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Monash University  
Victorian College of Pharmacy

## Course: Formulation Chemistry II (VCF2071)

Section Two: Lubricants – Liquid, semi-solid and dry powder

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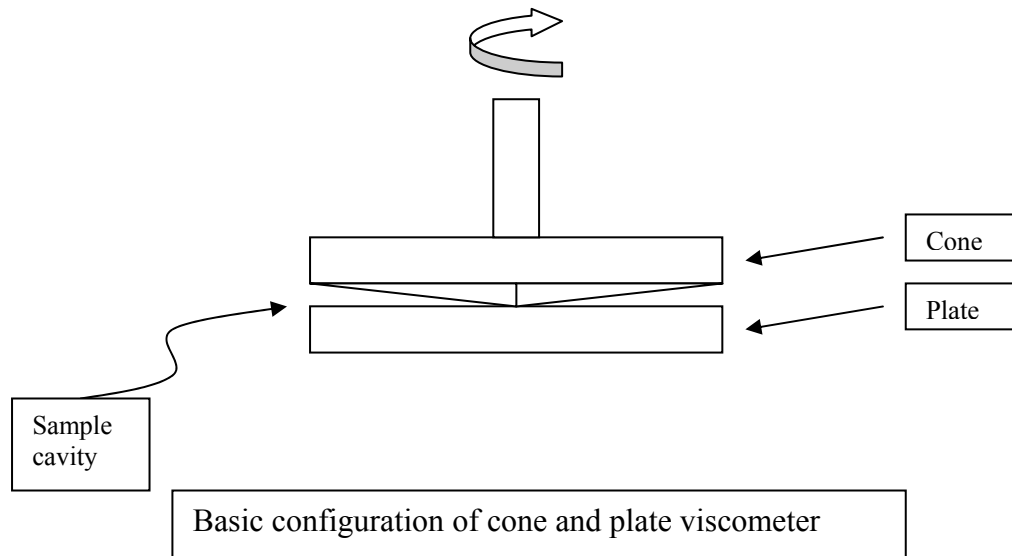
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## Lubricants

Lubricants, aqueous, gels, jellies, non-aqueous, silicones

Numerous liquid or semi-solid pharmaceutical, cosmetic and personal care products need to have a degree of “slipperiness” or lubricity as a component. This can be introduced through many different formulations, although these can be basically divided into aqueous based and non-aqueous based formulations. Aqueous formulations are most often some type of gel or jelly, while non-aqueous formulations are usually based on either mineral oils or silicones.

The extent of the lubricating properties can often be quantified by viscosity measurements. As these liquids and semi-solids have quite high viscosities, the measuring systems are often different to those used for measurement of viscosity in liquids that flow more easily. Although the capillary or the cup and bob viscometers can be used with viscous liquids, viscosities for semi-solids are most often measured with a temperature-controlled cone and plate viscometer. This geometry ensures that the semi-solid stays in contact with the shearing surfaces of the viscometer.



## Viscoelasticity

More complex viscosimetric techniques are also used to characterize semi-solids, including the study of **viscoelasticity**.

Viscoelasticity takes account of the fact that many complex semi-solids demonstrate behaviour that cannot be described in simple viscosity terms alone.

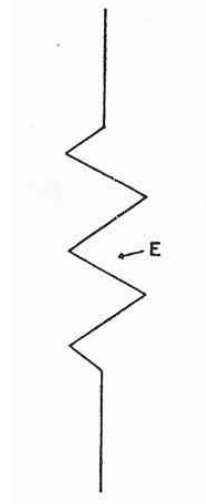
These semi-solids demonstrate behaviour that is divided into two components: a purely viscous component, and a purely elastic component.

The viscous component represents flow behaviour that is irreversible, while the elastic component represents flow that is reversible. In semi-solids, these flows are often called “deformation”

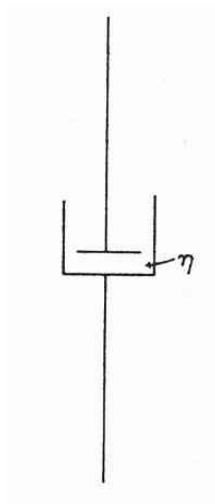
These concepts can be illustrated with a viscometer that instantly applies a weak shear stress to a semi-solid for a fixed time duration, then removes the stress. This is often called a “creep” viscometer, because the quantity that is measured is the slow, very small movement that occurs during the application of the stress and after its removal.

