BIO & PHARMA ANALYTICAL TECHNIQUES

Chapter 6 Particle Analysis: Powder Rheometry

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Rheometry
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http://ocw.ump.edu.my/course/view/php?id=611

Chapter Description

- Aims
  - Discuss theory, principles and application of analytical techniques used in material characterisation, pre-formulation development, manufacturing process and storage stability.

- Expected Outcomes
  - Explain type of fluid for finished pharmaceutical products
  - Discuss on the fluid viscosity and method of determination (viscometer)
  - Analyze selected powder rheometry techniques used in pharmaceutical laboratory
  - Discuss on the influence and significance of powder rheometry analysis in pharmaceutical industry

- References

  - Gunzler H. & Williams A. (2002). Handbook of Analytical Techniques. Wiley-VCH, Weinheim, Germany.
  - Mullertz, A., Perrie, Y. and Rades, T. (2016) Analytical Techniques in the Pharmaceutical Sciences (Advances in Delivery Science and Technology). Springer, United States.

History…

- The term 'Rheology' was invented by Professor Bingham (Lafayette College) in 1920s,and was inspired by a Greek quotation "panta rei" meaning "everything flows".

- This method of material analysis was first used by Professor Bingham and Reiner on the 29th of April 1929 when the American Society of Rheology was founded in Columbus, Ohio State, USA.

- Rheology mostly analyses mechanical properties which include physical properties of liquids and solids by describing the strain/force and flow behavior.

OVERVIEW

RHEOLOGY

- *Rheo = to flow*
- *logos = science / study*
- DEFINITION: Rheology is the study of the flow and deformation of matter under stress. (how the flow is affected by stresses or forces).
- These systems change their flow behavior when exposed to different stress conditions.
- It applies to substances which have a complex structure such as polymers, cheese, emulsion and other biological materials.

- **Deformation** is defined as the relative displacement of points in a body and it can be divided into **three types**:

  1.Flow: when the stress is removed the material does not revert into its original configuration. (Irreversible)

  2.Elasticity: removing the stress the applied work is largely recovered and the body retains its original configuration. (Reversible)

  3. Viscoelasticity: combination of both (flow and elasticity)

- Irreversible flows, reversible elastic deformations or their combination (viscoelasticity) can describe as a **rheological phenomenon.**

FUNDAMENTAL OF VISCOSITY

- An expression of the resistance of a fluid to flow
- The higher the viscosity, the great the resistance
- Fluid resistance to flow

$$\eta = F/G$$

- Viscosity is shearing stress divided by rate of shear
  - F: Shear stress
  - G: Shear rate

Source: https://en.wikipedia.org

- Viscosity is the measure of the internal friction of fluid.
- The greater the friction, the greater the amount of force required to cause the movement (shear)

DEFINITIONS

- **Shearing stress, F**

  The force per unit area, F'/A, required to initiate flow

- **Rate of shear, G**

  The velocity at which a fluid will travel

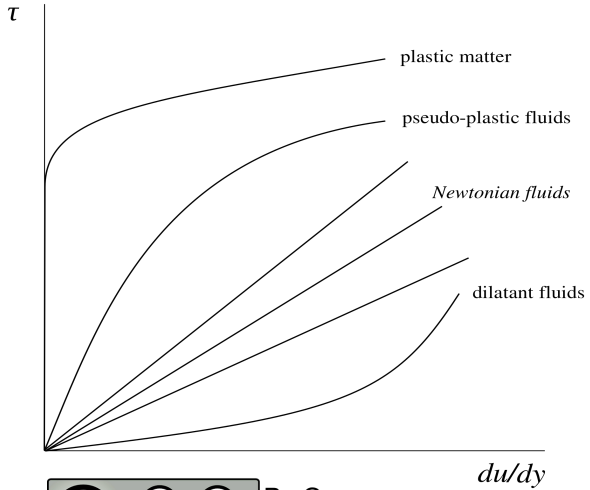
- **Velocity**

  The speed of „something" in a given direction

TYPE OF FLUIDS

1. NEWTONIAN FLUID (NF)

- Characterized by having a **constant viscosity** at a given temperature
- Shear stress and shear rate are **linearly proportion.**
- This plot will show constant slope = viscosity
- The simplest and the easiest fluids to measure in the lab
- Examples :
  - ✓ Water,
  - ✓ chloroform,
  - ✓ Castor oil (mineral oils)
  - ✓ Ethyl Alcohol etc.

