PHYSICS OF TABLET COMPRESSION

Tablet compression physics includes:

- Transmission of forces during compression
- Distribution of forces in tablets
- The effect of applied pressure on the relative volume of the powder
- Interparticulate adhesion and cohesion forces
- Tablet compression energies
- Mechanical strength of tablets
- Detailed description of the tools used in these studies and working methods.

The main criteria for tablet formulations are:

- To form tablets without sticking to the punch surfaces and to the die wall, and capping;
- To compress the tablets with acceptable mechanical properties in terms of hardness and friability;
- To meet pharmacopoeia limits for tablet weight variation and content uniformity;
- To provide appropriate disintegration time and dissolution rate for the tablets.

Manual hydroulic presses (simulator)

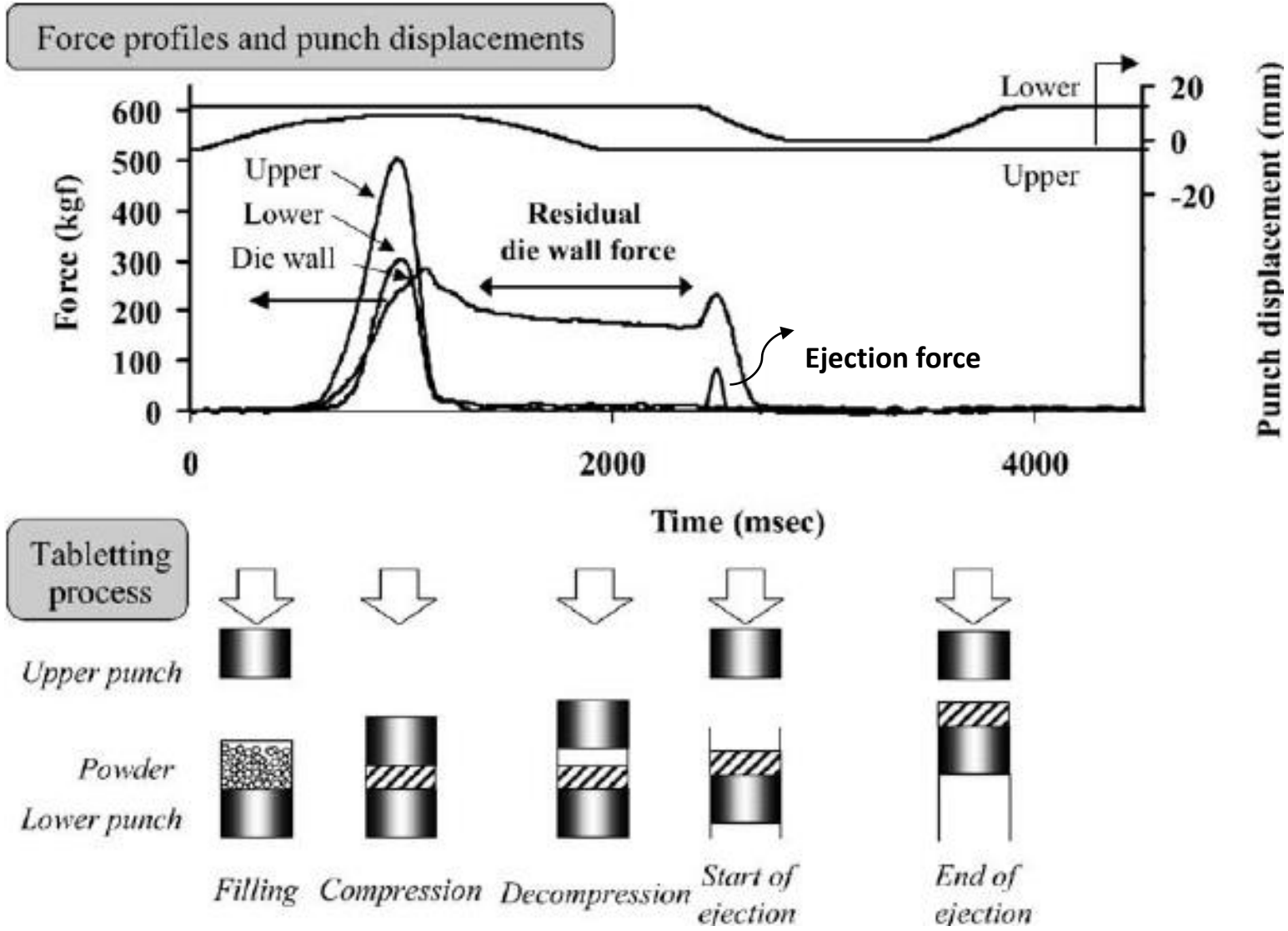
CARVER

Products

Pellet press for laboratories

25 - 40 t | AutoPellet

Typical pressure-time profile observed according to the stages involved in tableting process



