INTERNATIONAL COLLEGE OF PHARMACEUTICAL INNOVATION

国际创新药学院

Excipients in Solid Dosage Forms

Course BSc (Pharm) or BSc (ATT)

Year 2024-2025 II

Module Medicines: Pharmaceutics 2 (MP2)

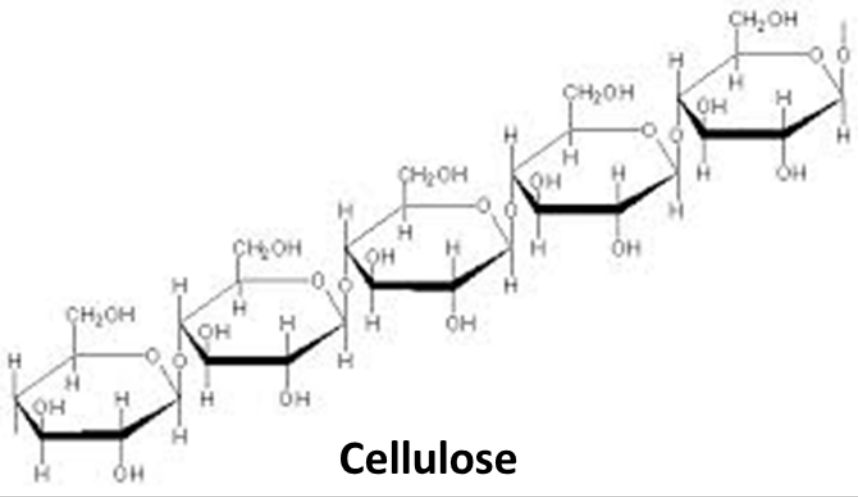
Lecturer Dr. Shi Du

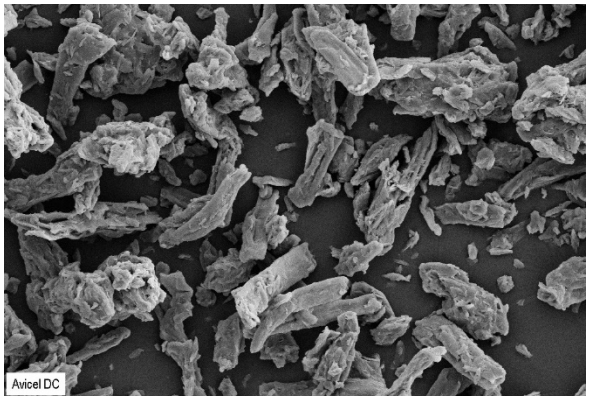
Learning Outcomes

1. List and describe the function of the principal types of excipients used in solid dose manufacture

2. Relate excipient function to its relevance in the tablet manufacture process

3. Describe specific examples of excipients within each type





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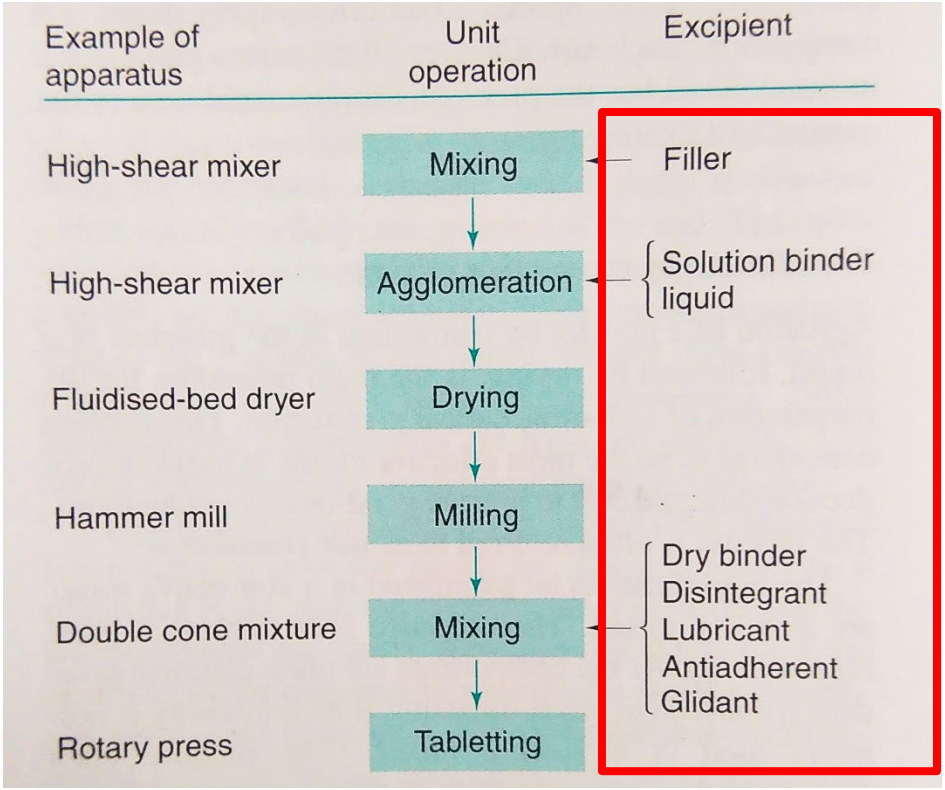
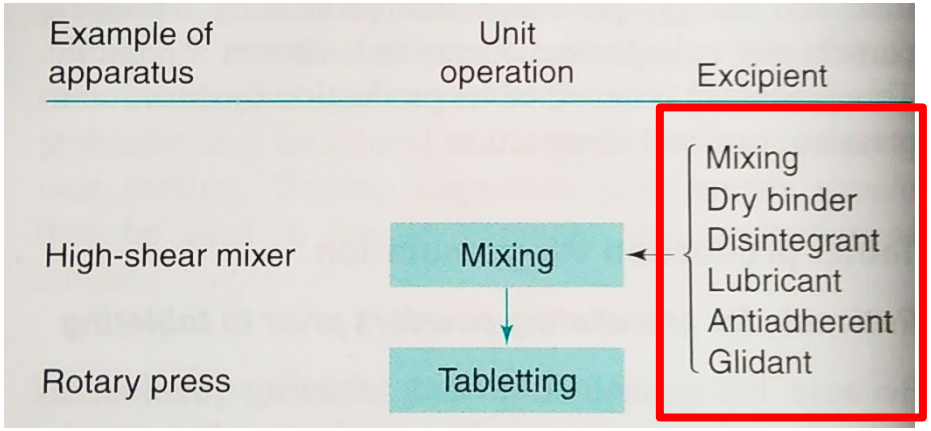
Unit Operations in Tabletting

