

Role of Pharmaceutical Excipients in Oral solid dosage forms

M.R. Avadi

2023



Definition

☺ (IPEC) defines an excipient as any substance other than the active drug or prodrug that is included in the manufacturing process or is contained in a finished pharmaceutical dosage form.

☺ More than 70% of the formulations contain excipients at a concentration higher than the drug.

☺ In reality, no single excipient would satisfy all the criteria; therefore, a compromise of the different requirements has to be made.



مجمع بين المللى مواد جانبى داروى

The role of excipients

- 😊 Modulating solubility and bioavailability of the drug
- 😊 Enhancing stability of the drug in its dosage forms
- 😊 maintaining pH and osmolarity of liquid products
- 😊 acting as antioxidants, suspending agent, emulsifier, aerosol propellants, glidant, lubricant, diluent....
- 😊 preventing aggregation or dissociation
- 😊 modulating the immunogenic response of drug (e.g. adjuvants) and many others

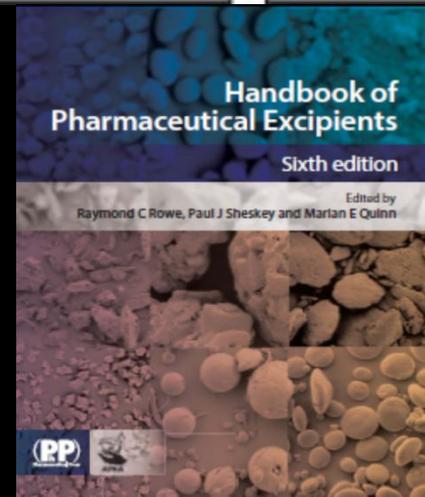
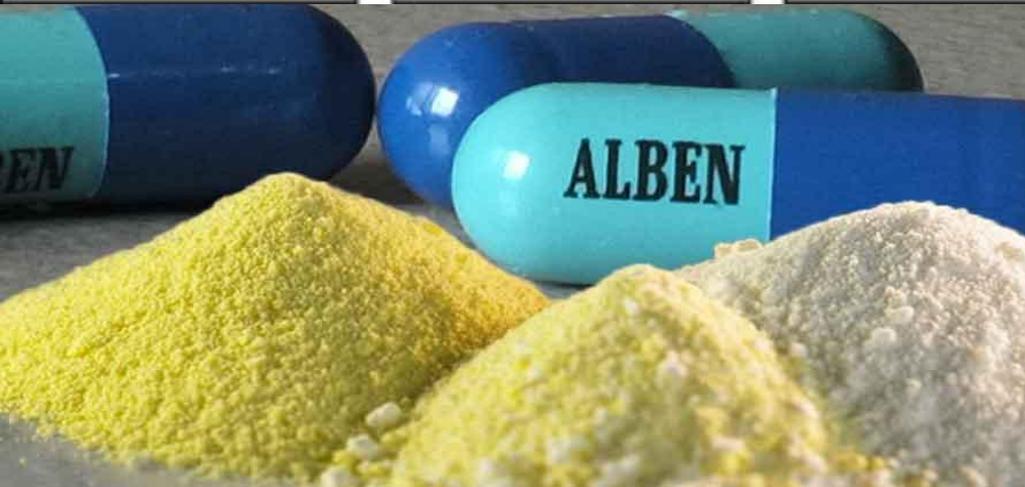
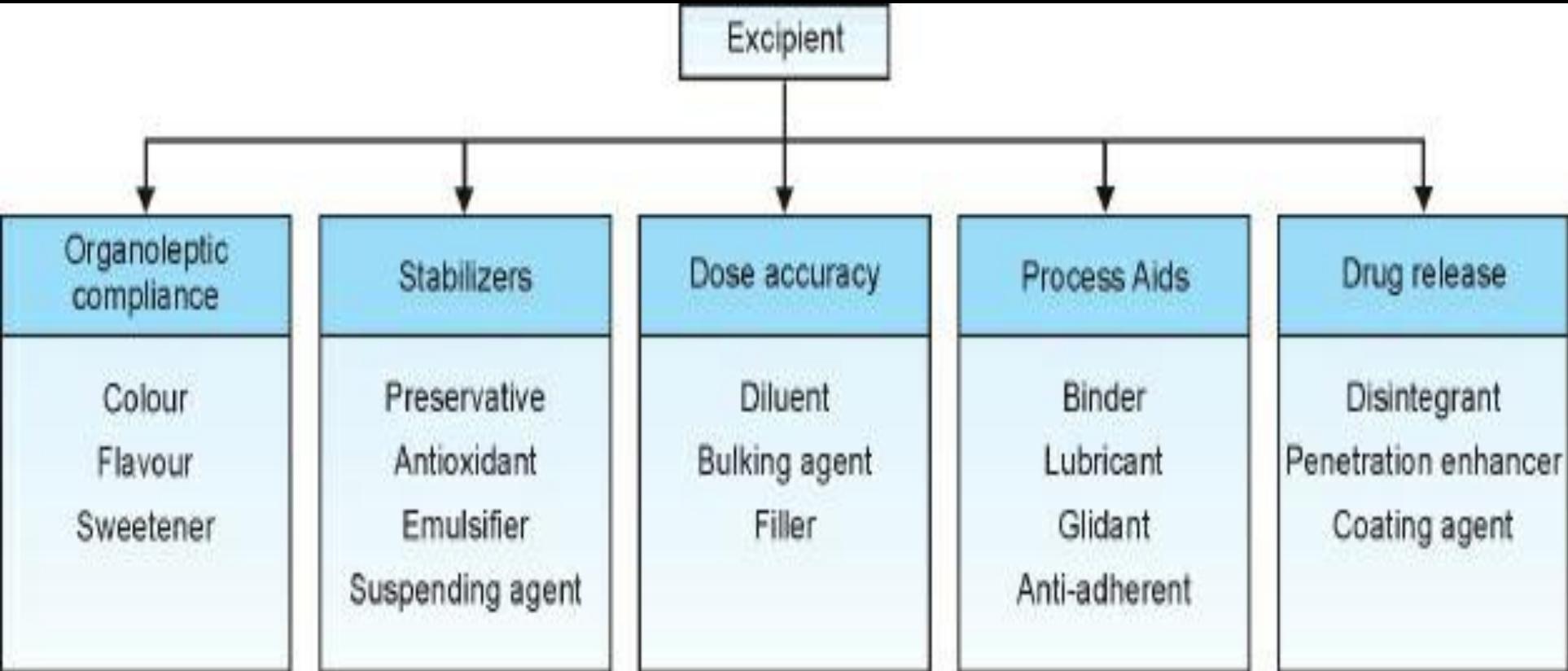