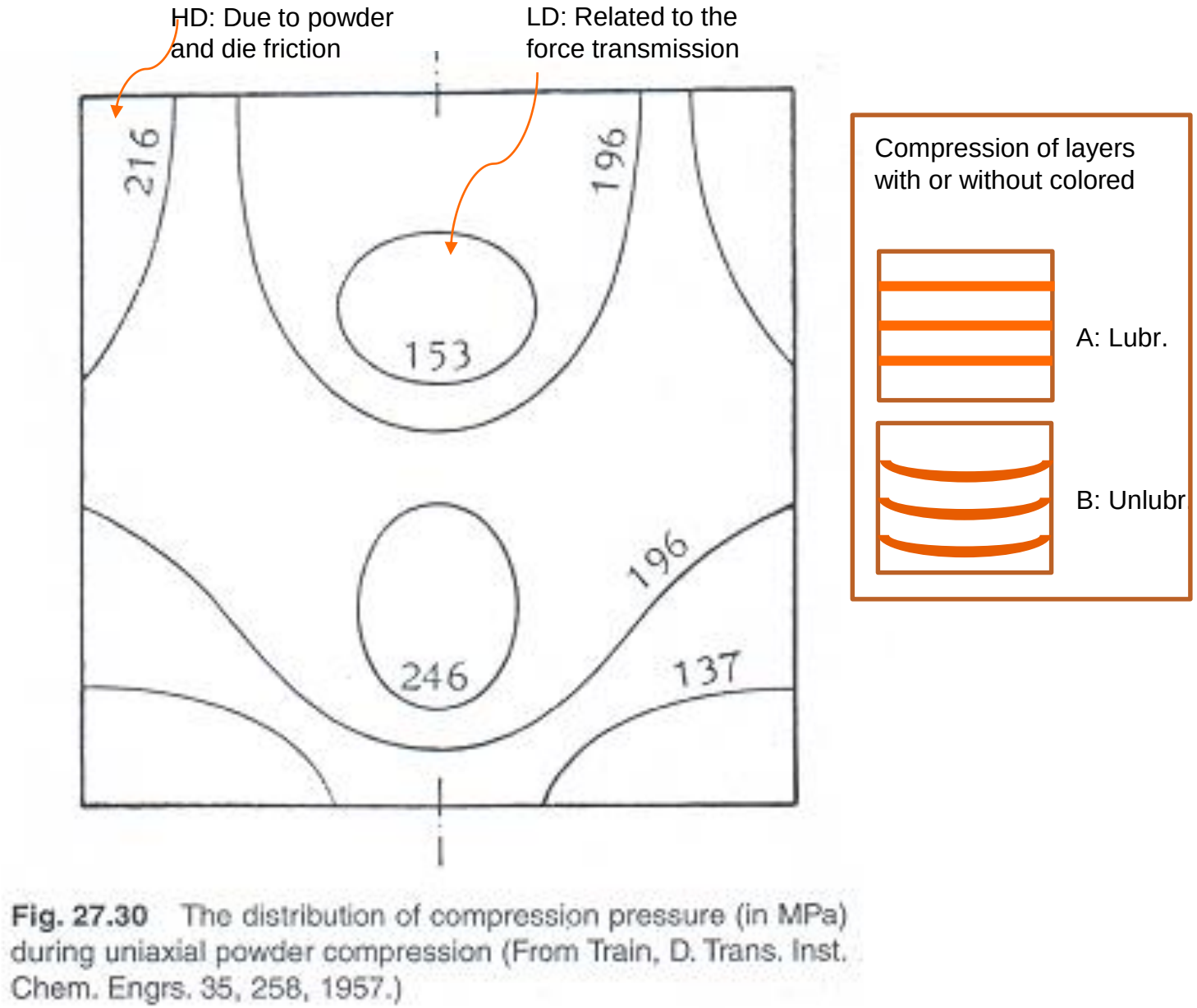
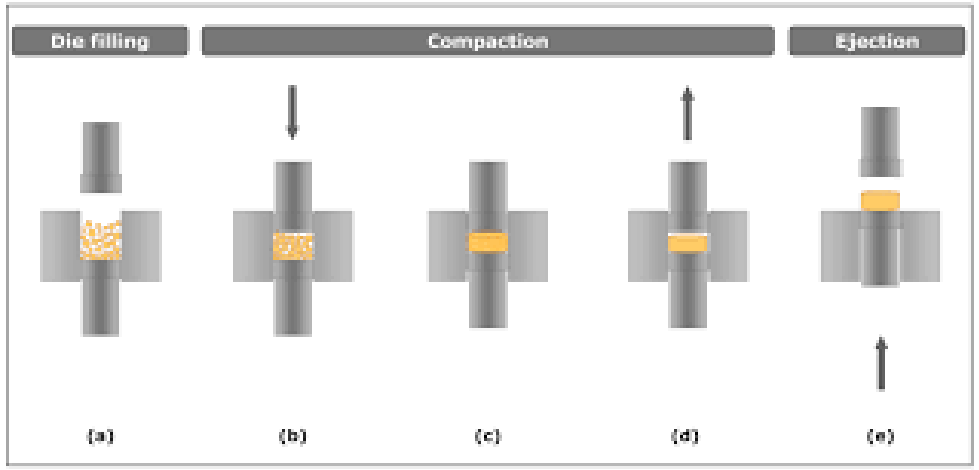