Tablet Production with Granulation



Tablet Production with Direct Compression



Excipients are added to solid dosage forms for various purposes:

- Helping the manufacture process
- Controlling dissolution of the drug from the tablet
- Disguising unpleasant taste/smell
- Cosmetic reasons- improving appearance
- Protecting the API

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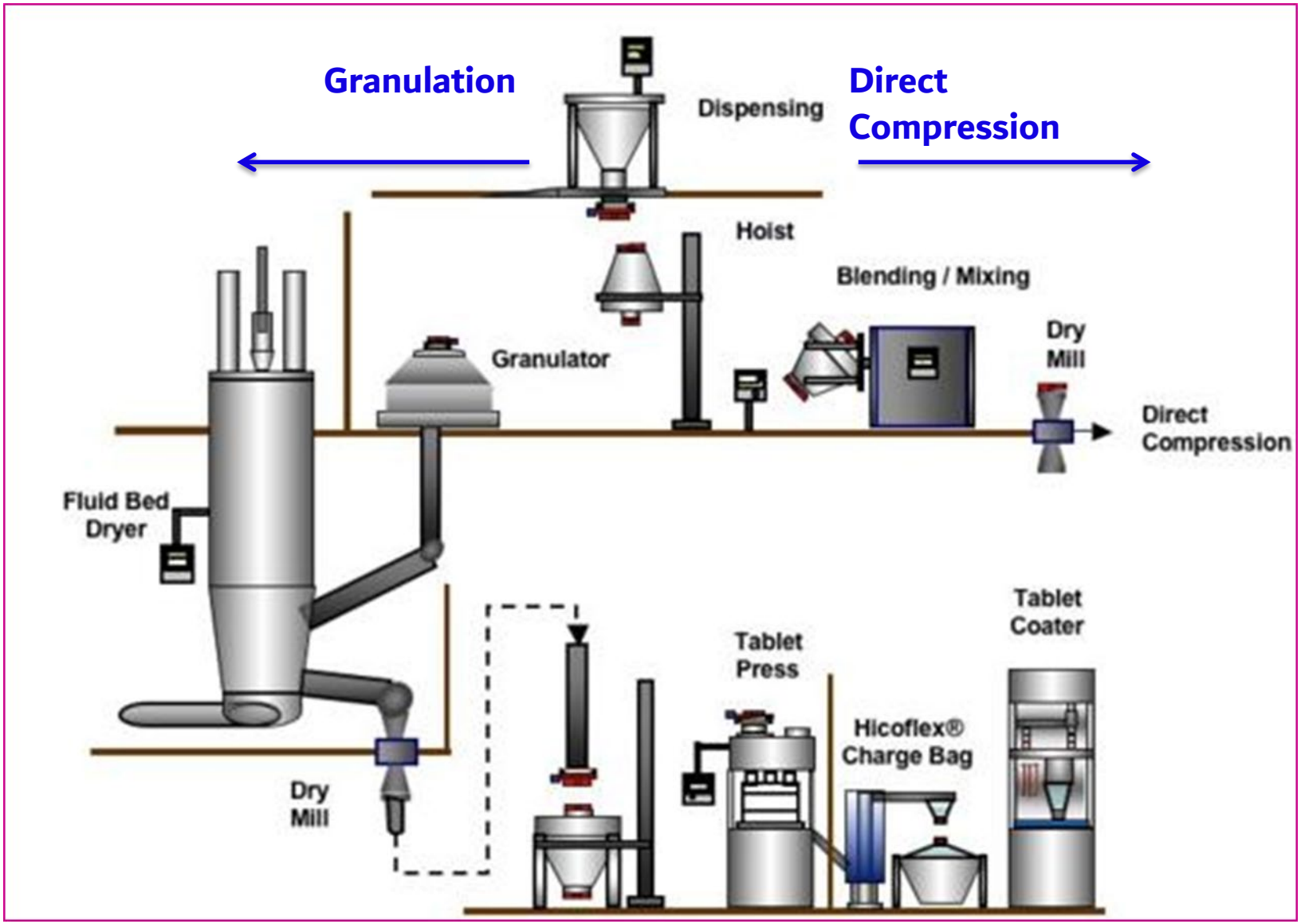
Tablet Manufacture: Summary of Processes



