

RHEOLOGY

The term 'rheology' was derived from the Greek words *rheo* (flow) and *logos* (science) and is used to describe the flow of liquids and the deformation of solids. Viscosity is an expression of the resistance of a fluid to flow: the higher the viscosity, the greater is the resistance.

Importance of Rheology in Pharmacy

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.

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.

The medicinal and cosmetic creams, pastes, and lotions must have an acceptable consistency and smoothness. These qualities must be reproducible each time a new batch is prepared. The rheology of a particular product, which can range in consistency from fluid to semisolid to solid, can affect patient acceptability, physical stability, and 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. Inappropriate equipment from this perspective may result in an undesirable product, at least in terms of its flow characteristics.

Newton's Law of Flow

Newton was the first to study now properties of liquids in a quantitative way. **Newton's Law of Flow** states that the shear stress between adjacent fluid layers is proportional to the velocity gradient between two layers or shear rate.

Two-plate model

The two-plates model provides a mathematical description for viscosity. There are two plates with fluid placed in-between. The lower plate does not move. The upper plate drifts aside very slowly and subjects the fluid to a stress, which is parallel to its surface: the shear stress. The force applied to the upper plate divided by this plate's area defines the shear stress (F'/A). Force/area results in the unit N/m^2 , which is named Pascal [Pa]

The two-plate model allows for calculating another parameter: the shear rate (dv/dr). The shear rate is the velocity of the upper plate divided by the distance between the two plates. Its unit is $[1/s]$ or reciprocal second $[s^{-1}]$.

Dynamic viscosity is shear stress divided by shear rate.

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

where η is the coefficient of viscosity or simply viscosity or absolute viscosity or dynamic viscosity.

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

For a Newtonian system, a representative flow curve or rheogram, by plotting F versus G is shown below where a straight line passing through the origin is obtained.

The cgs unit of viscosity is the *poise* (dyne sec/cm^2 or $\text{g cm}^{-1} \text{sec}^{-1}$), defined as the shearing force required producing a velocity of 1 cm/sec between two parallel planes of liquid each 1 cm^2 in area

and separated by a distance of 1 cm. A more convenient unit for most work is the *centipoise* (cp), 1P = 100cP. The SI unit is Pascal.sec (Pa.s or N.s/m² or kg/m.s). 1P=0.1Pa.s

Fluidity, ϕ is defined as the reciprocal of viscosity: $\phi=1/\eta$

Kinematic viscosity is the absolute viscosity divided by the density of the liquid, ρ at a specific temperature:

$$\text{Kinematic viscosity} = \frac{\eta}{\rho}$$

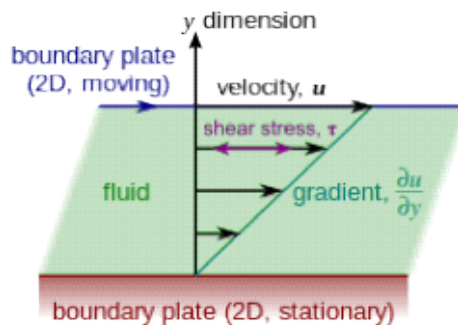
The cgs unit of kinematic viscosity is *stoke* (s) or cm²/sec and *centistoke* (cs) and SI unit of kinematic viscosity is m²/sec.



Two-plates model to calculate the shear stress. Shear stress is the force moving the upper plate divided by the plate's area.



Two-plates model to calculate the shear rate. Shear rate is the velocity of the moving plate divided by the distance between the plates.



Influence of Temperature and Pressure on Viscosity

Apart from the shear rate, temperature strongly influences a fluid's viscosity. A substance's viscosity decreases with increasing temperature. As temperature is raised, the fluidity of a liquid (the reciprocal of viscosity) increases with temperature. This inversely proportional relation applies to all substances. Any change in temperature always influences viscosity, but for different fluids, the extent of this influence varies. Even a 1 K (1 °C) temperature increase can raise the viscosity by 10%.

