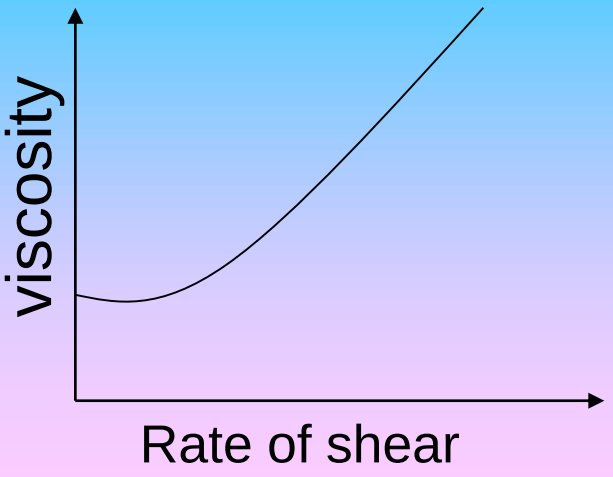
Gum mucilages are examples.

The viscosity during flow less than during stable situation..

Dilatants liquids السوائل المتمددة

The viscosity here increase when force is applied on.
The liquid consists of incompatible particles so they are far from each others but when force is applied they become close to each other and form network which resists flow and increase viscosity.
It happens in high concentration suspension.
It is undesirable phenomena.

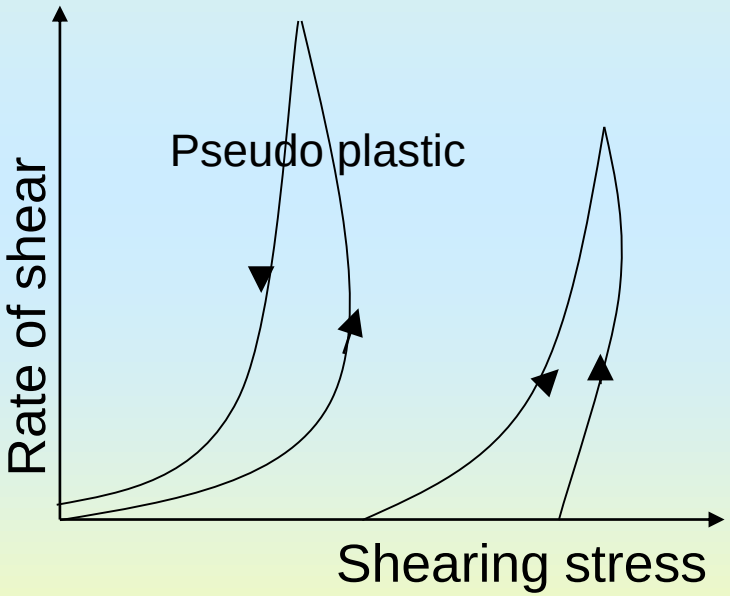




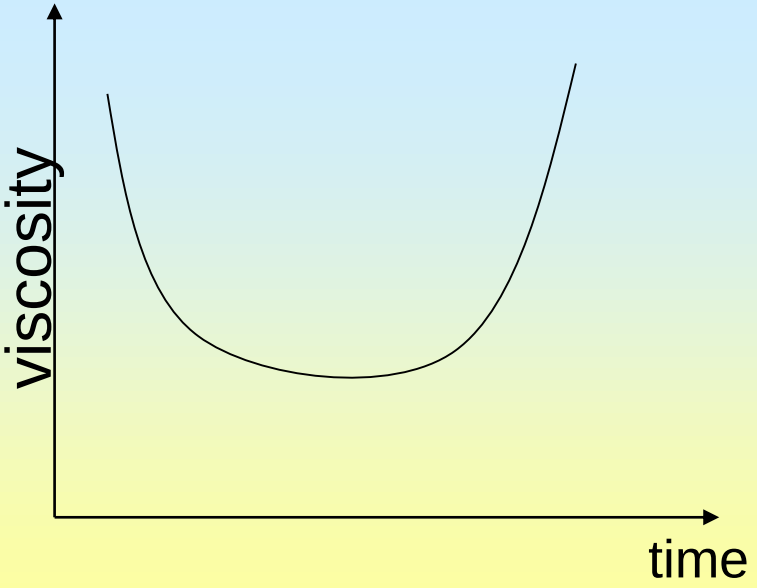
Another kind of flow it is called thixotropic

النظام التكسوتروبي

In case of rest the liquid change to gel and when exposed to shearing stress it becomes liquid.