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Solid Dosage: Excipients

Type of excipient	Example of substances
Filler	Lactose Sucrose Glucose Mannitol Sorbitol Calcium phosphate Calcium carbonate Cellulose
Disintegrant	Starch Cellulose Crosslinked polyvinyl pyrrolidone Sodium starch glycolate Sodium carboxymethyl cellulose
Solution binder	Gelatin Polyvinyl pyrrolidone Cellulose derivatives (e.g. hydroxypropylmethyl cellulose) Polyethylene glycol Sucrose Starch
Dry binder	Cellulose Methyl cellulose Polyvinyl pyrrolidone Polyethylene glycol
Glidant	Silica Magnesium stearate Talc
Lubricant	Magnesium stearate Stearic acid Polyethylene glycol Sodium lauryl sulfate Sodium stearyl fumarate Liquid paraffin
Antiadherent	Magnesium stearate Talc Starch Cellulose

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Fillers (Diluents)

- Function
  - Make tablet size a suitable size and weight for handling
  - Minimum weighable dose for tablet is normally ~50mg
  - Quantity of filler will be determined by quantity of API and other excipients in formulation

- Ideal properties
  - Chemically inert
  - Non-hygroscopic
  - Biocompatible
  - Favourable biopharmaceutical properties
  - Favourable material properties
  - Acceptable for patient
  - Cheap

Type of excipient	Example of substances
Filler	Lactose
	Sucrose
	Glucose
	Mannitol
	Sorbitol
	Calcium phosphate
	Calcium carbonate
	Cellulose

- Most fillers are carbohydrates or inorganic salts
  - Sugar molecules
  - Polysaccharides can also function as dry binders and disintegrants

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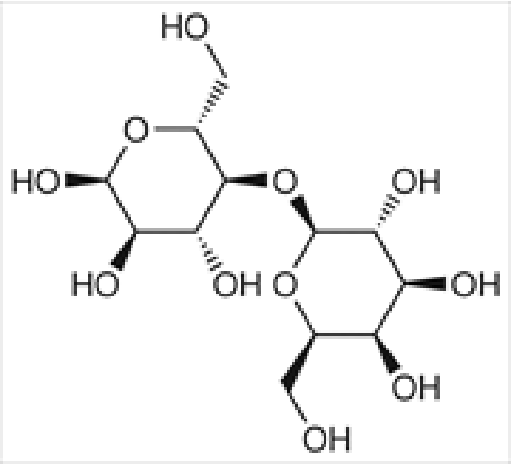
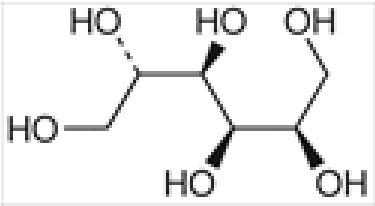
Fillers (Diluents)

- Lactose
  - Most common filler
  - Advantages: Relatively inert, water-soluble, non-hygroscopic, pleasant taste, good compactability
  - Limitation: Lactose intolerance
  - Crystalline and amorphous forms available



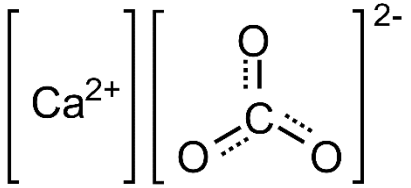
Lactose

- Other sugar derivatives (Sorbitol, mannitol)
  - Mannitol and sorbitol primarily used in chewable tablets and lozenges
  - They have a cooling effect on tongue
  - Laxative effect in large doses because not absorbed locally



Sorbitol

- Inorganic salts
  - Water-insoluble but still hydrophilic in nature
  - Easily wetted by water
  - Can be less inert than sugars