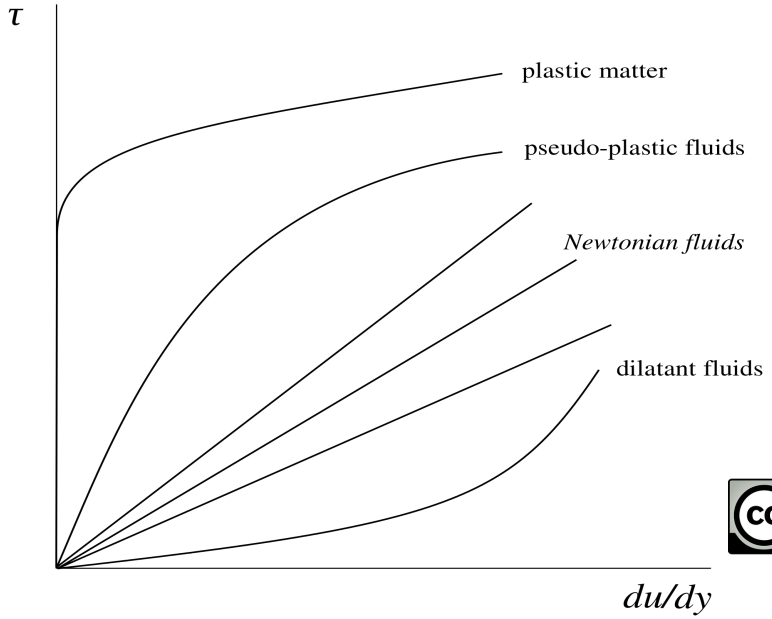


2. NON-NEWTONIAN FLUID (NNF)

- Characterized by **not having a unique value for viscosity**
- The viscosity of these fluids will **depend on the shear rate applied**.
- It can be seen in liquids and in solid heterogeneous dispersions such as **emulsions**, **suspensions**, **colloids** and **ointments**.
- They are classified into 3 types of flow:
  1. **Plastic Flow**
  2. **Pseu-doplastic Flow**
  3. **Dilatant Flow**

Rheogram

- A flow curve plot of F vs G.
- **Newtonian systems** will show a linear relationship (straight line), while **non-newtonian systems** have curved lines



- The majority of fluid pharmaceutical products are not simple liquids and **do not follow Newton's law** of flow.

HOW TO DETERMINE VISCOSITY

Selection of viscometer

Single point viscometer viscometer

Ostwald viscometer

Falling sphere viscometer

Application

Newtonian flow

Multi point

Cup and bob

Cone and plate

Application

non -Newtonian flow

Newtonian flow

- Viscosity can be determined by instruments called **viscosimeter or viscometer**
- Selection of instruments based on the **type of fluids and the analysis required**

