Hygroscop*icity* , *Powder Rheology* & *Compaction Properties*

(1) HYGROSCOPICITY:-

CONTENTS :-

A. **INTRODUCTION**
B. **METHOD OF DETERMINATION**
C. **IMPORTANCE OF MEASUREMENT**
D. **METHOD OF IMPROVEMENT**

(A) INTRODUCTION :

- ***Hygroscopicity: -*** It is the tendency of material to absorb moisture from atmosphere & get dynamic equilibrium with water in the atmosphere.

- ***Deliquescent: -*** It is the hygroscopic substance which absorb moisture from air and they can be liquefied by partially or wholly forming solution.

- ***Efflorescent: -*** a substance which loses water to form a lower hydrate or become anhydrous is termed as efflorescent.

(B) METHOD OF DETERMINATION :

- To carry out study, sample of compound are accurately weighed into container and placed at various humid condition for period of upto 2 weeks.
  - If Weight **gain** – Deliquescent or Hygroscopic
  - If Weight **loss** – Efflorescent

- Also determined by **TGA, GC, & KF titration**
- Versaperm has deviced a **WVTR meter** that can measure the permeability of package to moisture.so that humidity can be accurately controlled.

CLASSIFICATION OF SUBSTANCES :-

CLASS	***Essentially***		***After 1 Week***	
	Below %RH	***Moisture content (%)***	***Above %RH***	***Moisture content (%)***
(I)-Non hygroscopic	90	0	90	LT 20%
(II)- Slightly hygroscopic	80	0	80	LT 40%
(III)-Moderately hygroscopic	60	LT 5%	80	LT 50%
(IV)-Very hygroscopic	40-50	Higher	90	MT 30%

(C) IMPORTANCE OF MEASUREMENT :

- It affects the **chemical stability** of drug.
- It also affects the **flow property.** Hygroscopic compounds have poor flowability so that it causes weight variation problems.
- Moisture in cohesive material causes **solid bridges and liquid bridges** formation between the particles, which ultimately form **hard cake.**
- Hygroscopic compounds are generally sticky so that also affects the **compaction.** (e.g. picking & sticking)
- It is important for **aerosols containing powders.** Moisture content should be **below 300 ppm**. Higher moisture level generally results into particle agglomeration.

(D) METHODS OF IMPROVEMENT :

- For granulation of hygroscopic material, use **non-aqueous solvent.**
- For efflorescent material ,use **anhydrous salt.**
- Add finely powdered **adsorbants like MgO or Mg carbonate.**
- Perform the entire tableting operation under **controlled humidity condition**.eg-Very hygroscopic products are stored less than 40% RH.
- **Make complex to form dry physical form** suitable for tabletting. i.e. make clathrate of hygroscopic benzalkonium chloride with urea.
- **Store** hygroscopic compound **with desiccants** in well closed container.

Example:

Starch is hygroscopic,but on pregelatinization it exhibits lower propensity for moisture, thus providing excellent stabilization for moisture sensitive materials.

New smart excipient:

☐ **Galen IQ, a range of multifunctional excipient** by German company palatlinit

- It is based on hydrogenated isomaltulose,also known as isomalt
- Combined advantage of mannitol, sorbitol, lactose, MCC
- Low Hygroscopicity, at 25˚C temperature hardly absorb water untill 85% RH.
- This low hygroscopic nature combined with anti caking property makes easy mixing, agglomeration or tableting and helps in elimination of costly packing.

☐ **E.g. Relationship between powder characteristics & hygroscopicity of granule preparation by different methods :** Method with low hygroscopic granules are dry granulating & 2˚ swinging granulating method.

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(2) POWDER RHEOLOGY:-

CONTENTS:-

A. INTRODUCTION
B. IMPORTANCE OF FLOW PROPERTY STUDIES
C. FACTOR INFLUENCING FLOW PROPERTY
D. IMPROVEMENT OF POWDER FLOW PROPERTY
E. MEASUREMENT OF FLOW PROPERTY

(A) INTRODUCTION

- ❑ The flow properties of powder plays an important role in dosage form manufacturing process.
- ☐ When limited amounts of drugs are available these can be evaluated simply by measurement of bulk density and angle of repose.
- ☐ These are extremely useful derived parameters to assess the impact of changes in drug powder properties as new batches become available.