The lines don’t overlap because it needs time



Disperse Systems الأنظمة المبعثرة

١- المعلقات suspension

٢- المستحلبات emulsions

٣- الايروزولات aerosoles

المعلقات

تتألف المعلقات من طورين داخلي هو عبارة عن جسيمات صلبة موزعة ضمن طورخارجي سائل ص/س.

في المعلقات المائية الطور الخارجي مائي.

Features Desired in a pharmaceutical suspension

- The product should be elegant.
- The product should be effective.
- The product should be stable.

in addition to specific features.

A- the suspension should precipitate slowly and it should be ready to redisperse with gentle shaking of the container.

B-The size of the particles should stay stable for long time.

C- The suspension should be poured easily from its containers.

أهمية المعلقات

- Substances not stable in solution but stable in suspension. الثبات
- It is easily administered. سهولة التناول
- It is easy to mask the unaccepted taste of some drugs when they are suspended such as palpitate chloramphenicol the ester form which is not dissolved. لاخفاء الطعم السئ للمادة الفعالة

Sedimentation rate of the particles of the a suspension: معدل ترسب الجسيمات الصلبة في المعلقات

The rate of sedimentation may affected by several factors which are included in stokes equation.

Stoke's equation derived for ideal case where the suspended particles are spherical, and homogeneously suspended

- no attraction between particles
- no affinity toward the dispersing system.

Stocke's equation

$$\frac{dx}{dt} = \frac{d^2(Pi - Pe)g}{18\eta}$$

$\frac{dx}{dt}$ rate of settling

d : diameter of particles

Pi : densiyt of particle

Pe: density of medium

g: gravity constant

η viscosity of the medium

according to stocke’s equation reducing particle size is important for suspension stability.

But not reducing to fine particles because they tend to form compact cake.

The shape of particles may affect the stability of the suspension.

$CaCO_3$ barrel shaped more stable than needle shaped particles.

In order not to get rigid cake we intentionally form less rigid cake which is dispersable when suspension shaked:

1- try to form floccules.

2- these floccules when precipitate form a big sized, capillary, resdispersable precipitation.

Method to make floccules

- Using clays
- Changing pH
- Using electrolytes
- Using sufactants.

The oral suspension is designed to give the dose in 5 ml volume or in teaspoonful or drops for children.

PROPERTIES OF A GOOD PHARMACEUTICAL SUSPENSION

In preparing a pharmaceutically elegant product, several desirable properties are sought:

*There is ready redispersion of any sediment which accumulates on storage.

*After gentle shaking,the medicament stay in suspension long enough for a dose to be accurately measuerd.

*The suspension is pourable.

* Particles in suspension are small and relatively uniform in size, so that the product is free from a gritty texture.

The insoluble medicament may be a diffusible solid or an indiffusible solid:

Diffusible solids قابل للانتشار (dispersible solids) :these are insoluble solids that are light and easily wetted water. They mix readily with water and stay dispersed long enough for an adeguate dose to be measured. After settling they redisperse easily. Examples include magnesium trisilicate, light magnesium carbonate, bismuth carbonate and light kaolin.

Indiffusible solids:غير قابل للانتشار most insoluble solids are not easily wetted. And may form large porous clumps in the liquid. These solids will not remain evenly distributed in the vehicle long enough for an adequate dose to be measured. They may not redisperse easily. Example for internal use include aspirin, phenobarbital, sulfadimidine and chalk and for external use calamine, hydrocortisone, sulphur and zinc oxide.

Suspending agents

- Natural polysaccharides
- Semisynthetic polysaccharides
- Clays
- Synthetic thickeners
- Miscellaneous compounds

Dispersion medium

We need suspending agent to give dispersion medium a structure which may help the suspending we can use:

- CMC
- MC
- Micro crystalline cellulose
- PVP
- Bentonite
- Gums

This suspending agents should be compatible with A.S.

Shouldn’t increase the viscosity too much.