During application of the shear stress, some irreversible flow will take place, leading to a degree of permanent deformation of the sample. At the same time, some elastic deformation will also occur. Because elastic deformation is reversible, this component of the flow behaviour will be recovered when the shear stress is removed.

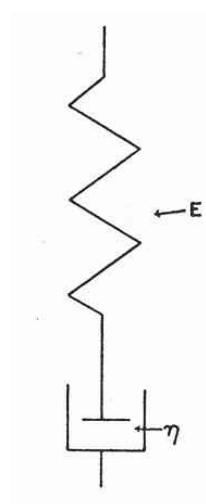
Viscoelastic measurements describe the analysis of semi-solids in terms of **Hookean springs** (which represent the reversible deformation) and **Newtonian dashpots** (which represent the irreversible deformation).



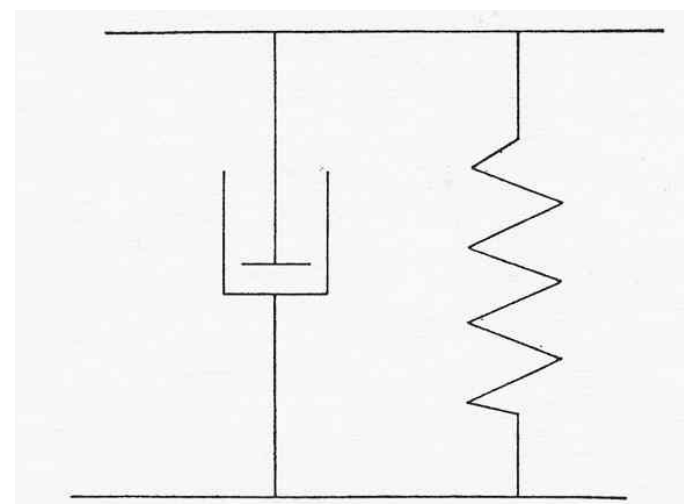
Hookean spring



Newtonian dashpot



Maxwell unit



Voigt unit

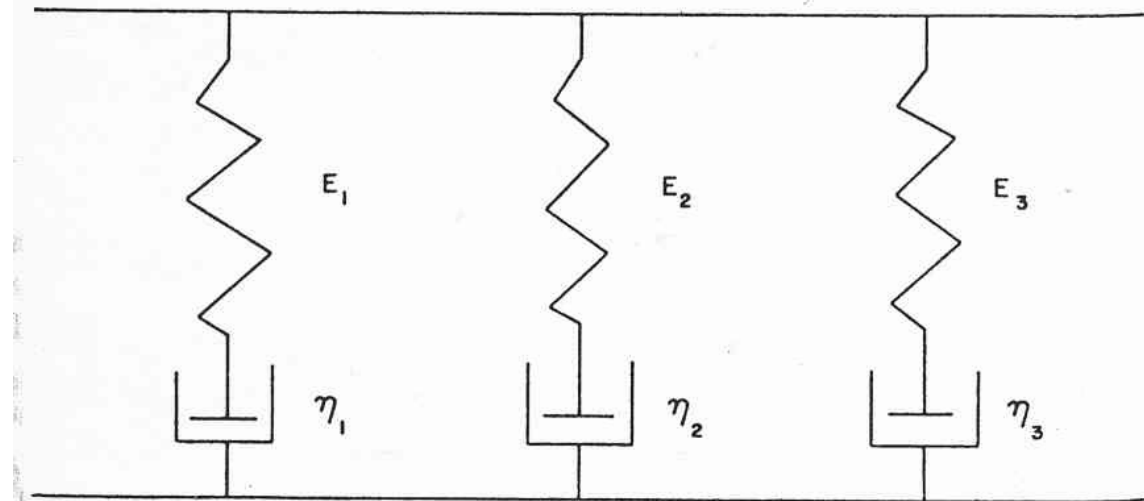
A Hookean spring is one that closely obeys Hooke's Law, for which Young's modulus ( $E$ ) can be measured. This is a normal characteristic of solids.