$CaCO_3$

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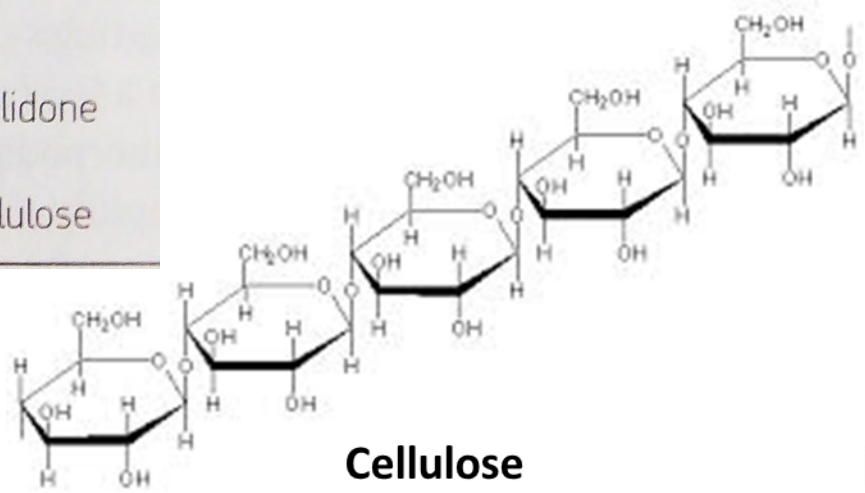
Disintegrants

- Function
  - Ensure that the tablet breaks into small fragments following exposure to liquid

- Main mechanisms
  1. Disintegrants facilitate water uptake into the tablet mass to facilitate breakdown into fragments by interaction of tablet particles with liquid
  2. Disintegrants swell during sorption of water and rupture the tablet mass into fragments
  3. Disintegrants dissolve to increase osmotic pressure that ruptures tablet (e.g. mannitol in ODTs)
  4. Effervescent gas formed upon reaction with water that ruptures tablet (e.g. citric acid with (bi-) carbonate salt)

Disintegrant	Starch
	Cellulose
	Crosslinked polyvinyl pyrrolidone
	Sodium starch glycolate
	Sodium carboxymethyl cellulose



Cellulose

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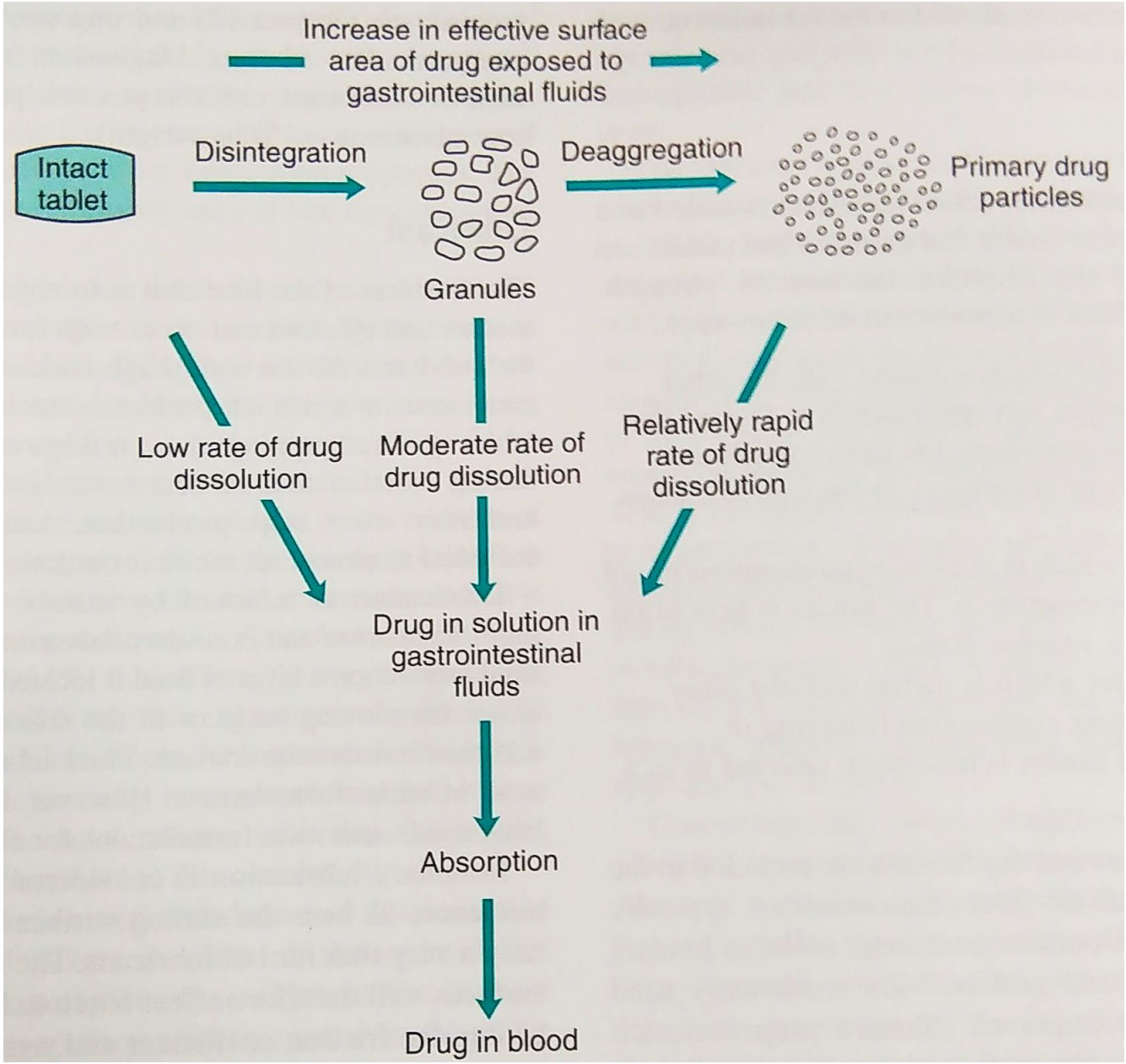
Disintegrants