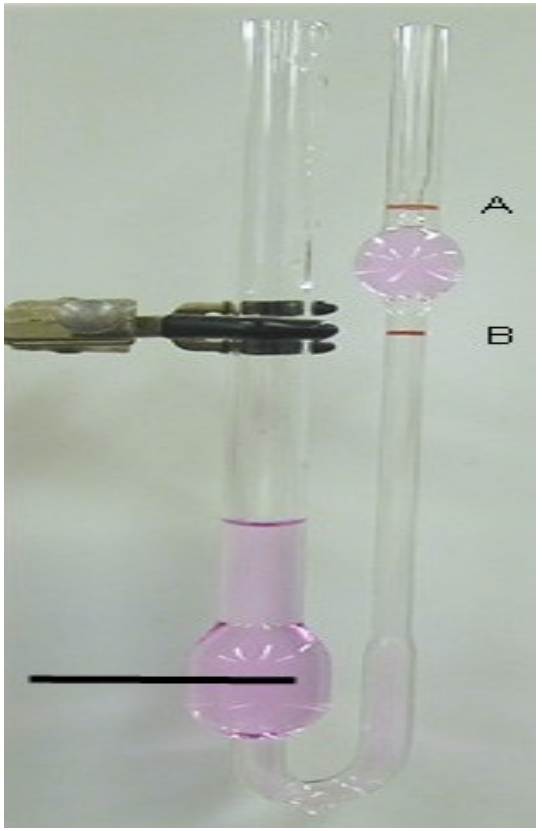
Single Point Viscometer

1. Ostwald viscometer (Capillary)

The Ostwald viscometer is used to determine the viscosity of **Newtonian fluid.**

- **by measuring time required for the fluid to pass between two marks.**

PRINCIPLE: When a liquid flows by gravity, the time required for the liquid to pass between two marks (A & B) through the vertical capillary tube. **The time of flow of the liquid under test is compared with time required for a liquid of known viscosity (Water).**



HOW DOES A CAPILLARY/OSTWALD VISCOMETER WORK?

Suction is applied to the liquid in the instrument, to bring the liquid up to a start mark.

↓

The liquid must flow down through a capillary, and the user times how long it takes to travel a specific distance.

↓

The time of flow of the liquid under test is compared with time required for a liquid of known viscosity (Water).

2. Falling Sphere Viscometer

- It is called as Hoppler falling sphere viscometers.
- **Principle**:

A glass or ball rolls down in vertical glass tube containing the test liquid at a known constant temperature.

The rate (time) at which the ball falls from top to bottom is measured

- Electrical sensor is used for opaque liquids

Multi Point Viscometer

3. Cup and Bob

Principle:

The sample is sheared in space between the outer wall of a bob & inner wall of a cup into which the bob is fits

↓

Either the bob or the cup is made to rotate

↓

Torque resulting from viscous drag is measured by spring or sensor at known speed

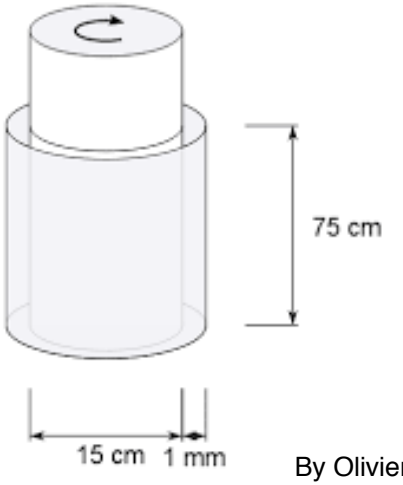
- Various instruments are available, differ mainly whether **torque results from rotation of cup or bob**

i. Coutte type viscometers:

-Cup is rotated

-The viscous drag on the bob due to sample causes to turn

- Example: *MacMicheal viscometer*



By Olivier Cleynen
https://commons.wikimedia.org

ii. Searle type viscometers:

-Bob is rotated

-The viscous drag of the system is measured by spring or sensor.

- Example: *Stormer viscometer*

4. Cone and plate viscometer (Rotational viscometer)

Principle:

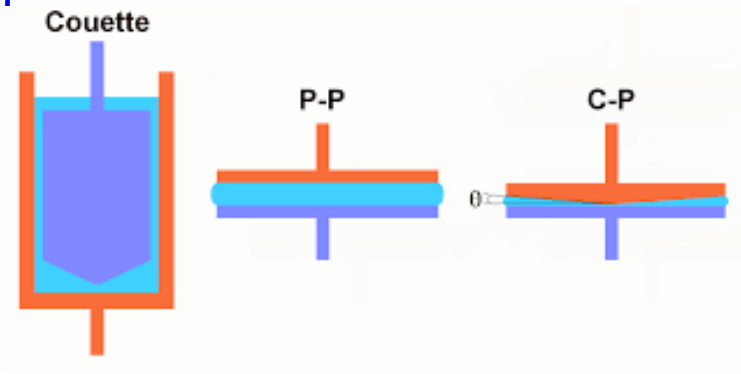
The sample is placed on the center of the plate, which is raised into the position under the cone.