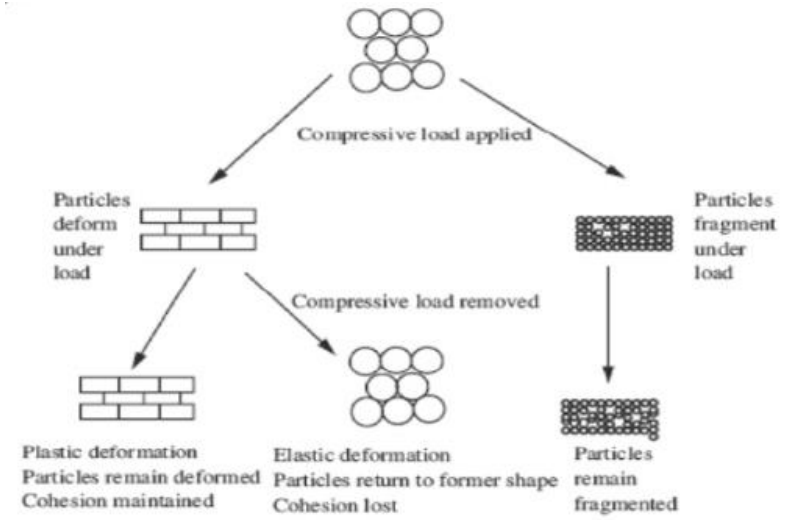
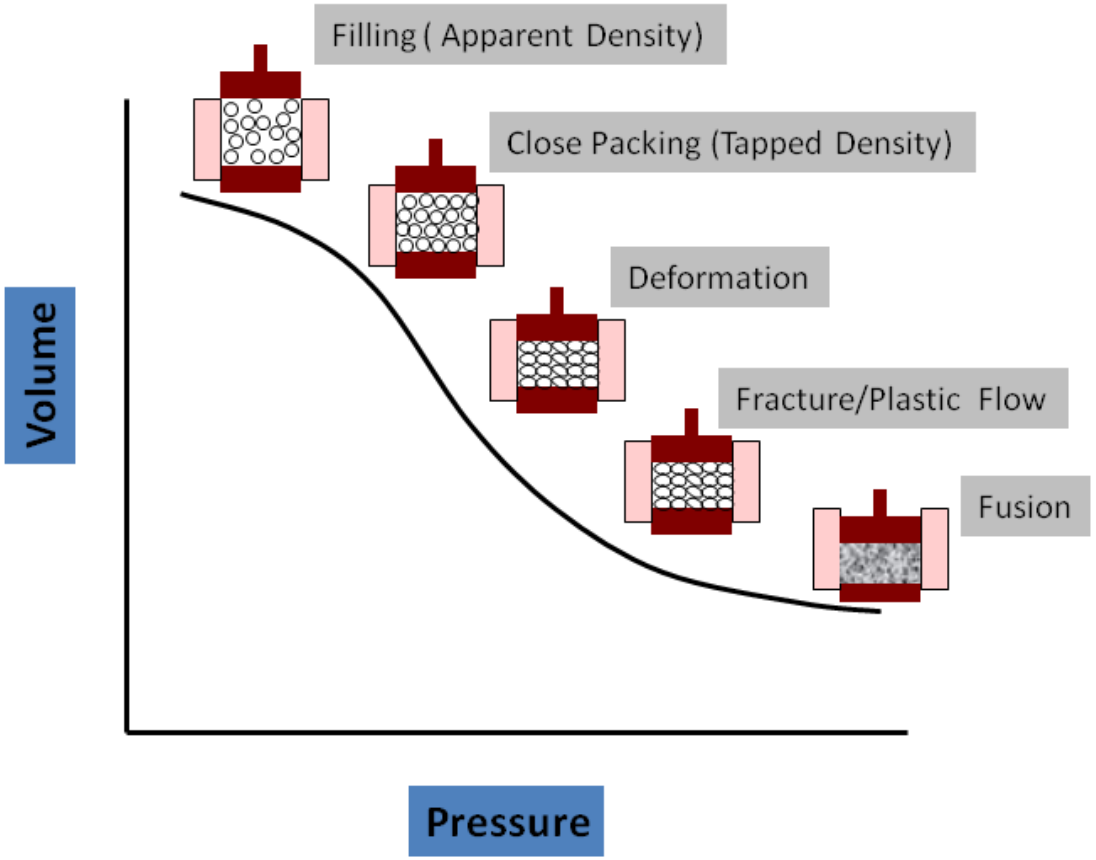