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Binders

Dry binder	Cellulose Methyl cellulose Polyvinyl pyrrolidone Polyethylene glycol

Solution binder	Gelatin Polyvinyl pyrrolidone Cellulose derivatives (e.g. hydroxypropylmethyl cellulose) Polyethylene glycol Sucrose Starch

- Function:
  - Ensure that granules and tablets of adequate mechanical strength can be manufactured
  - Binders facilitate bonding mechanisms between particles and also deform well

- Binders can be added in different ways
  1. As a dry powder that is mixed in before wet granulation
  2. As a solution in the granulation fluid for wet granulation (solution binder)
  3. As a dry powder that is mixed in before dry granulation or direct compression (dry binder)

- Most common binders used today
  - Solution binders: Povidone and hydroxypropylmethylcellulose (HPMC)
  - Dry binders: Crosprovidone and microcrystalline cellulose
  - Used in low concentrations generally
  - Solution binders are generally viewed as the most effective for granulation

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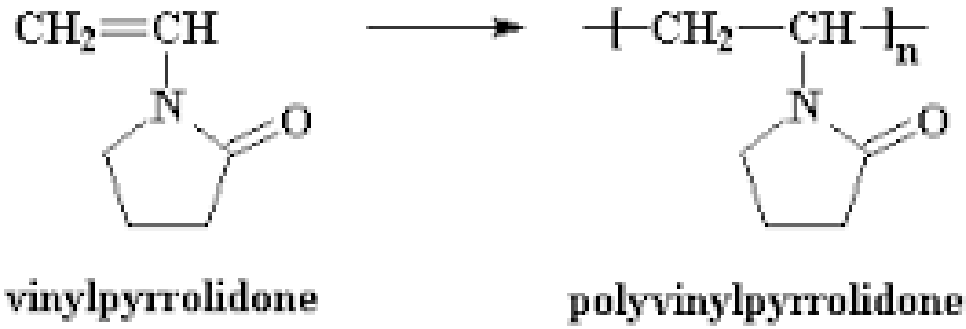
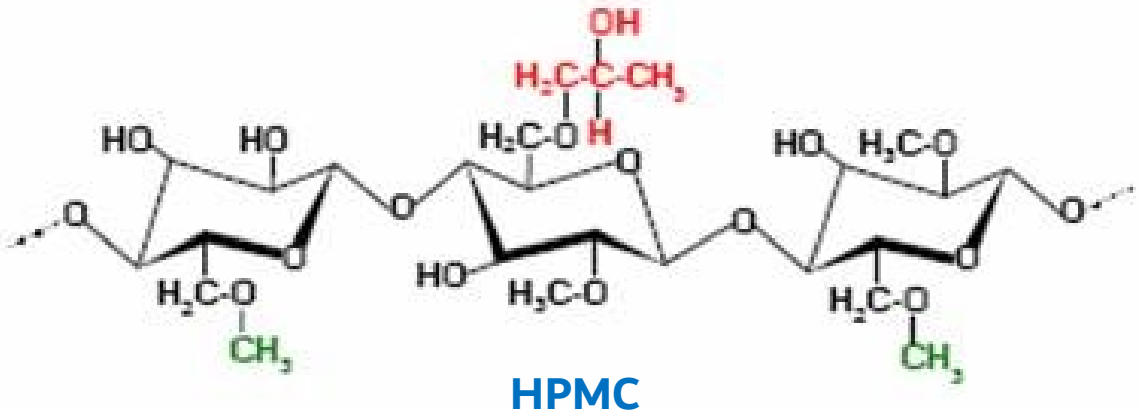
Binders