A Newtonian dashpot is represented by a closely fitting plunger inside a cylinder that is filled with a Newtonian fluid, which can be characterized by a viscosity,  $\eta$ .

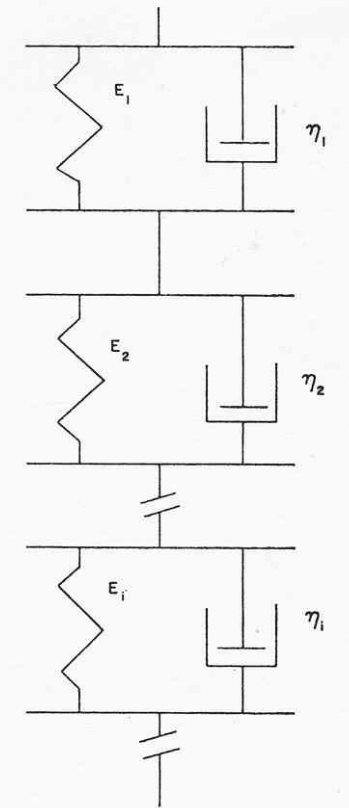
These two elements can be combined in the **Maxwell unit** (series; some permanent irreversible flow), or in the **Voigt unit** (parallel; all flow is reversible, but full recovery is slower than if the dashpot was not present)

### Semi-solids combine the elements of solids and liquids

Where a semi-solid system contains polymeric molecules, the type of viscoelastic behaviour is very often represented by a more complex combination of Maxwell and Voigt units:



Maxwell-Weichert model



Voigt-Kelvin model

From a formulation perspective, the ability to describe complex semi-solid systems is useful. It allows characterization of different polymeric excipients in terms of desired tactile properties. You can appreciate that systems which have a large amount of elastic character will feel different on the skin when compared to a system in which this behaviour is largely absent. Viscoelasticity is important in characterizing plastics for packaging and for medical devices, such as infusion tubing.

Furthermore, the overall behaviour of a system may change drastically with change in temperature.

Besides rheological properties, other factors also are important in design of semi-solids for application to the skin or body cavities. However, these are often more subjective, or else involve measurement with biological systems, such as skin properties, including epidermal moisture loss.

A gel was originally defined as “a two component system of a semi-solid nature, rich in liquid”. Although subsequent definitions have emphasized various aspects of gels, such as their very high viscosity, the one common characteristic at the molecular level is the presence of some form of continuous structure that provides solid-like properties.

In a typical polar gel, a natural, semi-synthetic or fully synthetic polymer at low concentration (typically <10% w/v) builds a three dimensional matrix throughout a hydrophilic liquid (primarily water). If the gelling agent dissolves completely, then the gel can be crystal clear, otherwise the presence of undissolved or aggregated components will make the gel more or less opalescent. These indicate aggregates of at least 400 nm in diameter.

Aqueous gels often display **viscoelastic** behaviour, especially carbopol gels. DNA solutions also display viscoelasticity.

The components which form aqueous gels are:

- (a) natural gums, e.g., tragacanth, carrageenan, pectin, agar and alginate salts. These contain numerous carboxyl groups which commence ionization at about pH 4 and are largely ionised in aqueous solutions at pH values >7.5;
- (b) semisynthetic polymers such as modified carbohydrates (methylcellulose, hydroxyethylcellulose, hydroxypropylcellulose, hydroxypropylmethylcellulose and carboxymethylcellulose), some of which also have ionised carboxylate groups as well as many hydroxyl groups; and
- (c) synthetics such as Carbopol (carbomer – has numerous carboxylates) and polyvinylalcohol (PVA) (many hydroxyl groups). Some clays (e.g., bentonite, veegum and laponite) have also been found to have gelling capability.