CLASSIFICATION OF PHARMACEUTICAL EXCIPIENTS

- 😊 Compendial or Noncompendial materials
- 😊 Origin (Animal, Plant, Mineral, Synthesis)
- 😊 Use and Objective



طبقه بندی مواد جانبی بر اساس هدف افزودن در شکل دارویی



EXCIPIENTS FOR SOLID DOSAGE FORMS

- 😊 Particle size and particle shape
- 😊 Density and porosity
- 😊 Moisture content
- 😊 Flow properties
- 😊 Compressability
- 😊 Compatibility



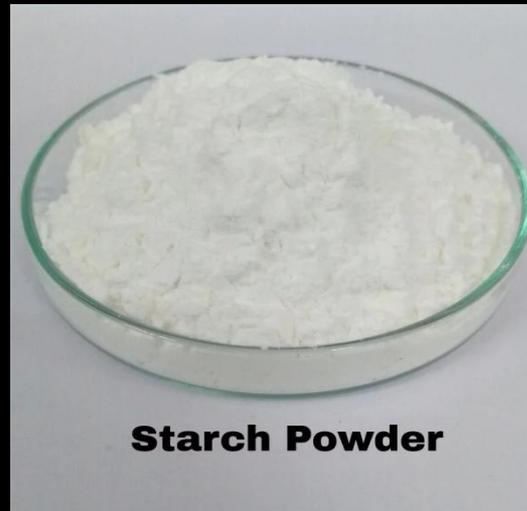
Diluents

- 😊 Lactose
- 😊 Sucrose
- 😊 Mannitol
- 😊 Avicel
- 😊 Dicalcium phosphate
- 😊 Calcium carbonate