Fig. 27.30 The distribution of compression pressure (in MPa) during uniaxial powder compression (From Train, D. Trans. Inst. Chem. Engrs. 35, 258, 1957.)



filling-compression-compaction-decompression-ejection





relative volume change of the powder vs. pressure

Heckel equation

$$\frac{dD}{dP} = K(1-D)$$

$$\ln\left[\frac{1}{1-D}\right] = KP + A$$

$$P_Y = \frac{1}{K}$$

$$\ln \frac{V_p}{V_p - V_\infty} = kP + \ln \frac{V_o}{V_o - V_\infty}$$

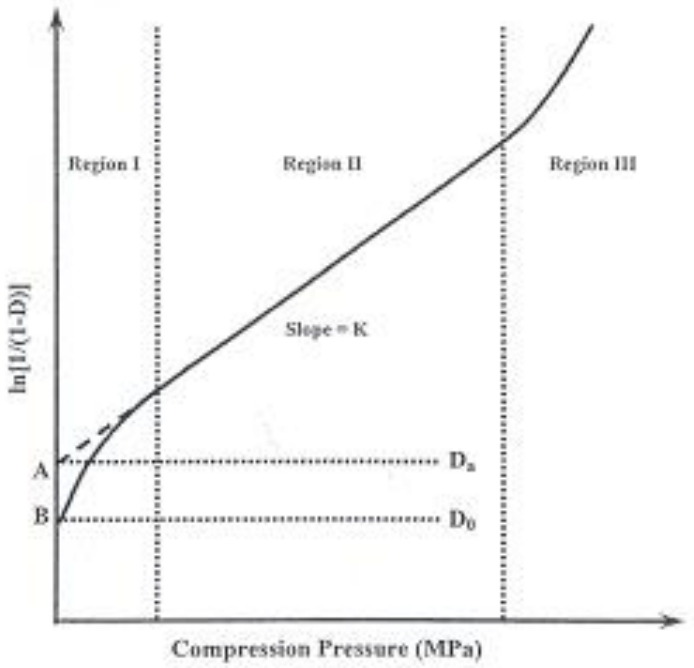
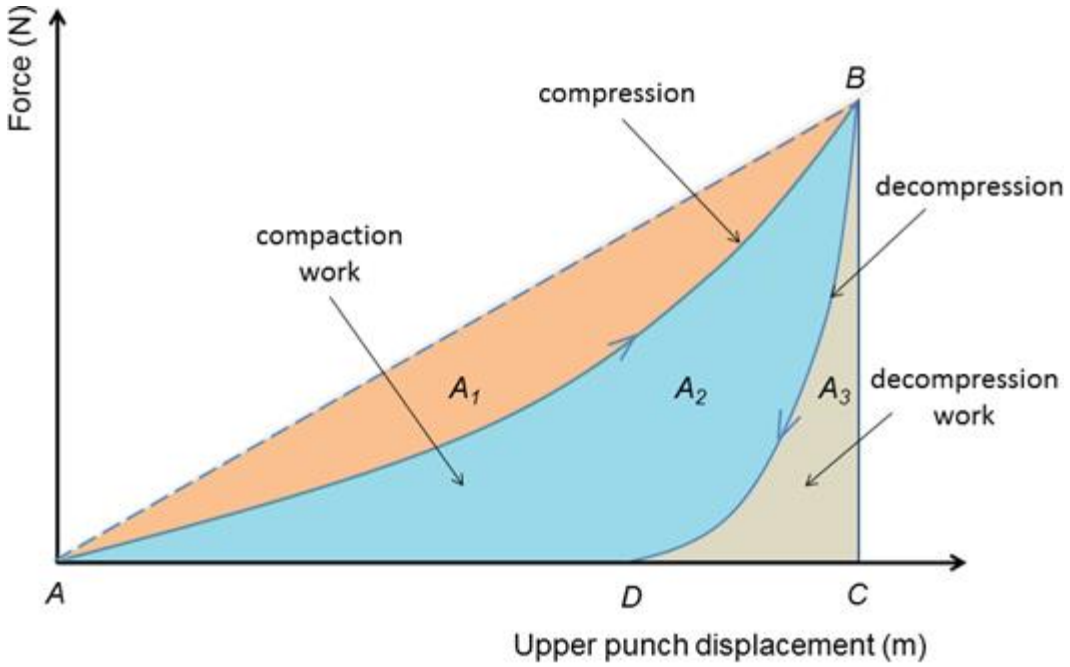


FIGURE 10. A typical Heckel plot derived from relative density and compaction pressure. Region I corresponds to particle rearrangement at low pressure, whereas region II, the linear part of the curve shows the ability of the material to deform plastically. At higher pressures, region III is observed due to work hardening. D_a gives densification due to initial particle rearrangement, whereas D_0 gives densification due to initial die filling. (Adapted from Ref. 13 with permission from Elsevier.)