↓

The cone is driven by variable speed motor and sample is sheared in the narrow gap between stationary plate and rotating cone.

↓

The resistance to the rotation of the cone produces a torque



HOW TO DETERMINE POWDER RHEOMETRY

1. Avalanching Tester

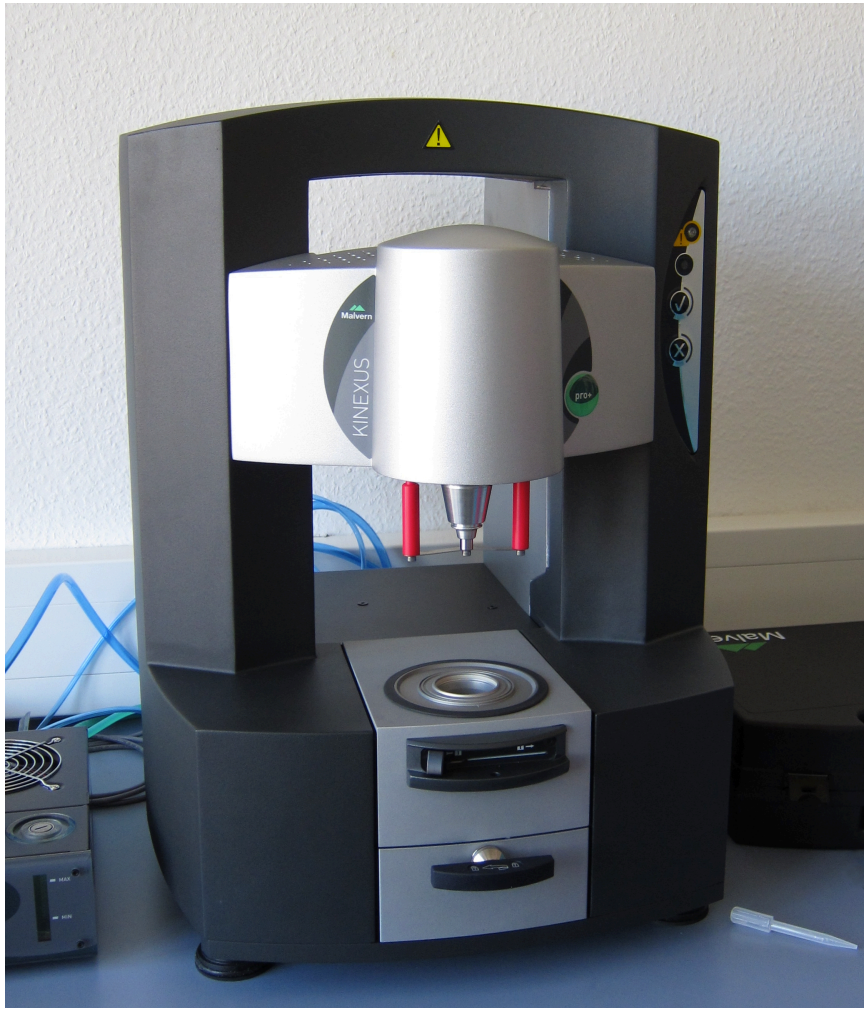
- Used to determine dynamic angle of repose.

- **Angle of repose**:

  "*The internal angle between the surface of the pile and the horizontal surface*" is known as the angle of repose.

- A static heap of powder, when only gravity acts upon it. Will tend to form a conical mount.