Binders

- 😊 Povidone
- 😊 Starch
- 😊 Gelatin
- 😊 HPMC
- 😊 HPC
- 😊 PEG
- 😊 Fatty acids
- 😊 Fatty alcohols
- 😊 Waxes

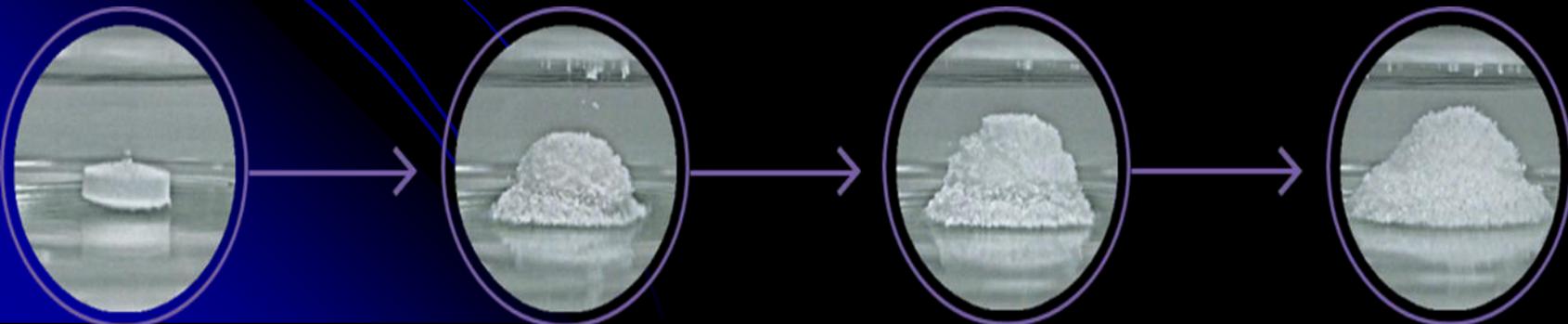


Disintegrating agents

Swelling

Wicking

- 😊 Sodium Starch Glycolate
- 😊 Croscarmellose
- 😊 Crospovidone



Glidants and Lubricants

- 😊 Improve flow properties
- 😊 Prevent the adherence of granules to punch and die faces
- 😊 Reduce interparticle friction
- 😊 Facilitate the ejection of the tablets from the die cavity