Tablet compression energies



$$A = \int_{X_{F=0}}^{X_{F=max}} F.dx$$

TABLET TESTING

- Controls of the starting materials

In-process and intermediate product controls at various stages of manufacturing

  - ✓ Bulk density
  - ✓ Flow properties
  - ✓ Moisture content
  - ✓ Drug content

- Finished product controls
- Stability

Finished product controls

- Organoleptic controls
- Thickness – diameter
- Uniformity of dosage units
  - Content uniformity
  - Weight variation
- Mass uniformity
- Decomposition products and impurities
- Hardness / tensile strength
- Friability
- Disintegration
- Dissolution
- Microbial quality

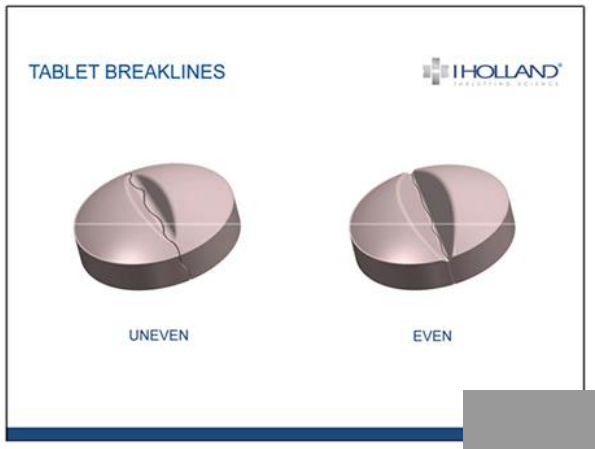
