C- Microcrystalline cellulose (MCC), Avicel®

- Compression aid, disintegrant.
- Commonly found into two grades, **Avicel PH 101 (powder) and Avicel PH 102 (granules).**

D- Others: Dextrose, mannitol (the most expensive one, used in chewable tablets and ODT), sorbitol and sucrose or sugar.

2- Inorganic diluents (soluble): such as

Dibasic calcium phosphate (Di-Tab®) and calcium sulfate which are hydrate powders, non hygroscopic with good flow properties.

Notes :

- ✓ **The most important considerations for diluents are type, amount, solubility, particle size, compatibility and moisture content.**
- ✓ **Diluent amount depend on total wt. of tablet , may be estimated as Q.S.**

Binders , granulating agents

- To bind powders together in the wet granulation process
- To bind granules together during compression.
- Added either (in dry or in liquid form) (Aqueous or non).
- Incorporated in different ways (pouring, spraying or admixing at low or high shear).
- Its amount can affect the tablet performance.
- Found into different types, mainly polymeric in nature, natural or semisynthetic polymer, hydrophilic or hydrophobic.

- **Natural gums like acacia and tragacanth (10-25% w/v).**
- **Proteins like gelatin (10-20% w/v).**
- **Poly saccharides like starch (paste), 10-20% w/v.**
- **Mono-saccharides like liquid glucose (50% solution in water).**
- **Semisynthetic polymers like alginates and cellulose derivatives (MC, HPMC, HPC and EC).**
- **Synthetic polymer like PVP 2%.**

- The type and concentration of binder affect the granule strength, friability, and the granule growth rate during the wet granulation process.
- Size and size distribution of granules can affect the flow and compressibility.
- Densification of granules can affect the rate of drug release.

Disintegrants

Used to promote breakup of the tablets to promote the release of the drug when it contacts water in the GIT.

There are different theories have been proposed for mechanisms of disintegrant action like:

1) Swelling: Depend on chemical structure and degree of cross-linking, porosity and pH. (ex. Starch)

2) Wicking (capillary action): Minor mechanism, depend on tortuosity, pore size and surface tension. (ex.MCC)

3) Strain recovery: When compacted disintegrants come in contact with the aqueous media, mechanical activation of disintegrant polymer chains help to partially recover their original shapes.

4) Interruption of particle-particle bonds: as in *MCC*

5) Heat of interaction: Minor mech., endo and exothermic interactions

6) Gas generation: ↑CO2, ↑O2

There are different types of disintegrants , each one may act with one mechanism or more like:

1) Starch 5-20% of tablet wt.

2) Pregelatinized starch (5%)

3) Clays like vee gum and bentonite (10%).

4) MCC (5-10%).

5) PVP (Cross-linked PVP), 5%.

6) Ac-Di-Sol® (internally cross linked sodium CMC)

7) Peroxide, effervescent base.

Super-disintegrants

- **Swell up to ten fold within 30 min when contact water. EX:**

Crosscarmellose (Cross-linked cellulose).

Crosspovidone (Cross linked povidone)

Sodium starch glycolate (Cross linked starch)

As questions??

- Can the method of incorporation (Intra, extra granular or both) affect disintegrant efficiency?
- What are the effects of other materials (Binder, lubricant and surfactant) on disintegrant efficiency?
- How can you increase the disintegrants efficiency?

Lubricants

- To reduce the friction during tablet ejection between the walls of the tablet and the walls of the die cavity
- Considerations? (type, amount, p.s., time of addition, and order of mixing)
- Types:

❑ Hydrophobic like stearic acid and its salts like (Ca and Mg salts), talc, waxes.

❑ Hydrophilic like PEG 4000, some surfactant

Glidants (Flow promotors)

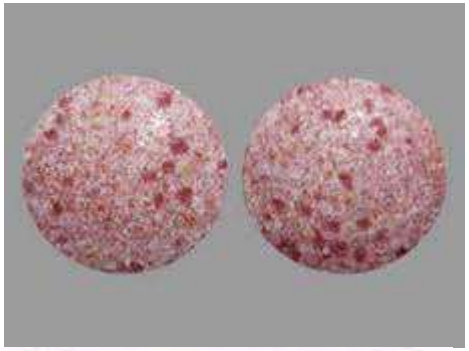
- Reducing friction between the particles (Mechanism?)
- To improve the flow properties of the granulations
- Considerations?
- Examples: Corn starch 5-10%, talc 5%, silica derivatives- colloidal silica (Cab-O-Sil®) in 0.25-3%.

Antiadherants

- To prevent adherence of the granules or powder to the punch faces and die walls (Picking problem).
- Ex. Starch, talc and Mg stearate.

Coloring agents

- For appearance and identification
- Its limitations? FDA approval
- Types? Soluble (solution) applied within
- The granulating agent, and insoluble
- (Lakes)??
- Examples? FD&C and D&C dyes
- (give different colors)



FD&C Red No.3

FD& C Yellow No.5

Mottling

Mottling is the term used to describe an unequal distribution of colour on a tablet.

The Causes And Remedies

Causes	Remedies
A coloured drug used along with colourless or white-coloured excipients.	Use appropriate colourants.
A dye migrates to the surface of granulation while drying.	Change the solvent system, Change the binder, Reduce drying temperature and Use a smaller particle size.
Improperly mixed dye, especially during 'Direct Compression'.	Mix properly and reduce size if it is of a larger size to prevent segregation.
Improper mixing of a coloured binder solution.	Incorporate dry colour additive during powder blending step, then add fine powdered adhesives such as acacia and tragacanth and mix well and finally add granulating liquid.

Flavoring agent

Used mainly in chewable tablets or dispersible types, flavor oils (0.5- 0.75%) are commonly used, more stable, added to tablet granulations in solvent, are dispersed on clays and other absorbents or emulsified in aq. granulated agent.

Sweeteners

Used mainly in chewable tablets, ex. Saccharine (with bitter aftertaste), aspartame (moisture sensitive), acesulfame potassium and mannitol.

- **Sorbents**
  - **With other materials (liq. Or semisolid like dyes or flavors)**
  - **Decrease hygroscopicity ex. Silicon dioxide**
  - **Fixing agent for drug or flavors ? Ex. PEG 400, Clays**
- **Dissolution modifiers (enhancers and retardants)= like???**
- **Wetting agents (why ??) ex. SLS**
- **Antioxidants: vit.C and Ascorbyl palmitate, Selenium, BHA**
- **Preservative: Parabens**

Co-processed excipients ? Give examples.