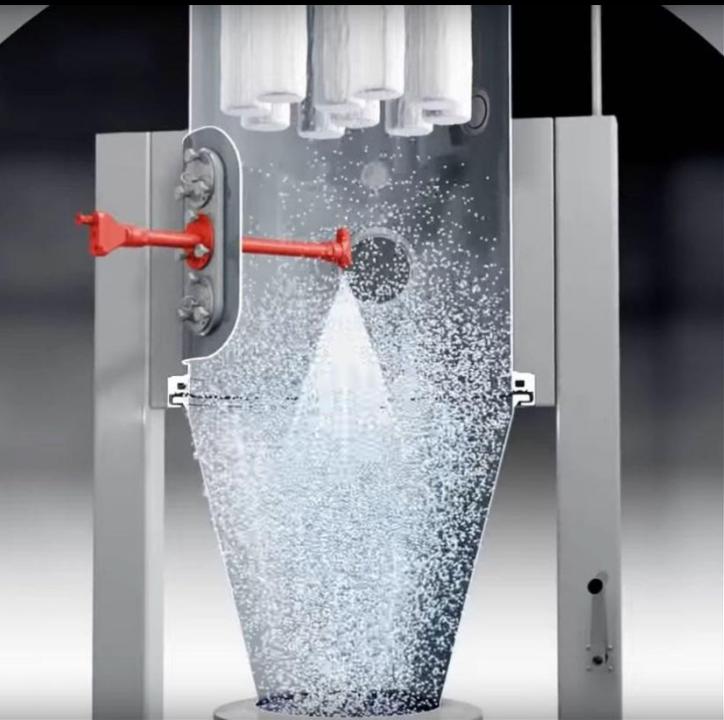
9/30/2023



10

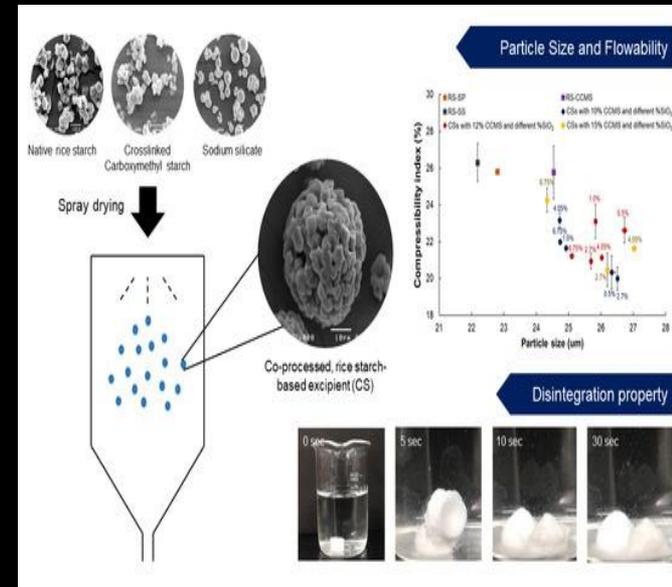
Multifunctional Excipients

😊 Multifunctional excipients or high-functionality excipients are those that contribute at least two functions to formulations through a single ingredient, require no complex processing and improve the performance of the formulations for better drug products.



Continue

- 😊 Decrease lubricant sensitivity
- 😊 Enhance flow properties
- 😊 Enhance the blending process
- 😊 Improve compression property
- 😊 Facilitate material handling
- 😊 Improve stability
- 😊 Decrease environmental concern



| Trade name | Coprocessed excipient | Added advantages |
|---------------|---|---|
| Ludipress | Lactose monohydrate (93%), Kollidon 30 (3.5%), and Kollidon CL (3.5%) | Lower hygroscopicity, good flow ability, tablet hardness independent of machine speed |
| Cellactose 80 | α -Lactose monohydrate (75%) and cellulose powder (25%) | Highly compressible, good mouth feel, better tableting at low cost |
| Avicel CE-15 | MCC and guar gum | Less grittiness, reduced tooth packing, minimal chalkiness, creamier mouth feel, improved |

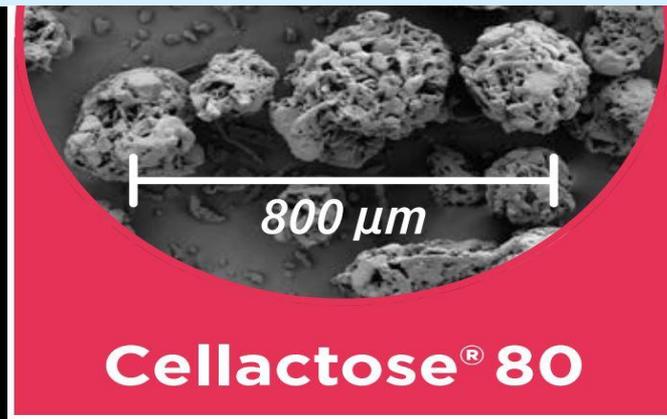
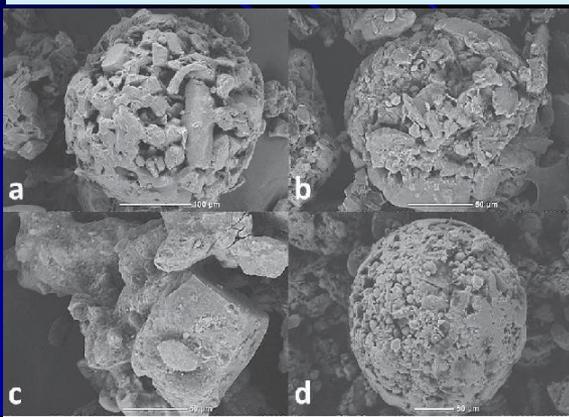


Table II: Typical physical properties of selected commercially available lactose, monohydrate.