(B) IMPORTANCE OF FLOW PROPERTY STUDIES:-

1.Weight uniformity
2.Content uniformity
3.Hardness
4.Disintegration
5.Speed of production
6.Scientific design of formulations and processing equipment

(C) FACTORS INFLUENCING FLOW PROPERTY :-

1.Particle size & Size distribution
2.Particle shape
3.Moisture

4.Electrostatic effects
5.Powder cohesion and storage compaction
6.Effect of temperature

1. PARTICLE SIZE & SIZE DISTRIBUTION :

If size (or) dimensions of particles altered

⇩

Particles shape changes

⇩

flow of particles changed

Size of Particle (µm)	Flow Property
More than 250	Free flowing
Less than 100	Poor flow
Less than 10	Resist flow

- Size distribution is carried out by using proper amounts of fines.

2. PARTICLE SHAPE & SURFACE MORPHOLOGY :

- **Spherical shape** is the best shape which give maximum flow.
- **Irregular shape** may cause bridging in hopper.

3. MOISTURE :

- The effect of moisture on flowability of particles varies from powder to powder.
- The particles become **cohesive** due to moisture absorption.
- Absorbed moisture in solids can exist in two forms :
  1. unbound state
  2. As a part of crystal structure

4. ELECTROSTATIC EFFECTS :

The charged material show poorer flow than uncharged material.

- **Particles acquire static charge by :**
  - Grinding
  - Attrition
  - collision
  - mixing
  - sieving
  - Moisture
- Electro static charge may be **positive** or **negative.**

+ve charge particles ⇒ **plastic surfaces**

-ve charge particles ⇒ **metal or glass surfaces**

5. POWDER COHESION & STORAGE COMPACTION :

- When solid remains **at rest or stored in a hopper or bin ,** it can become **more cohesive** and gives **poor flow.**
- **Flow chacteristics depends on :**
  - Intrinsic cohesiveness of the material
  - Temperature of storage
  - Load levels of Hopper and bin
  - Time of storage
  - Vibratory forces

(D) METHODS OF IMPROVING FLOW PROPERTIES OF POWDERS :-

1: By addition of glidant :- Effect depend on particle size of material to which they are added.
E.g..Magnesium stearate, Talc, Colloidal silicone are effective in finer particles,
Corn starch is more effective in coarser particles.

2: By size reducing or addition of fines:- both should be up to optimum level.

3: By wet granulation:- gives regular spherical shape and also reduces static charge .

4: By removing static charge:- increase flow property.

5: By making more denser:- as density increases,flow property increases.

6: By addition of flow activator like MgO:- here MgO dose not act as flow activator directly but it increases flow by absorbing moisture which affect the flow property.

7: For hygroscopic and moist powder:- use silicon treated powder
eg. Silicon coated TALC or $NaHCO_3$.

8: Alteration of process :-use force feeder, use vibrating hopper.

(E) MESUREMENT OF FLOW PROPERTIES :-

1) Bulk Density
2) Tapped Density
3) Carr's Compressibility Index
4) Hausner Ratio
5) Angle of Repose
6) Shear Cell Determination
7) Kava, Keta, Kuno parameter

1. Bulk density :-

- Bulk density of a compound varies substantially with the method of crystallization, milling, or formulation.

- **Bulk density measurement** :The bulk density of a powder is dependent on particle packing and changes as the powder consolidates. A consolidated powder is likely to have a greater arch strength than a less consolidated one and may therefore be more resistant to powder flow. The ease with which a powder consolidates can be used as an indirect method of quantifying powder flow.

- ☐ It is determined by pouring presieved (40-mesh) bulk drug into a graduated cylinder via-a large funnel and measuring the volume and weight.

2. Tapped density :-

- ☐ It is determined by placing a graduated cylinder containing an known mass of drug or formulation on a mechanical tapper apparatus, which is operated for a fixed numbers of taps(about-1000)untill the powder bed volume has reached a minimum volume. using the weight of a drug in the cylinder and this minimum volume,the tapped density is calculated.

3.Carr's Index:-

- ☐ Neumann and carr developed a simple test to evaluate flowability of a powder by comparing the poured (fluff)density and tapped density of a powder and the rate at which it packed down.