Mechanisms of gelation depend on the type of gelling agent:

- Chemically modified celluloses form colloidal dispersions in water. Extensive hydrogen bonding between these large, linear polymers (MW up to  $10^6$  g/mol) generates structure in the gelled system. As the hydrogen bonding depends entirely on dipole-dipole interactions, fairly high concentrations (up to 10% w/w, depending on molecular weight and extent of chemical modification) are required for gel formation. Tangling of the polymer chains adds to the structure.
- Sodium alginate gels are formed when low concentrations (1-3% w/v) are cross-linked by the addition of small amounts of divalent cations, i.e., magnesium or calcium ions. This mimics the naturally occurring carbohydrate gums, which contain a greater or lesser proportion of divalent cations. The cross-linking extends the structure of the gelling agent in giant networks.
- Bentonite (hydrated aluminium silicate) and other naturally occurring clays (veegum – magnesium aluminium silicate) occur in hydrophilic colloid-sized particles. These are essentially insoluble in water, but hydrate and swell considerably to form gels when mixed with 8 to 10 parts by weight of water. The hydrated exterior surfaces are polar and form numerous sites for hydrogen bond formation and cross-linking to neighbouring particle surfaces.
- Carbopols are used extensively for gel formation. Their synthetic nature permits (a) a wide range of properties to be specifically designed, such as controlled molecular weight, viscosity, type and extent of cross-linking; and (b) more rigid quality control, a factor which is not always so well developed with naturally occurring gums. Several gelling mechanisms occur with the carbopols. The untreated polymers form opalescent, somewhat viscous dispersions that are slightly acidic, due to their extensive carboxyl groups. Under these conditions, the polymer exists mainly as flexible coils. A wide variety of alkaline bases may then be used to sequentially ionise the COOH functions, e.g., alkali metal hydroxides, such as sodium, potassium and ammonium; and organic bases, especially amines. Ionization forms negatively charged networks, in which the charges are subject to coulombic repulsion. This forces the anionic groups apart, extending the chains and making them stiffer. Increased ionisation also increases the strength of direct ion-dipole interactions with water molecules, leading to more extensive hydrogen bonded networks throughout the gel. The nature of the cation can be controlled to superimpose a range of more subtle and subjective effects, such as smoothness and moisturizing properties. Carbopol gels can form with amounts as low as 0.1 to 1%, depending on the extent of ionisation (a function of the pH), molecular weight and degree of cross-linking. Another mechanism involves swelling that occurs when the cross-linked carbopol structure absorbs water. See Banker and Rhodes, *Modern Pharmaceutics*, 2<sup>nd</sup> ed., pp. 300-302 and also <http://www.carbopol.com/>



**Bath/shower gel constituents**

Cussons Imperial Leather Shower Gel formulations advertised as hypoallergenic; dermatologically tested; suitable for sensitive skin (all these are essentially meaningless terms in a legal sense):

Normal	Fresh Burst - for a feeling of freshness and energy	Moisture Plus for softer smoother skin
Water sodium laureth sulphate (C12-(oxyethylene) <sub>n</sub> -sulphate) (n = 4 to >20) sodium cocoylisethionate (medium chain alkyl ether of 2-hydroxyethanesulphonic acid, sodium salt) cocamidopropylbetaine glycerin PEG-7 glycerylcocoate PEG-200 hydrogenated glyceryl palmate Fragrance cocamidopropyl PG-dimonium chloride phosphate hydroxypropylguar gum hydroxypropyltrimonium chloride disodium phosphate disodium EDTA citric acid hexylene glycol benzophenone-1 methyldibromoglutaronitrile phenoxyethanol sodium chloride	Water sodium laureth sulphate cocamidopropylbetaine PEG-7 glyceryl cocoate cocamidopropylamine oxide NaCl Fragrance hydroxypropyl guar gum hydroxypropyl trimonium chloride disodium EDTA hexylene glycol citric acid disodium phosphate methyldibromoglutaronitrile phenoxyethanol CI 42090 (Brilliant Blue FCF; FD&C Blue No. 1) CI 19140 (Tartrazine; FD&C Yellow No. 5)	Water sodium laureth sulphate cocamidopropylbetaine PEG-7 glyceryl cocoate cocamidopropylamine oxide NaCl Fragrance PEG-6 caprylic/capric glycerides PEG-5 octanoate Trideceth-9 glycol distearate cocamide MEA Laureth-10 guar gum hydroxypropyl trimonium chloride disodium EDTA hexylene glycol citric acid disodium phosphate methyldibromoglutaronitrile phenoxyethanol CI 17200

## Safety

The question of safety of compounds used in cosmetic products has been under continual evaluation by the Cosmetic Ingredient Review, a US industry body set up in 1976 to evaluate the safety of materials used in personal care products. See <http://www.cir-safety.org/index.html> (homepage) and <http://www.cir-safety.org/SAFETY.html> (safety updates). See below under Product Types for further discussion.