| Supplier/grade | Density (bulk) (g/cm ³) | Density (tapped) (g/cm ³) | Water content (%) |
|--------------------------------------|-------------------------------------|---------------------------------------|-------------------|
| DMV-Fonterra Excipients | | | |
| <i>Pharmatose 50M</i> | 0.70 | 0.82 | — |
| <i>Pharmatose 60M</i> | 0.80 | 0.98 | — |
| <i>Pharmatose 70M</i> | 0.81 | 1.02 | — |
| <i>Pharmatose 80M</i> | 0.75 | 0.92 | — |
| <i>Pharmatose 90M</i> | 0.72 | 0.90 | — |
| <i>Pharmatose 100M</i> | 0.73 | 0.88 | — |
| <i>Pharmatose 110M</i> | 0.72 | 0.88 | — |
| <i>Pharmatose 125M</i> | 0.68 | 0.85 | — |
| <i>Pharmatose 130M</i> | 0.65 | 0.96 | — |
| <i>Pharmatose 150M</i> | 0.62 | 0.90 | — |
| <i>Pharmatose 200M</i> | 0.57 | 0.84 | — |
| <i>Pharmatose 350M</i> | 0.54 | 0.80 | — |
| <i>Pharmatose 450M</i> | 0.48 | 0.74 | — |
| <i>SuperTab 30GR</i> | 0.53 | 0.66 | — |
| Friesland Foods Domo | | | |
| <i>Lactochem Coarse Crystals</i> | 0.75 | 0.88 | — |
| <i>Lactochem Crystals</i> | 0.74 | 0.86 | — |
| <i>Lactochem Fine Crystals</i> | 0.73 | 0.85 | — |
| <i>Lactochem Extra Fine Crystals</i> | 0.73 | 0.86 | — |
| <i>Lactochem Coarse Powder</i> | 0.71 | 0.95 | — |
| <i>Lactochem Regular Powder</i> | 0.62 | 0.92 | — |
| <i>Lactochem Powder</i> | 0.64 | 0.89 | — |
| <i>Lactochem Fine Powder</i> | 0.61 | 0.84 | — |
| <i>Lactochem Extra Fine Powder</i> | 0.45 | 0.74 | — |
| <i>Lactochem Super Fine Powder</i> | 0.47 | 0.74 | — |
| Meggle GmbH | | | |
| <i>Capsulac 60</i> | 0.59 | 0.70 | 5.2 |
| <i>Granulac 70</i> | 0.72 | 0.90 | 5.2 |
| <i>Granulac 140</i> | 0.66 | 0.89 | 5.2 |
| <i>Granulac 200</i> | 0.54 | 0.80 | 5.2 |
| <i>Granulac 230</i> | 0.47 | 0.76 | 5.2 |
| <i>Primalac 40</i> | 0.47 | 0.54 | 5.2 |
| <i>SacheLac 80</i> | 0.60 | 0.71 | 5.2 |
| <i>Sorbolac 400</i> | 0.36 | 0.78 | 5.2 |
| <i>Spherolac 100</i> | 0.69 | 0.84 | 5.2 |
| <i>Tablettose 70</i> | 0.51 | 0.62 | 5.2 |
| <i>Tablettose 80</i> | 0.57 | 0.72 | 5.2 |
| <i>Tablettose 100</i> | 0.54 | 0.74 | 5.2 |
| Sheffield Pharma Ingredients | | | |
| <i>Monohydrate 80M</i> | 0.66 | 0.92 | 4.8–5.2 |
| <i>Monohydrate Impalpable</i> | 0.53 | 0.81 | 4.8–5.2 |



جرم حجمی اولیه - جرم حجمی متراکم شده

$$\text{اندیس کار} = \frac{\text{جرم حجمی اولیه} - \text{جرم حجمی متراکم شده}}{\text{جرم حجمی متراکم شده}} \times 100$$

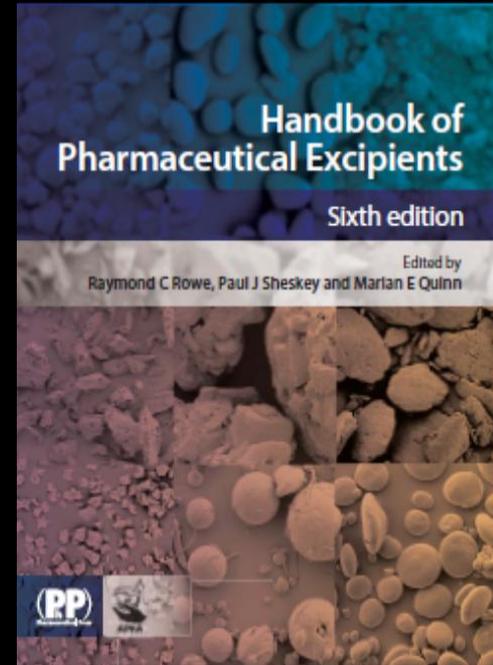
| | Tapped D. | Bulk D. | Results |
|---------------------|------------------|----------------|----------------|
| Lactose 60M | 0.98 | 0.8 | 18.37 |
| Lactose 80M | 0.92 | 0.72 | 21.74 |
| Lactose 200M | 0.84 | 0.57 | 32.14 |