vinylpyrrolidone polyvinylpyrrolidone



HPMC

Ludipress®

Lactose monohydrate 93%
Povidone 3.5%
Crospovidone 3.5%

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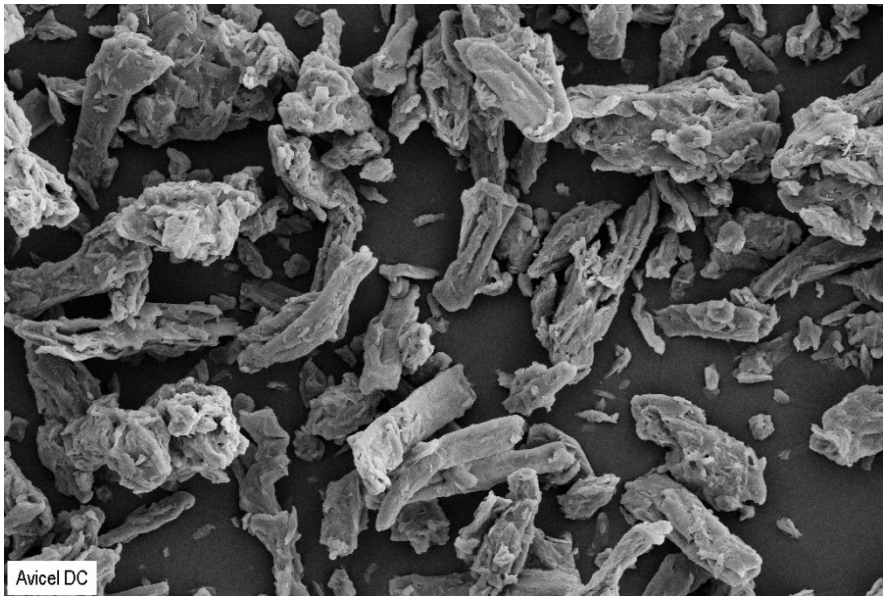
Microcrystalline Cellulose: Multipurpose Excipient

- Microcrystalline cellulose:
  - Most commonly used cellulose powder in tablet formulation
  - Has crystalline and amorphous regions
  - Prepared by hydrolysis of cellulose followed by spray drying
  - Agglomerations of smaller cellulose fibres
  - Different grades available with different degrees of crystallinity

- Function
  - Filler
  - Binder
  - Disintegrant

Avicel ®
Pharmacel®
Emcocel®



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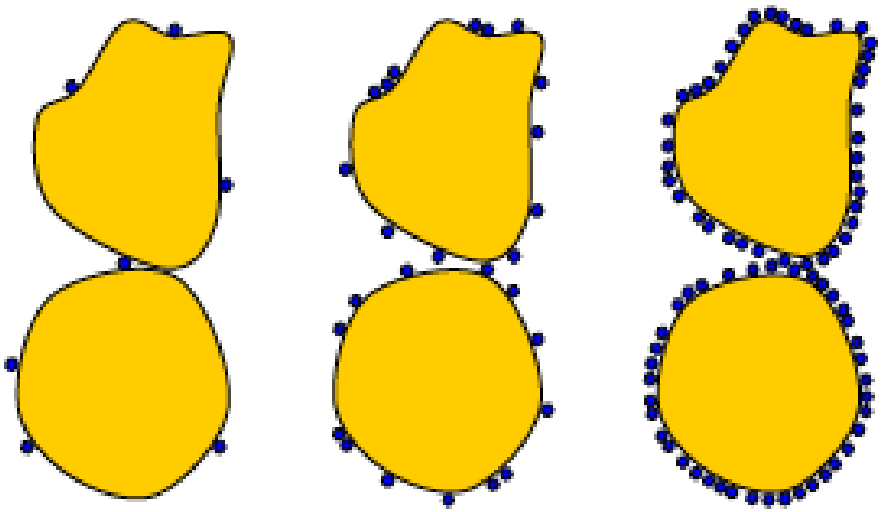
Glidants

- Function
  - Improve powder flowability
  - Ensure tablet weight uniformity and prevent defects
  - Used in low concentrations (~1-2% weight): Enough to coat particles
  - Often added before compaction after granules have dried
  - Colloidal silica most common

- Colloidal silica (~0.2% weight)
  - Has very small particle size (~15nm) and high surface area
  - Coats powder particles to interfere with cohesion
  - Has absorbent properties and will absorb moisture, preventing dampness & cohesion due to trapped moisture

Glidant	Silica Magnesium stearate Talc



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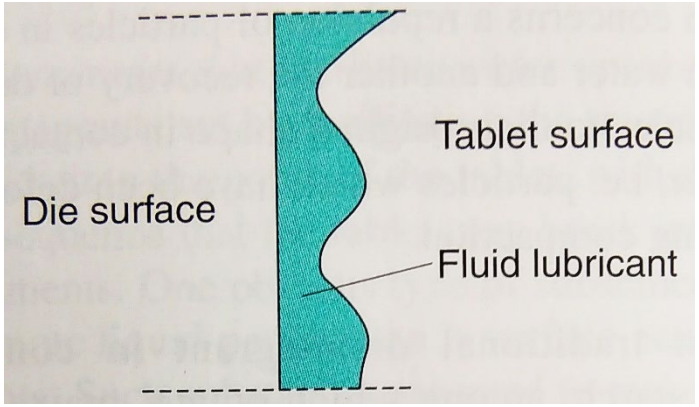
Lubricants