☐ % Compressibility (Carr's index) $= \frac{\text{Tapped Density - Bulk Density}}{\text{Tapped Density}} \times 100$

% COMPRESSIBILTY RANGE	**FLOW DESCRIPTIONS**
5-15	Excellent (free flowing granules)
12-16	Good (free flowing powder granules)
18-21	Fair to passable (powder granules)
23-28	Poor (very fluid powder)
28-35	Poor (fluid cohesive powder)
35-38	Very poor (fluid cohesive powder)
>40	Extremely poor (cohesive powder)

4. HAUSNER RATIO:-

- ☐ Hausner predict the flow properties of powder by using interparticle friction.
- ☐ This is a simple index that can be determined on small quantities of powder.
- ☐ Hausner ratio = tapped density /poured density

HAUSNER RATIO	**TYPE OF FLOW**
< 1.25	**Good flow**
> 1.25	**Poor flow**

Typical values of Bulk Density,Tapped Density, Hausner Ratio & Carr's index :-

Lactose -product Lactochem- Domo	Bulk density	Tapped density	Hausner ratio	Carr's index
Coarse crystals	0.75	0.88	1.2(good flow)	15(excellent)
Crystals	0.74	0.86	1.2(good flow)	15(excellent)
Extra fine crystals	0.73	0.86	1.2(good flow)	15(excellent)
Powder	0.64	0.89	1.3(poor flow)	>25(poor)
Fine powder	0.61	0.84	>1.3(poor flow)	>25(poor)
Extra fine powder	0.45	0.74	>1.3(poor flow)	>25(poor)
Super fine powder	0.47	0.74	>1.3(poor flow)	>25(poor)

5. Angle Of Repose :-

- Angle of repose is defined as the angle of the free surface of a pile or heap of powder to the horizontal plane.
- Characterize the flow properties of solids.

If material is **not cohesive** ⇩ Flows well ⇩ Low heap

If material is **cohesive** ⇩ Poor low ⇩ High heap

Angle Of Repose is measured by the equation :

Angle of Repose = $\theta = \tan^{-1}(h / r)$

where, h = height of conical heap &

r = radius of horizontal plane of powder

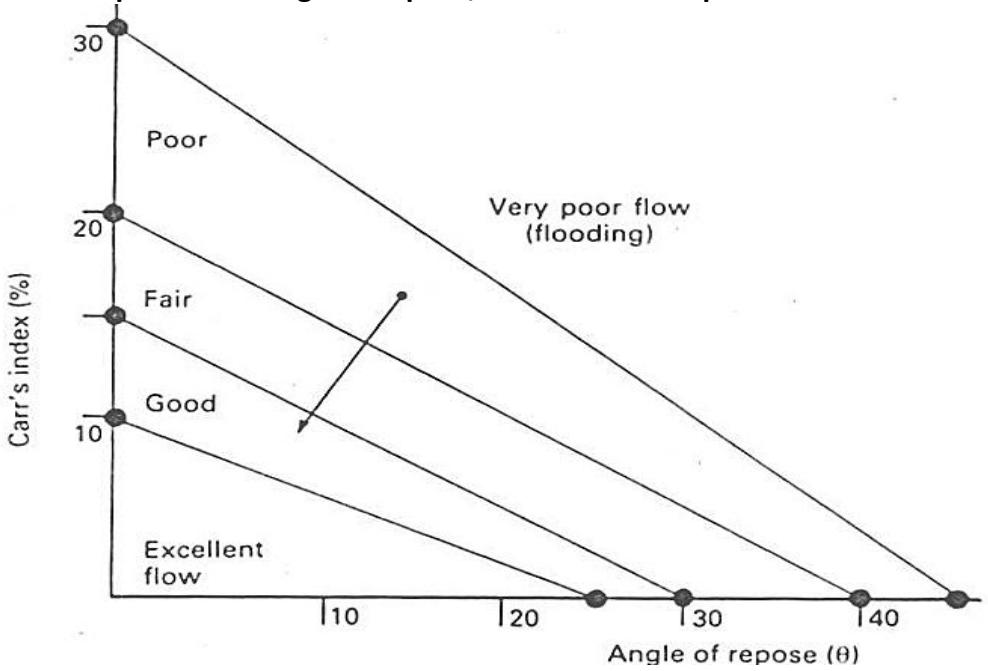
Angle Of Repose as an indicatior of powder flow properties :-

Angle of repose(degrees) (θ)	Type of flow
<25	Excellent
25-30	Good
30-40	Passable
>40	Very poor

- **REPOSOGRAPH :**

- It is a stable instrument which at best can only indicate comparative flow properties.
- The formation of **sharp cone** would mean poor flow property while a good spread would indicate a superior flow property.