| Flow character | Carr's index (%) | Hausner ratio |
|-----------------------|-------------------------|----------------------|
| Excellent | ≤ 10 | 1.00-1.11 |
| Good | 11-15 | 1.12-1.18 |
| Fair | 16-20 | 1.19-1.25 |
| Possible / Passable | 21-25 | 1.26-1.34 |
| Poor | 26-31 | 1.35-1.45 |
| Very poor | 32-37 | 1.46-1.59 |
| Very, very poor | > 38 | > 1.60 |

DRUG-EXCIPIENT, EXCIPIENT-EXCIPIENT INTERACTIONS

 Drug

 Excipients



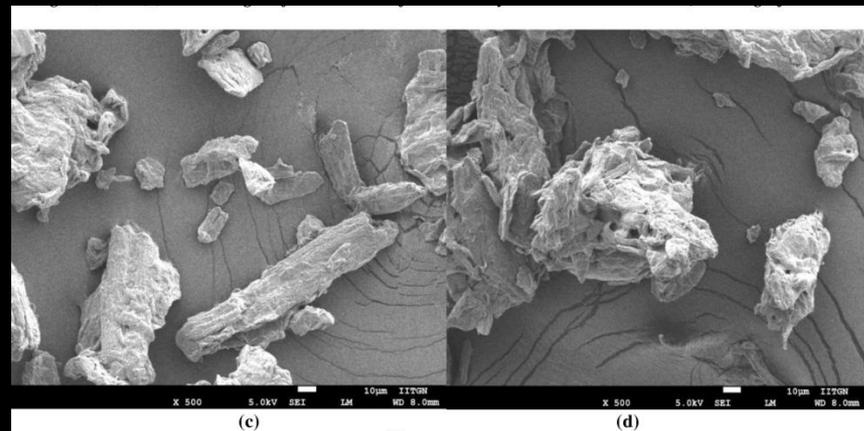
Physical Interactions

😊 Physical interactions involving excipients are quite common

😊 Used in pharmaceutical science to aid processing and to aid or modify drug dissolution

😊 Silicied microcrystalline cellulose

It is thought that the fumed silica particles prevent the structural collapse of the microcrystalline cellulose that can occur on drying after wet massing during wet granulation.



Continue

😊 Physical interaction between primary amine drugs and microcrystalline cellulose is an example of drug-excipient interaction. drug may bound to the microcrystalline cellulose and is not released when dissolution is carried out in water. It is not a major issue for high-dose drugs but for low-dose drugs it can lead to dissolution failures.



Chemical Interactions

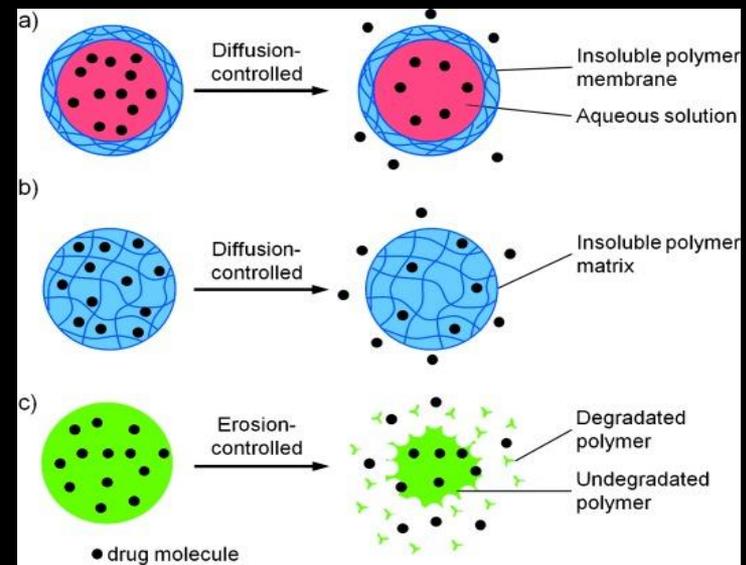
- 😊 Sodium bicarbonate with citric acid.
- 😊 Manufacturing and packing at very low RH (< 20%) to prevent premature activation of the couple.
- 😊 The packaging also needs to be impermeable to moisture for the same reason.