Normally, an increase in pressure causes a fluid's viscosity to increase. However, fluids are not dramatically affected if the applied pressure is low or medium: liquids are almost non-compressible in this pressure range. Most liquids react to a significantly altered pressure (from 0.1 MPa to 30 MPa) with a viscosity change of about 10%.

In case the pressure goes up from 0.1 MPa to 200 MPa, the viscosity can rise to 3 to 7 times the original value. This applies to most low-molecular liquids. Highly viscous mineral oils react with a viscosity increase of times 20000 under identical circumstances.

[**Conversion of pressure units:** 1 bar = 0.1 MPa = 10⁵ Pa = 10⁵ N/m²]

In most liquids, pressure reduces the free volume in the internal structure, and thus limits the movability of molecules. Consequently, internal friction and viscosity increase.



This is the simplest form of a rheogram is produced by Newtonian systems. A *rheogram* is a plot of shear rate, G , as a function of shear stress, F . Rheograms are also known as consistency curves or flow curves. For this system, the greater the slope of the line, the greater is the fluidity or, conversely, the lower is the viscosity.

Fluids which obey the Newton's law of viscosity are called as **Newtonian fluids** or a fluid whose viscosity does not change with shear rate or a **Newtonian fluid** is one where there is a linear relationship between shear stress and shear rate.

Non-Newtonian Systems

The majority of fluid pharmaceutical products 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.

Non-Newtonian Flow

- (a) Plastic
- (b) Pseudoplastic
- (c) Dilatant

(a) Plastic Flow

The materials that exhibit plastic flow, such materials 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. The

slope of the rheogram 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

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

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. As a result, a continuous structure is set up throughout the system. A yield value exists because of the contacts between adjacent particles (brought about by van der Waals 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. Once the yield value has been exceeded, any further increase in shearing stress ($F - f$) brings about a directly proportional increase in G , rate of shear. In effect, a plastic system resembles a Newtonian system at shear stresses above the yield value.

Pseudoplastic Flow

Many pharmaceutical products, including liquid dispersions of natural and synthetic gums (tragacanth, sodium alginate, methylcellulose, and sodium carboxymethyl cellulose) exhibit pseudoplastic flow. Pseudoplastic flow is typically exhibited by polymers in solution in contrast to plastic systems, which are composed of flocculated particles in suspension. 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.



Furthermore, because no part of the curve is linear, the viscosity of a pseudoplastic material cannot be expressed by any single value. The viscosity of a pseudoplastic substance decreases with increasing rate of shear and this system is known as shear thinning system.

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. In addition, some of the solvent associated with the molecules may be released, resulting in an effective lowering of both the concentration and the size of the dispersed molecules. This, too, will decrease apparent viscosity.

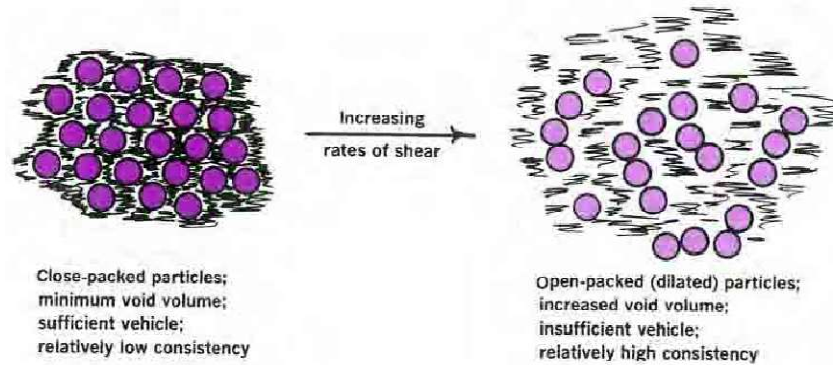
Dilatant Flow

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 *dilatants*. This type of flow is the inverse of that possessed by pseudoplastic systems. Whereas pseudoplastic materials are frequently referred to as "shear-thinning systems," dilatant materials are often termed "shear-thickening systems." When stress is removed, a dilatant system returns to its original state of fluidity.