Relationship between angle of repose, carr's index of a powder and its flow characteristics:-



- When only small quantities of powder are available, an alternative is to determine the **'angle of spatula'** by picking up a quantity of powder on a spatula and estimating the angle of the triangular section of the powder heap viewed from the end of the spatula.this is obviously crude but is useful during preformulation,when only small quantities of drug are available.

METHODS OF DETERMINATION :-

TYPE OF ANGLE OF REPOSE	METHOD
Static Angle of Repose	Fixed Height Cone
	Fixed Based Cone
	Tilting Table
Dynamic Angle of Repose	Rotating Cylinder
	Rotating drum
Drained Angle of Repose	Ledge Type
	Crater Type
	Platform Type

6. SHEAR CELL DETERMINATIONS :-

- ❖ Characterize the flowability from the behavior of powder in a shear cell
- ❖ The powder bed was subjected to shear and its applied load for shear also noted
- ❖ Graph plotted between shear stress and applied load
- ❖ Flow factor can be obtained by determining the reciprocal of slope.

FLOW FACTOR	TYPE OF FLOW
> 10	**Free flow**
4 – 10	**Easy flow**
1.6 - 4	**Cohesive**
< 1.6	**Very cohesive**

7. Kava, Keta, Kuno parameter :-

It is the recent parameter that is introduced by Japanese scientists.
It is used for the measurement of **flow property of crystals**.

NEW MEASUREMENT SYSTEM TO EVALUATE POWDER FLOWABILITY BASED ON VIBRATIONAL CAPILLARY METHOD :

- ☐ Evaluates flowability of micrometer sizes particles under actual flow condition.
- ☐ The amplitude and frequency of vibration is controlled by computer and mass of powder discharged from vibrating capillary tube is measured by digital balance.
- ☐ The mass flow rate is measured by digital processing.

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(3)COMPACTION PROPERTIES:-

CONTENTS:-

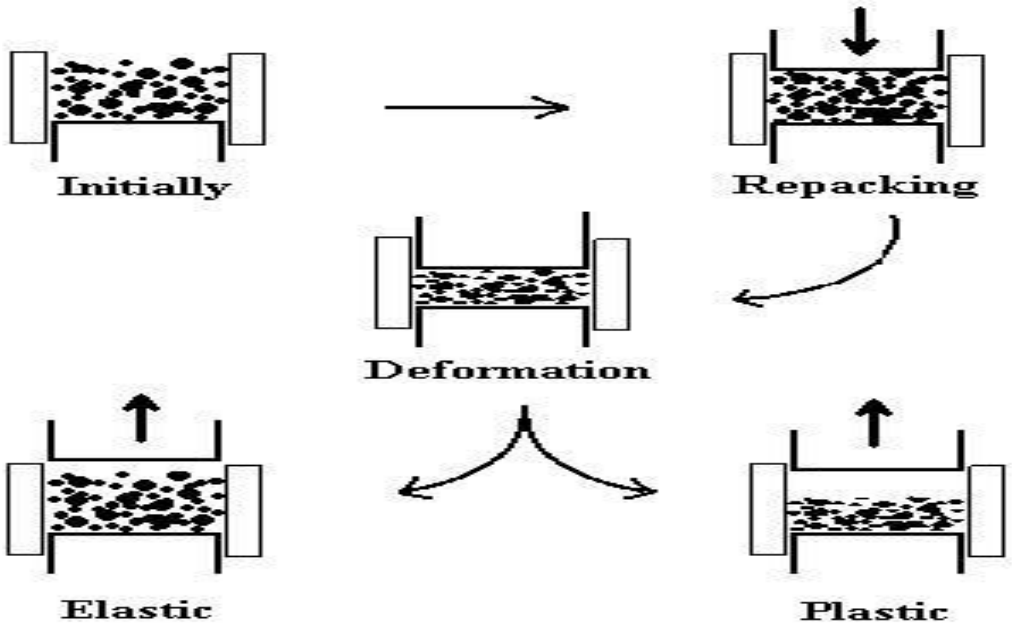
A. DEFINITION
B. DIFFERENT STAGES OF POWDER COMPACTION
C. METHOD FOR IMPROVEMENT
D. EFFECT OF COMPACTION ON DIFFERENT FACTORS
E. MOISTURE AND COMPRESSION
F. EVALUATION OF COMPACTION

A. DEFINITION:-

- ☐ **COMPACTION :-** Compaction of powder is term used to describe the situation in which material are **subjected to some level of mechanical force.**
- ☐ **COMPRESSION :-** Compression is **reduction in the bulk volume** of the material as a result of displacement of the gaseous phase.