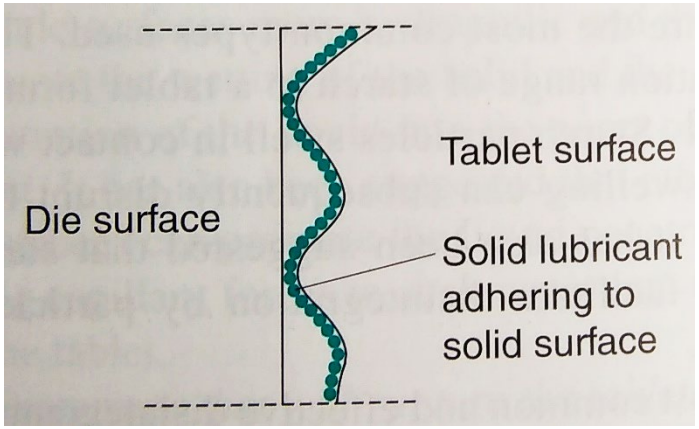
- Function
  - Ensure compaction and tablet ejection with low friction
  - Used in low concentrations (<1% weight): Enough to coat particles

- Mechanisms
  1. Fluid lubrication: Fluid separates surfaces; e.g. liquid paraffin and effervescent tabs
  2. Boundary lubrication: Fine particulate solids form a thin layer to separate boundary; e.g. Mg stearate

- Boundary lubricants
  - Substances have low shear resistance
  - Can interfere with bonding mechanism in compaction
  - Can interfere with disintegration and dissolution

Lubricant	Magnesium stearate
	Stearic acid
	Polyethylene glycol
	Sodium lauryl sulfate
	Sodium stearyl fumarate
	Liquid paraffin





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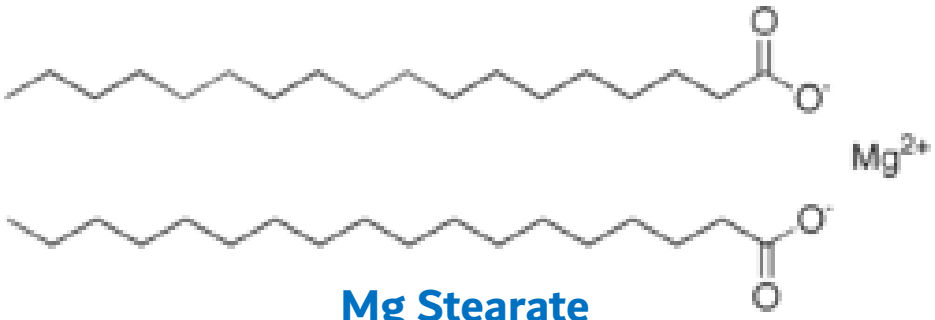
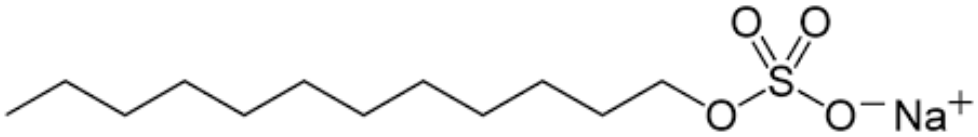
Lubricants



Mg Stearate



Na Lauryl Sulphate

PEG

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Anti-adherents: Secondary Function of other Excipients

Antiadherent	Magnesium stearate
	Talc
	Starch
	Cellulose

- Function
  - Reduce adhesion between powder and equipment
  - Multipurpose excipients

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Other Excipients in Oral Solid Dosage Forms

- Sorbent
  - Can remove residual moisture in powder beds
  - E.g. Microcrystalline cellulose and silica

- Flavouring
  - Mask taste in uncoated tablets
  - Sugars and sweeteners
  - Alternatively, can mask taste by coating