Substances possessing dilatant flow properties are invariably suspensions containing a high concentration (about 50% or greater) of small, deflocculated particles.

Dilatant behavior can be explained as follows. At rest, the particles are closely packed with minimal inter-particle volume (voids). The amount of vehicle in the suspension is sufficient, however, to fill voids and permits particles to move relative to one another at low rates of shear. Thus, a dilatant suspension can be poured from a bottle because under these conditions it is reasonably fluid.



As shear stress is increased, the bulk of the system expands or dilates; hence the term *dilatant*. The particles, in an attempt to move quickly past each other, take on an open form of packing, as depicted in the above figure. Such an arrangement leads to a significant increase in inter-particle void volume. The amount of vehicle remains constant and, at some point, becomes insufficient to fill the increased voids between particles. Because the particles are no longer completely wetted or lubricated by the vehicle, the resistance to flow increases. Eventually, the suspension will set up as a firm paste.

Thixotropy

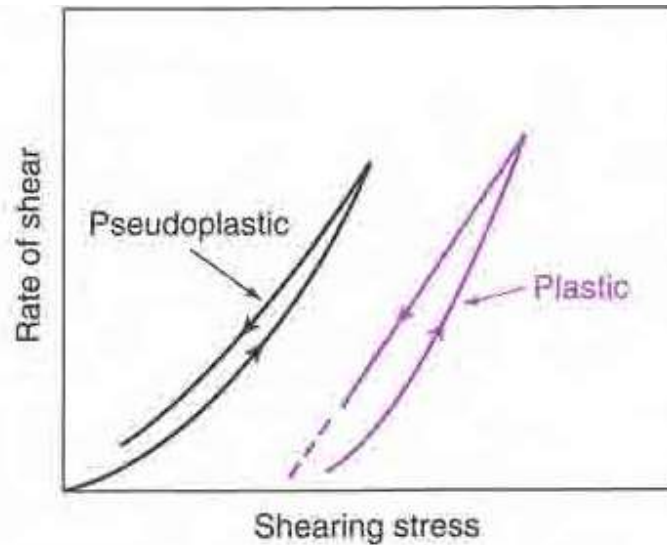
Thixotropy is defined as the progressive decrease in viscosity with time for a constant applied shear stress followed by a gradual recovery when the stress is removed.

Thixotropy is a time-dependent shear thinning property.

Thixotropy can be defined as an isothermal and slow recovery of material consistency, lost through shearing.

If the rate of shear is reduced once the desired maximum is reached, the down-curve would be superimposable on the up-curve. This is true for Newtonian systems.

In case of non-Newtonian systems, the down-curve can be displaced relative to the up-curve. With shear-thinning systems (i.e., pseudoplastic), the down-curve is frequently displaced to the left of the up-curve, showing that the material has a lower consistency at any one rate of shear on the down-curve than it had on the up-curve. This indicates a breakdown of structure (and hence shear thinning) that does not reform immediately when stress is removed or reduced. This phenomenon is known as *thixotropy*. Typical rheograms for plastic and pseudoplastic systems exhibiting this behavior are shown below.



Thixotropic systems usually contain asymmetric particles. These particles set up a loose three-dimensional network in the sample through numerous points of contact. 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.

The most apparent characteristic of a thixotropic system is the hysteresis loop formed by the up-curves and down-curves of the rheogram. The **area enclosed** between the “up” and “down” **curves** (the **hysteresis loop**) is an indication of the extent of **thixotropy** of the **material**. This relates to the energy needed to breakdown reversible microstructure of tested material. Thus, a highly thixotropic material is characterized by having a large area within the loop. If up- and down-curves coincide perfectly, the material is non-thixotropic. In a thixotropic system, the nature of rheogram largely depends on the rate at which shear is increased or decreased. Typically, the time period over which the shear rate is increased (up-curve) is equal to the time period over which it is decreased (down curve). The response in terms of material shear stress is recorded and plotted against time.