In vitro dissolution tests for immediate release solid oral dosage forms are used:

(1) to assess the lot-to-lot quality of a drug product;

(2) to assess the stability of the drug product;

(3) to ensure continuing product quality and performance after certain changes, such as changes in the formulation, the manufacturing process, the site of manufacture, and the scale-up of the manufacturing process; and

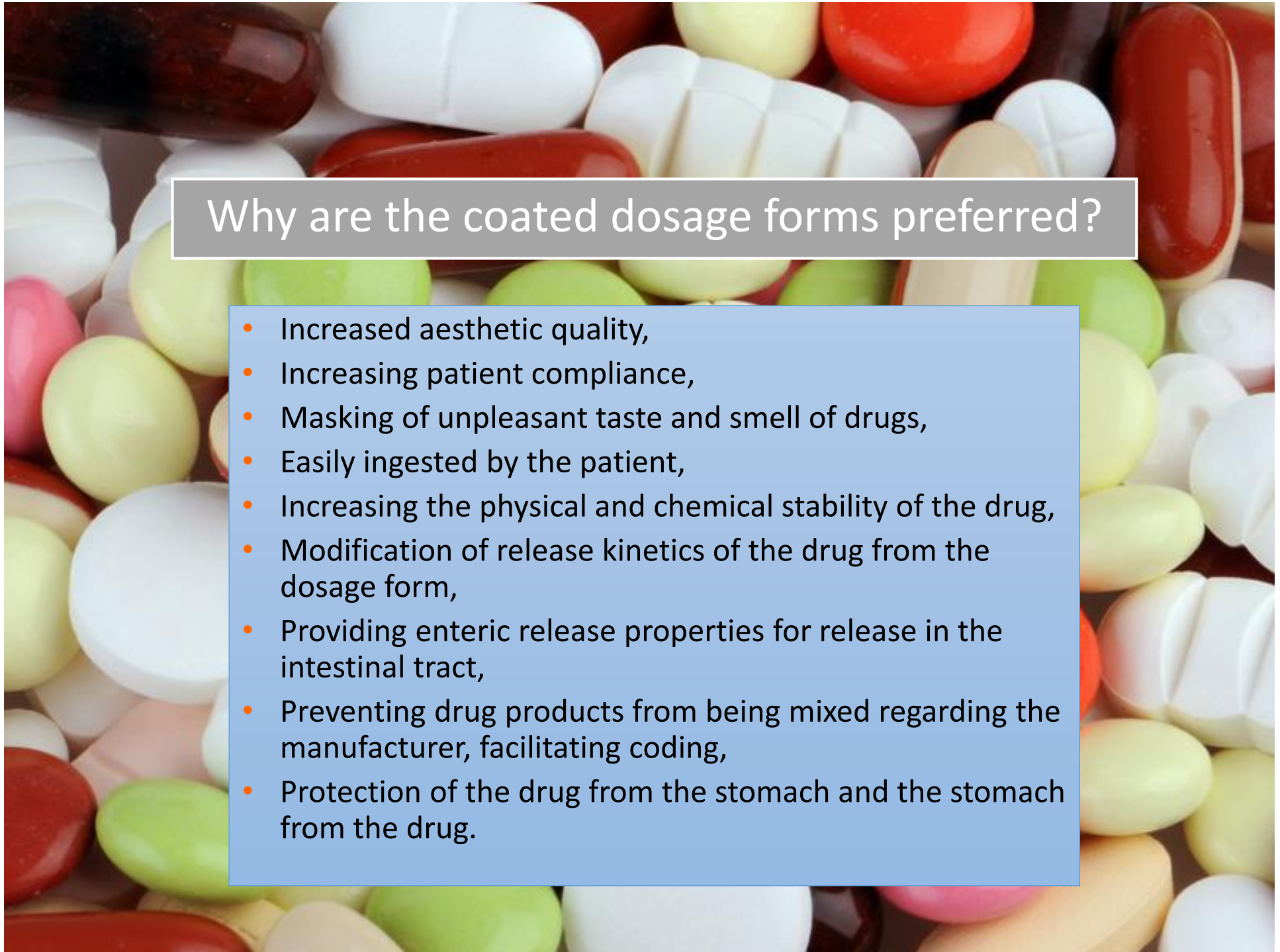
(4) to develop new formulations. In formulation development, dissolution testing can aid in the selection of excipients, help optimize the manufacturing process, and enable formulation of the test product to match the release of the reference product.