Physiological/Biopharmaceutical Interactions

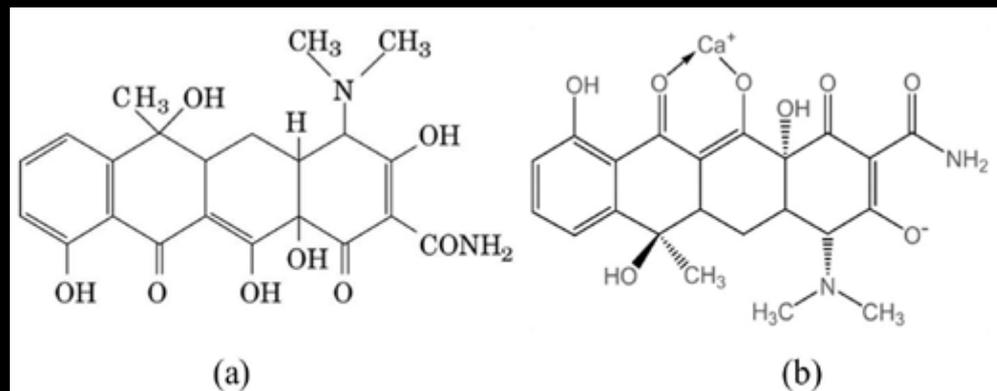
😊 Disintegrants are added in immediate release tablet and capsule formulations.

😊 Hydrophilic colloid matrices swell and create a diffusion barrier.



Continue

😊 A classic biopharmaceutical incompatibility is the interaction between tetracycline antibiotics and calcium and magnesium ions. A complex is formed that is not absorbed from the GIT. This is a well-known interaction, and tetracycline antibiotics usually carry a warning against taking them with certain types of food.



Continue

Handbook of Pharmaceutical Excipients

Sixth edition

Edited by
Raymond C Rowe, Paul J Sheskey and Marian E Quinn

Lactose anhydrous is a reducing sugar with the potential to interact with primary⁽⁵⁾ and secondary amines⁽⁶⁾ (Maillard reaction) when stored under conditions of high humidity for extended periods.