Thixotropy can be measured by two methods:

- (a) At constant shear rate
- (b) At variable shear rate

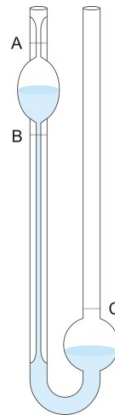
Determination of viscosity

- (a) For Newtonian system, single-point instruments that operate at a single shear rate are used. Example: **Ostwald viscometer** and **falling sphere viscometer**.
- (b) For non-Newtonian system, multi-point instruments operate at a variety of shear rates are used. Example: a single-point determination is virtually useless in characterizing its flow properties. Example: **Brookfield viscometer**

Therefore, 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.

Capillary Viscometer

The viscosity of a Newtonian liquid can be determined by measuring the time required for the liquid to pass between two marks as it flows by gravity through a vertical capillary tube known as an *Ostwald viscometer*.



The time of flow of the liquid under test is compared with the time required for a liquid of known viscosity (usually water) to pass between the two marks. If η_1 and η_2 are the viscosities of the unknown and the standard liquids, respectively, ρ_1 and ρ_2 are the respective densities of the liquids, and t_1 and t_2 are the respective flow times in seconds, the absolute viscosity of the unknown liquid, η_1 is determined by substituting the experimental values in the equation

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

The ratio η_1/η_2 is known as the relative viscosity of the liquid under test.

The above equation is obtained from Poiseuille's law for a liquid flowing through a capillary tube as follows.

$$\eta = \frac{\pi r^4 t \Delta P}{8lV}$$

where r is the radius of the inside of the capillary, t is the time of flow, ΔP is the pressure head (dynes/cm²) under which the liquid flows, l is the length of capillary and V is the volume of liquid flowing. The radius, length, and volume of a given capillary viscometer are constants and can be combined into a constant, K . Then the equation can be written as:

$$\eta = Kt\Delta P$$

The pressure head ΔP depends on density, ρ of the liquid being measured, the acceleration of gravity, and the difference in heights of liquid levels in the two arms of the viscometer (hydrostatic pressure = $h\rho g$). Acceleration of gravity is a constant, however, and if the levels in the capillary are kept constant for all liquids, these terms can be incorporated in the constant and the viscosities of the unknown and the standard liquids can be written as

$$\eta_1 = K't_1\rho_1$$

$$\eta_2 = K't_2\rho_2$$

Therefore, when flow periods for two liquids are compared in the same capillary viscometer, the two equations give the following relationship:

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

Deformation of Solids

Deformation means change of form of materials upon application of force. When any solid body is subjected to opposing forces, there is finite change in its geometry, depending upon the nature of the applied load. The relative amount of deformation produced by such forces is a dimensionless quantity called strain. The deformation of a solid due to stress is strain. Three of the commonest types of strain are illustrated below:

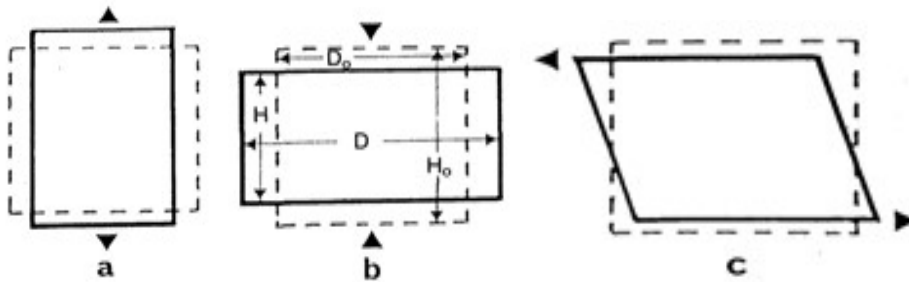


Diagram shows change in geometry (strain) of a solid body resulting from various types of applied force: tensile strain (a), compressive strain (b), and shear strain (c)