Personal care products see: <http://www.personalcare.noveoninc.com/applications/default.html> (web site for Carbopol and related products)

## Non-Aqueous Lubricants

Mineral oils (paraffins) are the higher boiling saturated hydrocarbon fractions from the petroleum industry. They are obtained from crude oil by distillation (330 to 390 deg C) and are liquid and moderately viscous at room temperature. The fraction boiling from 330 – 360 deg C is separated by a second distillation and described as Light Mineral Oil, while the higher boiling fraction is simply called mineral oil.

Even higher boiling grades are semi-solid to solid at room temperature. These are separated from mineral oil by chilling the distillate and collecting solid fractions that precipitate at various temperatures. They are usually called soft paraffin, petroleum jelly or petrolatum. The material is usually white or yellow, the white form being made from the yellow form by chemical bleaching.

**Mineral oils** are frequently used in skin and personal care products for their **emollient** properties. This word means that they have the property of softening the skin. The mechanism for this process is based on their hydrophobic, water repellent nature. On the skin, mineral oils prevent the loss of perspiration, thus increasing the moisture content of the skin. As a consequence, the horny keratin layer absorbs the water and becomes less rigid.

**Silicones** are synthetic polymers based on the element silicon. Take care to not confuse the words “silicon” (which is the element) and “silicone” which describes thousands of compounds that have the Si-O group as part of a repeated structure.

Silicones provide formulations with similar properties to mineral oils, although in recent years, novel silicones have been developed with significantly altered properties. The archetypal silicone oil is dimethicone,  $(\text{CH}_3)_3\text{Si-O}[\text{Si}(\text{CH}_3)_2\text{-O}]_n\text{-Si}(\text{CH}_3)_3$ . Similar compounds have phenyl rings or cyclohexane rings in place of the methyl groups.

These compounds are hydrophobic and water repellent, and have similar barrier function and emollient properties to the mineral oils.

Look at <http://www.personalcare.noveoninc.com/literature/default.html> for a bunch of stuff on silicones:

“Traditional silicones, such as dimethicones and cyclomethicones are known for their ability to improve feel and spreading, to impart lubricity, provide barrier properties, and add conditioning benefits to personal care products. Silicone fluids have long been recommended as potential replacers, extenders or enhancers for oil phases in cosmetic formulations.”

“Silicones are also known for their hydrophobic, and oleophobic nature. Their insolubility in both water and mineral oils, along with their tendency to defoam has limited their utility in many personal care formulations. The need that emerged was for silicone properties in products without the drawbacks of fluids or emulsions. The answer to that need comes in the form of Ultrasil™ and Ultrabee® Specialty Silicones for Personal Care.”

“Ultrasil™ and Ultrabee® Specialty Silicones were created through the pairing of traditional oleochemistry with silicone chemistry. These organo silicone surfactants feature both a hydrophilic and hydrophobic group. When silicone is used as the hydrophobe in the preparation of surfactants, these novel ingredients yield properties that cannot be achieved through the use of silicones or oleochemical surfactants alone.” (quoted from Noveon, Inc., website)

Chemically modified silicones include polar groups on the side chains. These impart hydrophilic properties and consequently, they have some surfactant character. They have been designed for use in the personal care industry and find much use as emulsifiers. See web site (above).

## Dry Powder Lubricants

Lubricants, solid, microfine powders (graphite, starch, talc, other tablet lubricants)

See P.York, Tablet Lubricants, pp. 37-70 in Florence, Materials used in Pharmaceutical Formulation; also Handbook of Pharmaceutical Excipients (Wade and Weller, 2<sup>nd</sup> Edn.; or Kibbe, 3<sup>rd</sup> Edn.)