- **CONSOLIDATION :-** Consolidation is an **increase in mechanical strength** of material resulting form particle – particle interactions

B. DIFFERENT STAGES OF POWDER COMPACTION :-



The Characteristics Of Material :-

1. PLASTICITY

- Plastic material are capable of permanent deformation, also exhibit a degree of brittleness (fragmentability)
- But plastic material will get bonding after Viscoelastic deformation.

2. FRAGMENTABILITY

- If material is fragmentable, neither lubricant mixing time nor dwell time affecting the tablet strength.

3. ELASTICITY

- E.g. PCM, MCC, ASPIRIN,etc.
- If material is elastic, it rebound when compression force is released.
- Elastic material may lead to capping & lamination
- They require wet massing to induce plasticity or plastic tableting material.

4. PUNCH FILMING [STICKING]:

- This may lead to chipping of tablet.

❖ **A new directly compressible excipient:**

c*pharmamannidex DC is mannitol based.

- permit higher dose of active ingredient. Helpful for those companies that are looking for animal derivative to non animal derivative excipient.

- ☐ non hygroscopic, non carcinogenic, chemically stable, **suitable for diabetics.**
- ☐ high compressibility, high binding capacity, low friability.
- ☐ excellent diluent, binder, ideal for **chewable tablet.**

C. METHOD FOR IMPROVEMENT :-

- ➢ If material is **Elastic**, it can be improved
  - By plastic tableting matrix (like MCC).
  - By wet massing to induce plasticity.
  - By precompression.
- ➢ If material is **Sticky**, it can be improved
  - By change in salt form.
  - By using high excipient ratios.
  - By using abrasive inorganic excipient.
  - By wet massing.
  - By addition of colloidal silica as a polishing agent.
  - By addition of magnesium stearate up to 2%.

- ➢ If material is **Plastic**, it can be improved
  - by addition of fragmentable excipients (like lactose,calcium phosphate)

D. EFFECT OF COMPACTION ON DIFFERENT FACTORS :-

- ☐ Compression force affects **surface area,granule density,porosity, hardness and disintegration time** of pharmaceutical tablets.
- ☐ Surface area increased to a maximum and then decreased.
- ☐ Porosity decrease and density increased as a linear function of the logarithm of the compression force.
- ☐ As the compression increase the tablet hardness and fracture resistance also rise.

E. MOISTURE & COMPACTION :-

- ☐ Moisture is **essential** for the formation of the tablet.**(2-4%)**
- ☐ Moisture **increases the tensile strength** of the tablet by increasing contact area for bonding.
- ☐ Moisture **decreases particle surface energy** & thus decreases adhesion of the tablet to the die wall.
- ☐ In case of **MCC**, moisture present within the pores ,that facilitate the flow during the compaction.
- ☐ Lack of moisture leads to **lamination** because of elastic recovery.
- ☐ Excessive moisture produces capillary state of powder aggregation and thus surface tension effects are insignificant to have better compaction.
- ☐ Reported e.g. is that of Naproxen tablet which help of lactose. When moisture as more then 2% ,hardness of tablet decreased (at both low & high pressure).

F. EVALUTION OF COMPACTION:-

1. **Strain index (SI) :-** Measures internal strain associated with a powder when compacted.
2. **Bonding index (BI) :-**Ability of material to bonds.
3. **Brittle fracture index (BFI) :-** Measures brittleness of material.

Higher is the BI index, stronger is the tablet.
Higher is the SI index, softer is the tablet.

- **e.g.<u>Silicified MCC as a multifunctional pharmaceutical excipient</u>:** having high compressibility,high intrinsic flow, enhanced lubrication efficiency & improved Blending properties.

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