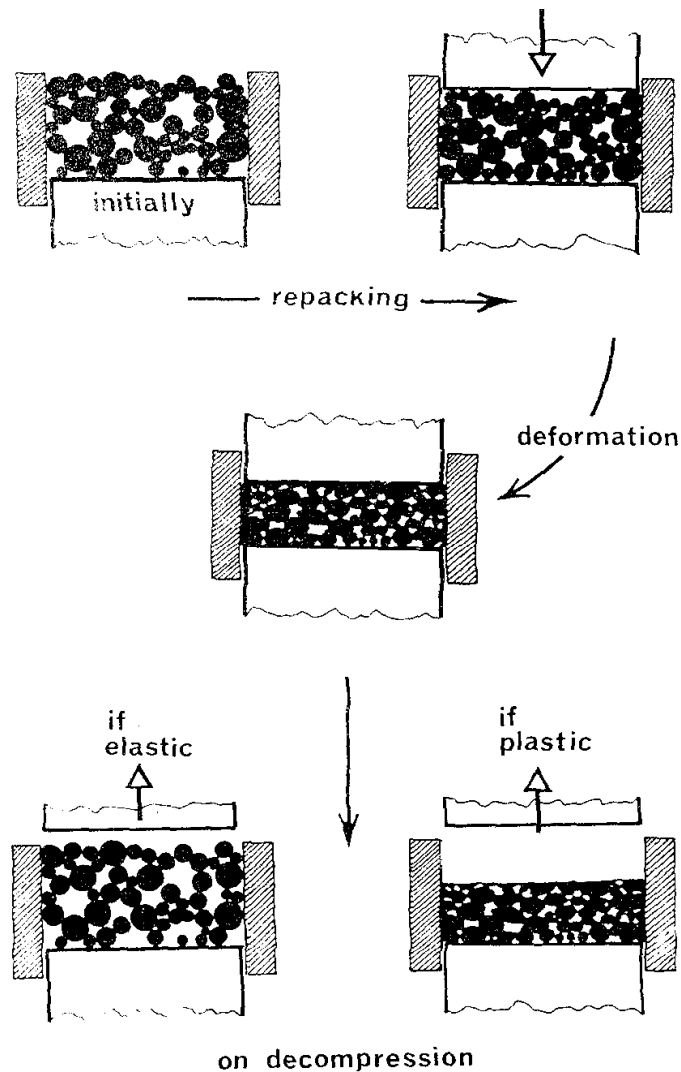
For example, if a solid rod is compressed by forces acting at each end to cause a reduction in length of ΔH from an unloaded length of H_0 (Diagram b), then the compressive strain Z is given by the equation:

$$Z = \frac{\Delta H}{H_0}$$

The ratio of force, F necessary to produce this strain to the area A over which it acts is called the stress σ , that is

$$\sigma = \frac{F}{A}$$

The deformation may be **plastic** or **elastic**. A deformation that does not recover completely after release of stress is known as plastic deformation. A deformation that returns to original shape upon release of stress is known as elastic deformation. The force required to initiate a plastic deformation is known as yield stress.



The particle size distribution and shape of the granules determine initial packing or bulk density as the granulation is delivered into die cavity. At low pressure, the granules flow with respect to each other, with the finer particles entering the void between the larger particles and the bulk density of the granulation is increased. Spherical particles undergo less particle rearrangement than irregular particles as spherical particles assume a close packing arrangement initially. When the particles of a granulation is so closely packed that no further filling of void occur, a further increase in compression force causes deformation at the points of contact. Deformation increases the area of true contact, thereby increasing potential bonding areas.