Dry powder lubricants are needed for numerous formulated products, e.g.,

- Graphite powders – general purpose lubricant
- Glove lubricants – e.g., surgical gloves
- Make up powders
- Tablet formulations
- Capsule formulations
- Oral granule and powder formulations
- Soap and laundry detergent powders
- Photocopier and laser printer toner cartridges

## Mechanisms of surface friction

Solid surfaces are universally rough – they differ only in the **degree** of roughness or **rugosity**

Two mechanisms are proposed –

- the more important involves the interlocking of asperities or **projections** on the rough surfaces. These must be slid over or around each other for the friction to be overcome
- **Adhesion** between the contact areas of the surface projections is also important
- The second mechanism accounts for additional energy that is found to be needed to allow rough surfaces to slide over each other. It involves a degree of deformation of the projections from each surface. This is mainly relevant to the friction found in tablet formulations.

Friction needs to be overcome in two situations:

- Making powders and granules flow readily
- Preventing compressed powders or granules sticking to machinery used for making compressed tablets

Lubricants and glidants are used for these purposes

- Glidants are required for making powders flow readily in all cases
- Dry lubricants are used for making the stainless steel surfaces of tablet compression and other machinery slippery

## Lubricant and Glidant Materials

Typical materials for lubricant and glidant purposes are:

- Graphite powder is a laminar system at the atomic level – it has very weak forces between planes of strongly bonded carbon atoms arranged in six-membered rings – a useful general purpose lubricant although generally not used in formulated products (colour, lack of assimilation by biological systems)
- Magnesium and calcium stearates are the archetypal metallic soaps – their largely non-polar, hydrocarbon properties mean they stick to very little apart from other hydrocarbons. Magnesium stearate is the most widely used of all tableting lubricants. It contains mainly stearic acid (C18), but also some palmitic acid (C16), as their magnesium salts. It adheres easily to surfaces, but acts a very good lubricant as the solid powder is a very flaky material which easily fractures along slip planes. It is polymorphic, with a second form that is acicular, with poorer lubricant properties. Its biggest problem is that it is relatively hydrophobic, thus does not dissolve easily and can retard the dissolution of drugs from tablets. GRAS listed
- Surfactants, e.g., sodium and magnesium lauryl sulphate
- Stearic acid (octadecanoic acid) and other fatty acids have intrinsic lubricant properties, but can also form soaps *in situ*. They have no glidant properties. They will react with bases and may form undesirable products, such as insoluble or poorly absorbed materials. They are GRAS listed and widely used in formulated products for internal and external use.
- Fatty acid esters, including materials such as Sterotex (various grades and types of hydrogenated vegetable oils, such as castor, cottonseed, palm and soybean) and Cutina HR (castor seed oil) are solid at lower temperatures. Other solid esters with good lubricant properties are the monoglycerides (e.g., glyceryl monostearate) and triglycerides (e.g., glyceryl tristearate). GRAS listed

- Talc (also known as French chalk, soapstone or steatite) is a hydrated magnesium silicate (a type of clay) which exists as very fine powder. Various grades exist with most particles less than 40 microns or less than 70 microns (specific surface area, 12 m<sup>2</sup>/g). It is a very widely used tableting lubricant and as a component of external skin powders. It has been used for lubricating rubber gloves, but should not be, as there is a risk of granuloma if it gets past broken skin. It also has glidant properties, but not very good. Talc can be a severe respiratory irritant. It does not dissolve in all common solvents and is not absorbed by the body. GRAS listed
- Colloidal (fumed) silica is the best material available for use as a glidant. The extremely minute size of the particles (7-16 nm) means that it has very high specific surface (up to 400 m<sup>2</sup>/g) and fills in the most minute spaces between the surface projections. Colloidal silica also tends to aggregate with itself, so it is able to mold itself to fit irregularly shaped cavities. It is extremely light and one of the least dense powders known (>0.04 g/cm<sup>3</sup>). Colloidal silica is hygroscopic and can absorb quite large amounts of water without appearing to be damp, making it a good desiccant and anti-caking agent.
- Starch also has glidant properties when dry – skin powders, gloves (not always used)
- Leucine and sodium benzoate have weak lubricant properties, but the advantage of aqueous solubility, which makes them suited to be the lubricant in effervescent tablets, e.g., soluble aspirin. Both GRAS listed

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