- Colourant
  - Tablet appearance and identity
  - Often by coating

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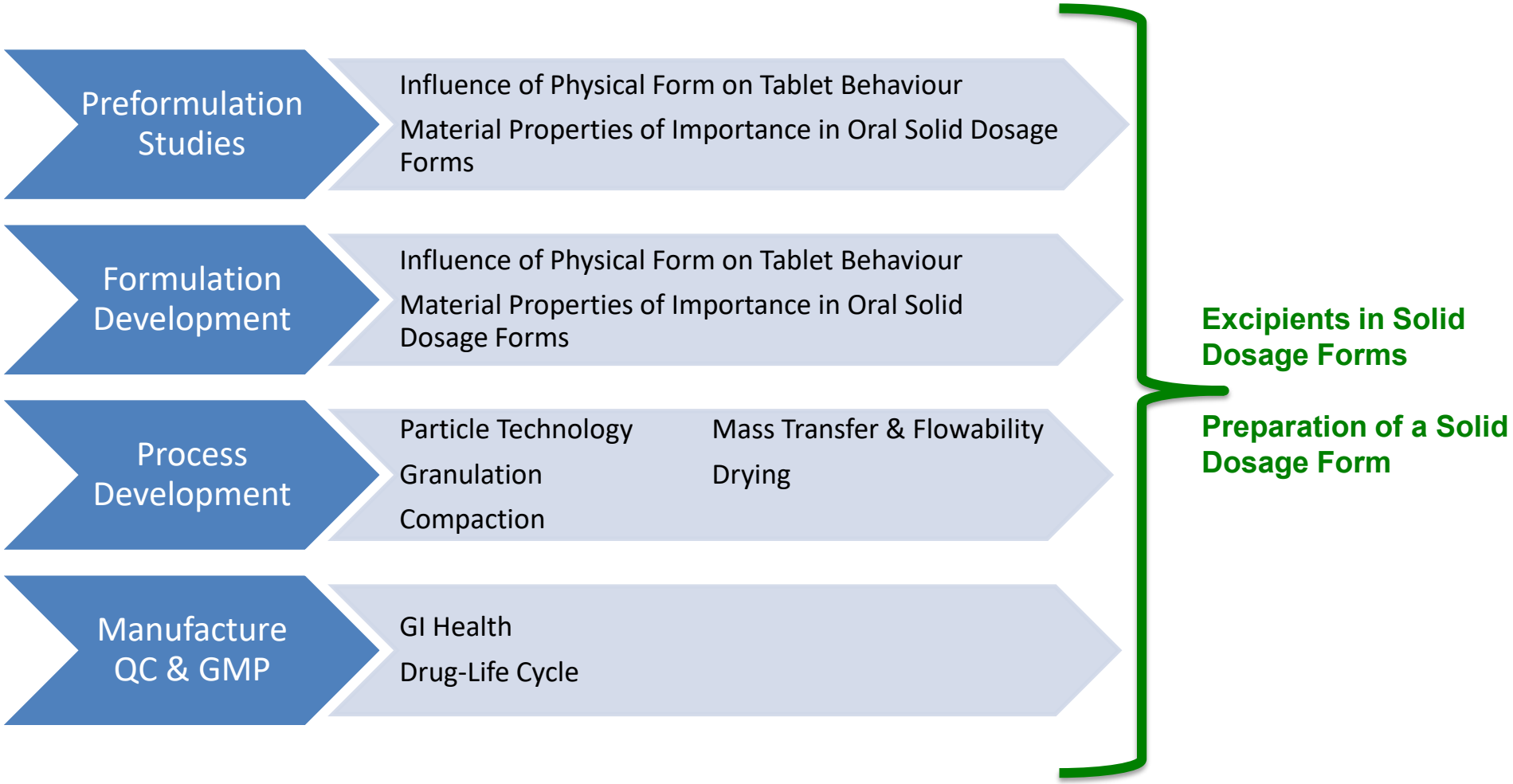
Solid Dosage Form Lecture Series



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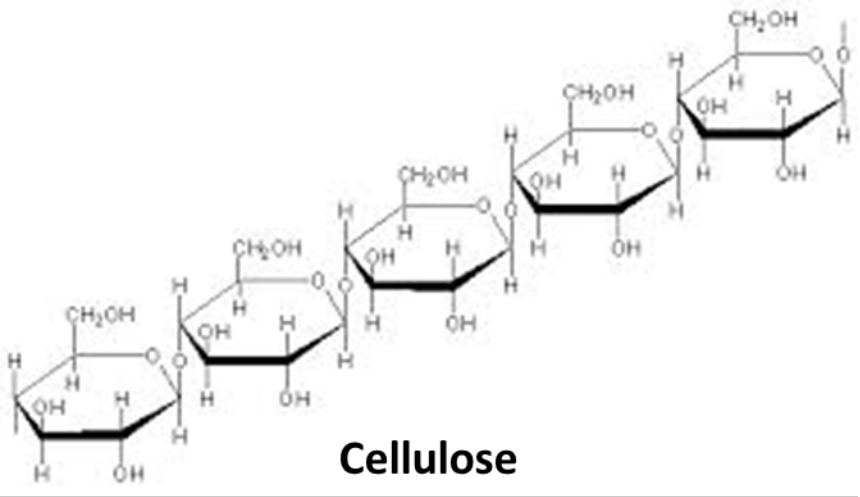

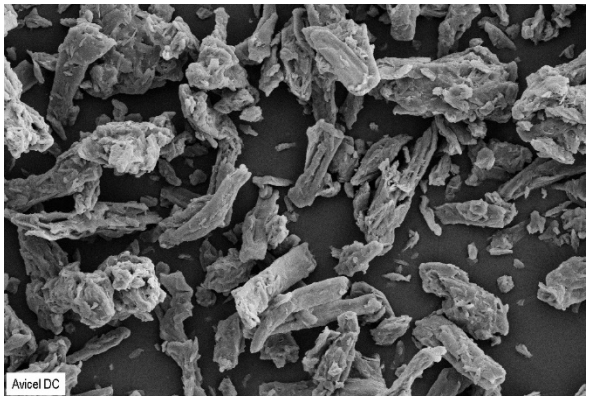

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Further Reading

- Aulton's Pharmaceutics Chapter
  - Tablets and Compaction

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