Emulsions المستحلبات

Oil-in-water O/w can be diluted with water

Water-in oil W/O can be diluted by oil

Emulsions could be liquid or semi solids

Liquid emulsions can be employed orally, topically or parentraly.

Semi solid emulsion are employed topically.

Preparation of emulsions:

- Surfactant should be compatible with all ingredients in the emulsion
- No effect on the stability or efficacy of the active substance.
- Stable
- Not toxic.

Classification of surfactants
تصنيف العوامل الاستحلابية

1- carbohydrates:

- Acacia, tragacanth, agar, chondrus, pectin
    - They produce o/w emulsion
- Acacia is used as emulsifier while agar or tragacanth are thickening agents.
- Microcrystalline cellulose increases viscosity in emulsion.

2- proteins

- Gelatin, eggyolk, casein
- Produce 0/w emulsion
- But the emulsion produced from gelatin is very liquid

3- high molecular alcohols:

- Stearyl alcohol, cetyl alcohol.,glyceryl monostearate, cholesterol,.
- All of them are emulisifier which can enhance the stablilty of o/w emulsions

4- Wetting agents which could be:

- Anionic :sodium stearate,
- Cationic benzalkonium chloride
- Nonionic:Spans and Tweens
- Amphoteres.

5- colloidal clays

- Bentonitn,
- Al hydroxide]
- Mg hydroxid

Volume of the two phases is important: increasing the volume of internal means increasing the viscosity, then viscosity decrease rapidly and emulsion is inverted

75% is the maximum of internal phase.

The Hydrophilic Lipohpilic Balance HLB

Each surfactant has two parts: lipophilic one
hydrophilic one

The stronger part among both will determine the type of the surfactant weather it is hydrophilic or lipophilic.

Table 3.B Determine the activity of some surfactants according to their HLB

Activity	HLB
Antifoaming	1 – 3
Emulsifiers (w/o)	3 – 6
Wetting agent	7 – 9
Emulsifiers (o/w)	8 – 18
Solubilizers	15 – 20
detergents	13 - 15

The substances which are polar or hydrophilic will take high values, while those which are less polar or lipophilic will take low values.

In general, substances which have HLB from 3 to 10 are greatly lipophilic and give w/o emulsions, and those who have HLB from 8 to 18 are highly hydrophilic and give o/w emulsions.

STABILITY OF EMULSIONS
ثبات المستحلبات

Generally speaking, an emulsion is considered to be physically unstable if (*a) the internal or dispersed* phase upon standing tends to form aggregates of drops,

(*b) large drops or aggregates* of drops rise to the top or fall to the bottom of the emulsion to form a concentrated layer of thin ternal phase,

and (*c) if all or part of the liquid* of the internal phase separates and forms a distinct layer on the top or bottom of the emulsion as a result of the coalescing of the drops of the internal phase.

In addition, an emulsion may be adversely affected by microbial contamination and growth and by other chemical and physical alterations.

Aggregation and Coalescence

التجمع والاندماج

Aggregates of drops (globules) of the internal phase have a greater tendency than do individual particles to rise to the top of the emulsion or fall to the bottom.

Such a preparation of the drops is termed the creaming of the emulsion, and provided coalescence is absent, it is a reversible process.

The term is taken from the dairy industry and is analogous to creaming, or rising to the top of cream in milk that is allowed to stand.

Creaming التقشد

The creamed portion of an emulsion may be redistributed rather homogeneously upon shaking, but if the aggregates are difficult to disassemble or if insufficient shaking is employed before each dose, improper dosage of the internal phase substance may result. Furthermore, a creamed emulsion is not esthetically acceptable to the pharmacist or appealing to the consumer.

More important, it increases the risk that the drops will coalesce.

Separation and breaking
الانفصال والانكسار

More destructive to an emulsion than creaming is coalescence of the drops of the internal phase and separation of that phase into a layer.

Separation of the internal phase from the emulsion is called breaking, and the emulsion is described as being cracked or broken. This is irreversible, because the protective sheath about the drops of the internal phase no longer exists. Attempts to reestablish the emulsion by agitation of the two separate layers are generally unsuccessful. Additional emulsifying agent and reprocessing through appropriate machinery are usually necessary to reproduce an emulsion.