  - Example: Aero-Flow™ Automated Powder Flowability Analyzer



2. Carr's Compressibility Index and Hausner Ratio

- Both are determined by measuring the bulk volume and the tapped volume of a powder.
- by calculating the compressibility index (CI)
- CI is an indirect measure of bulk density, size and shape, surface area, moisture content and cohesiveness of material.

Compressibility is the ability of powder to decrease in volume under pressure

Compressibility Index (%)	Flow Character	Hausner Ratio
≤10	Excellent	1.00-1.11
11-15	Good	1.12-1.18
16-20	Fair	1.19-1.25
21-25	Passable	1.26-1.34
26-31	Poor	1.35-1.45
32-37	Very poor	1.46-1.59
≥37	Very, very poor	≥1.60

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3. Flow Through an Orifice:

Useful **only for free-flowing materials.**

Two types of flow rate of powder determined:

- Mass flow rate
- Volume flow rate

4. Shear Cell Method:

In the shear cell method, the force necessary to shear the powder bed by moving the upper ring is determined.

Shear cell tester : to check on the interparticle adhesion, which often makes them cohesive.

This will help manufacturer to determine the amount of flow agent needed.

5. Powder Rheometer:

This methodologies allow **measurement of Flow energy**

Flow energy

= Total resistance of powder to flow, whilst the powder is in motion.

A precision 'blade', or impeller, is rotated and moved downwards and upwards through the powder to establish a precise flow pattern.

↓

This causes many thousands of particles to interact, or flow relative to one another, and the resistance experienced by the blade represents the difficulty of this relative particle movement, or the bulk flow properties.

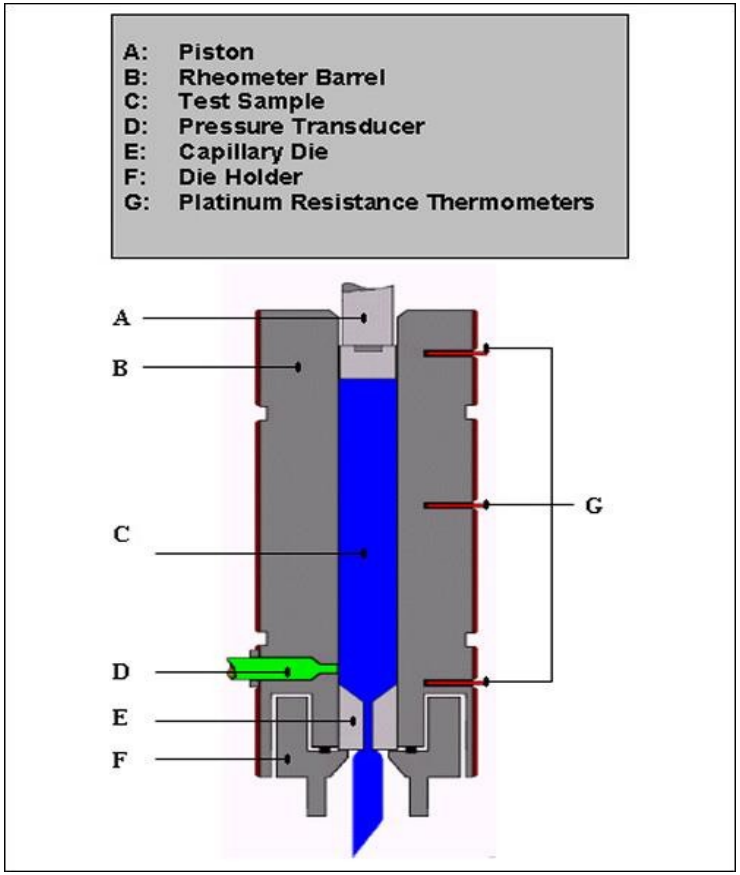
↓

The more the particles resist motion and the harder it is to get the powder to flow, the more difficult it is to move the blade.