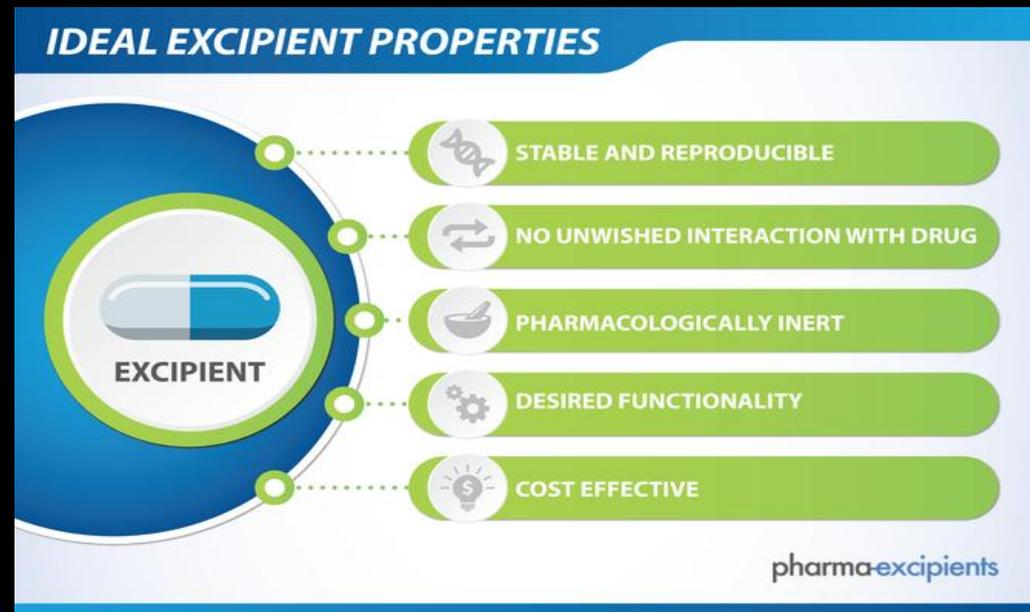


Incompatible with strong acids, alkalis, and iron salts. Avoid mixing with strong oxidizing materials. Magnesium stearate cannot be used in products containing aspirin, some vitamins, and most alkaloidal salts.



EXCIPIENT SELECTION

- 😊 The nature and properties of the active ingredient dictate the choice of an excipient, the dosage form to be elaborated, and the process by which it is manufactured.
- 😬 patient group and clinical condition
- 😊 Candidate excipients should then be evaluated to demonstrate that they function in the manner intended and do not adversely interact with the drug, or with other excipients.



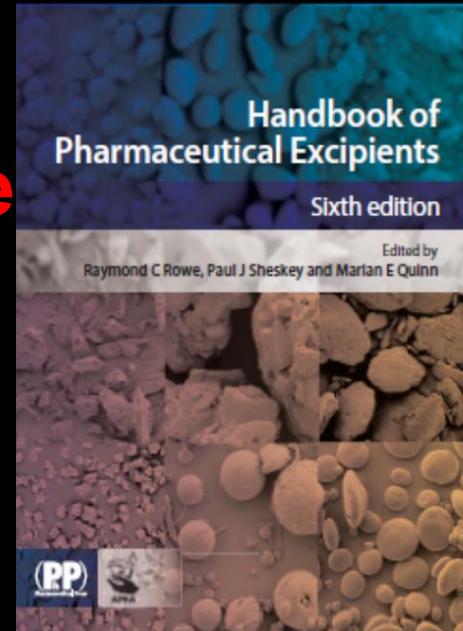
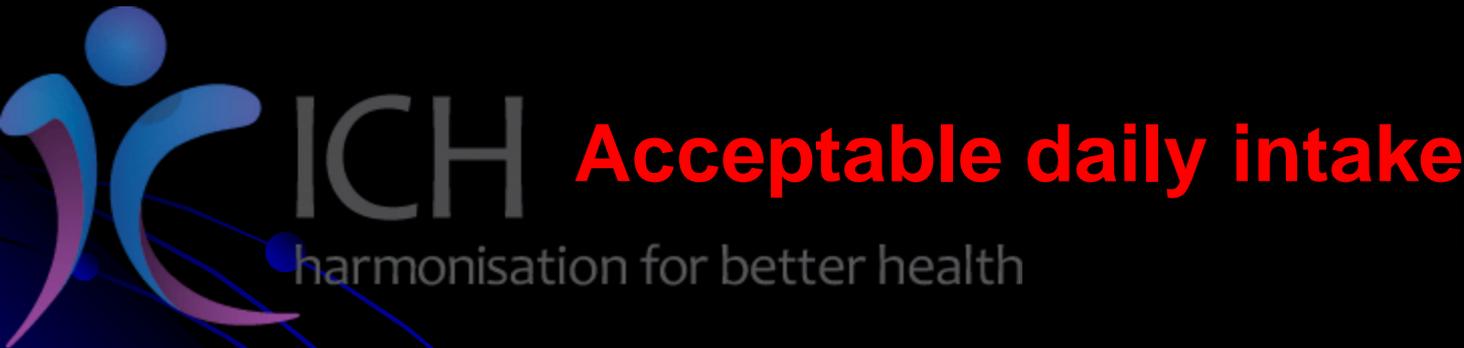
EXCIPIENT TOXICITY

😊 Pharmaceutical excipients have a vital role in drug formulations, a role that has tended to be neglected as evidenced by the lack of mechanisms to assess excipient safety outside a new drug application process.



Continue

- 😊 International Conference on Harmonization (ICH)
- 😊 Food and Drug Administration/Center for Drug Evaluation and Research (FDA/CDER)
- 😊 Handbook of Pharmaceutical Excipients



Thank you