Heckel Equation

For the compression process, Heckel proposed the following equation:

$$\ln \frac{V}{V - V_{\infty}} = kP + \frac{V_0}{V_0 - V_{\infty}}$$

$$\text{Porosity} = \frac{V - V_{\infty}}{V}$$

$$\frac{V}{V - V_{\infty}} = \frac{1}{\text{porosity}}$$

Hence we can write,

$$\log \frac{1}{E} = \frac{kP}{2.303} + \frac{1}{2.303E_0}$$

$$\log \frac{1}{E} = \frac{kP}{2.303} + A$$

Where, V= volume at pressure P, V₀=original volume of the powder including of voids, K is a material dependent constant (Heckel constant), inversely proportional to the yield value of the powder and V_∞= volume of solid material.

$$\ln \frac{V/M}{V/M - V_{\infty}/M} = kP + \frac{V_0}{V_0 - V_{\infty}}$$

$$\ln \frac{1}{1 - \frac{V_{\infty}M}{MV}} = kP + \frac{V_0}{V_0 - V_{\infty}}$$

$$\text{Relative density } (\rho_r) = \frac{\text{density of a sample, } \rho \text{ under specific condition}}{\text{true density of material } (\rho_T)}$$

Therefore,

$$\ln \frac{1}{1 - \frac{\rho}{\rho_T}} = kP + \frac{V_0}{V_0 - V_{\infty}}$$

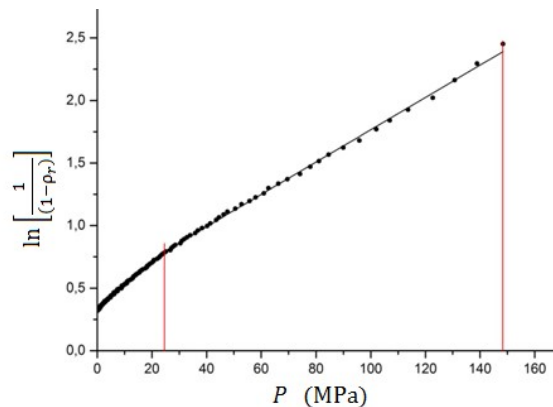
$$\ln \frac{1}{1 - \rho_r} = kP + \frac{V_0}{V_0 - V_{\infty}}$$

$$\log \frac{1}{1 - \rho_r} = \frac{kP}{2.303} + A$$

Thus, Heckle relationship may be written in terms of relative density rather than volume.

Heckel constant is inversely related to the yield pressure. The curved portion of the Heckel plot at low pressure represents a value due to densification by particle rearrangement.

The intercept obtained from the slope of the upper portion of the curve is a reflection of the subsequent deformation process including densification after consolidation. A large value of Heckel constant indicates the onset of plastic deformation at relatively low pressure.



Heckel plot

Application of Heckel equation

- A Heckel plot permits the interpretation of mechanisms of bonding. For NaCl, Heckel plot is linear indicating that NaCl undergoes plastic deformation during compression.
- The crushing strength of tablets can be correlated with value of K of Heckel plot.
- Larger k values indicate harder tablets
- Such information can be used as means of binder selection when designing tablet formulations
- Heckel plots can be influenced by the overall time of compression, the degree of lubrication, and even the size of the die, so that the effects of these variables are also important and should be taken into consideration.

Elastic modulus

Young's modulus or modulus of elasticity (E) is a measure of a material's stiffness. The higher the Young's modulus value, the stiffer is the material. Young's modulus has a unit of pressure. Its SI unit is Pascal (N/m^2). It can be used to predict the elongation or compression of an object when exposed to a force.

$$\begin{aligned}
 E &= \frac{\text{tensile stress}}{\text{tensile strain}} \\
 &= \frac{\sigma}{\epsilon} \\
 &= \frac{F/A}{\Delta L/L} \\
 &= \frac{FL}{A\Delta L}
 \end{aligned}$$

ΔL =change in length and L is the initial length.

Reference:

Martin's Physical Pharmacy and Pharmaceutical Sciences: physical, chemical and biopharmaceutical principles in the pharmaceutical sciences. 6th edition. Editors: Patrick J Sinko, Yashveer Singh. Wolters Kluwer Health, Lippincott Williams & Wilkins, Philadelphia, 2006.