- As the blade moves through the sample, **rheometer measures both rotational and vertical resistances**, in the form of **Torque** and **Force** respectively.

- It is important to capture both signals as it is the composite of these two values that **quantifies the powder's total resistance to flow.**

Capillary Extrusion Rheometer



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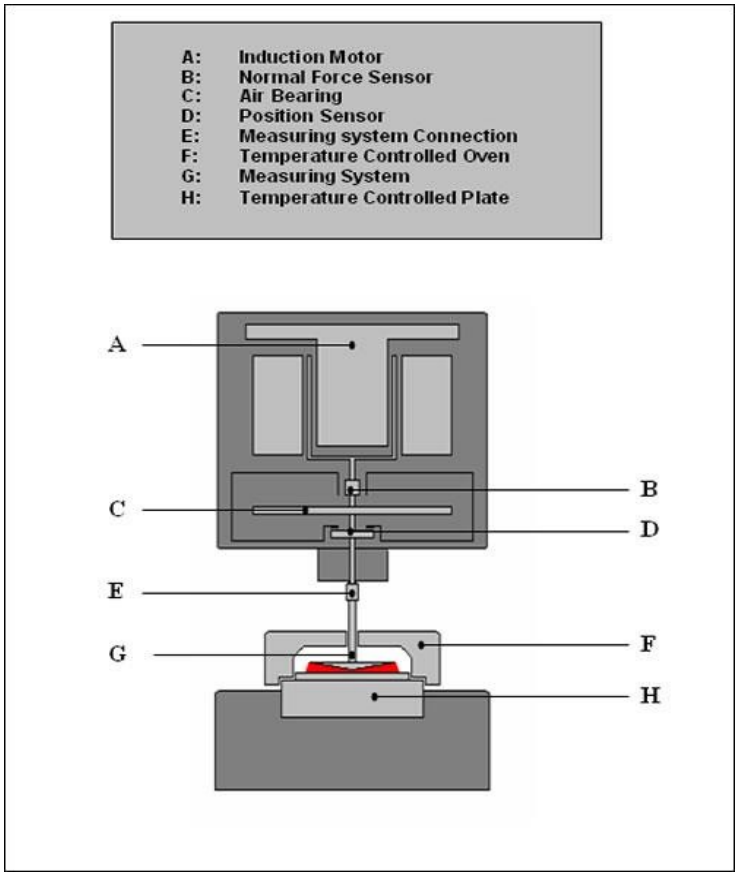
Controlled Stress / Rate Rotational Rheometer



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IMPORTANCE OF RHEOLOGY

FORMULATION

- Ensuring acceptable and reproducible consistency/smoothness of creams, pastes, lotions.

MIXING (PROCESS)

- Influence the choice of processing equipment in the pharmaceutical system.

PRODUCT PERFORMANCE (PACKAGING)

- Packaging of materials into containers
- Removal of materials from containers (pouring from bottle, passing through syringe needle, extrusion of ointment from tubes)

IMPORTANCE OF VISCOSITY

- Patient's acceptability of the product, physical stability, biological availability, **absorption rate** of drugs in the gastrointestinal tract.

- **How can viscosity affect biological activity?**

→ Drugs will diffuse more slowly out of a more viscous fluid, affecting absorption from GI tract or skin

1. The **viscosity of creams and lotions** may affect the rate of **absorption** of the products by the skin.
2. A greater release of active ingredients is generally possible from the **softer, less viscous bases.**
3. The viscosity of semi-solid products may affect absorption of these products due to the **effect of viscosity on the rate of diffusion of the active ingredients.**

Conclusion of the Chapter

1. Rheology gives a relationship between the **properties, structure and processing of the materials.**

2. Rheology helps describe the mechanical **behavior** of materials as a **function of stresses, strain, temperature and pressure** in order to develop materials with the correct processing behavior based on their viscosity and elasticity

3. The rheology of these formulations /products must be optimum during mixing, stirring, pumping, coating, spraying or extrusion processes.

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Any Question?

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