(EP 6.0 V1, Subdivision of tablets, ease of intake or **posology – uniformity of mass**)

IMPORTANT...
Products that are not intended to be split, e.g. enteric coated tablets, tablets which are film coated to maintain stability and some modified release preparations, should not be split. However, those modified release preparations using matrix technology or using compressed film coated components could be split.

COATING OF TABLETS:
Sugar coating - dragees
Film coated tablets
Formulations
Manufacturing processes

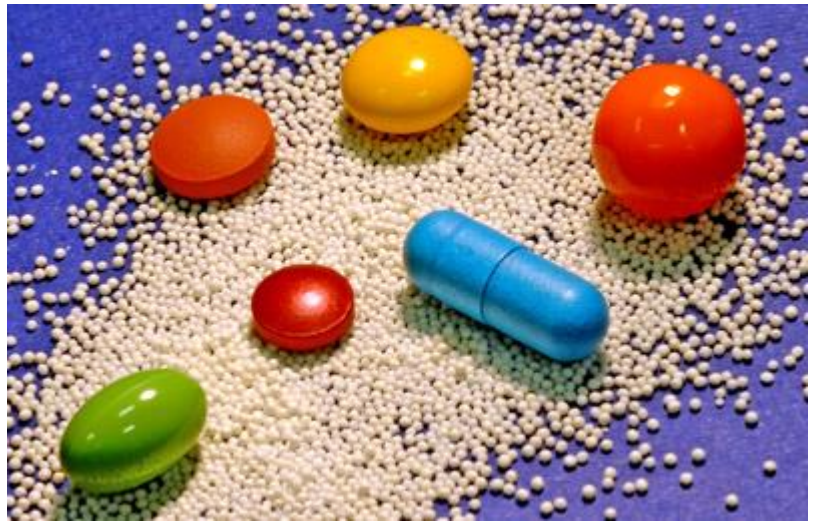


Why are the coated dosage forms preferred?

- Increased aesthetic quality,
- Increasing patient compliance,
- Masking of unpleasant taste and smell of drugs,
- Easily ingested by the patient,
- Increasing the physical and chemical stability of the drug,
- Modification of release kinetics of the drug from the dosage form,
- Providing enteric release properties for release in the intestinal tract,
- Preventing drug products from being mixed regarding the manufacturer, facilitating coding,
- Protection of the drug from the stomach and the stomach from the drug.

The types of cores (substrate) for coating

- Crystals
- Different types of granules
- Pellets
- Tablets
- Soft and hard gelatin capsules



Properties

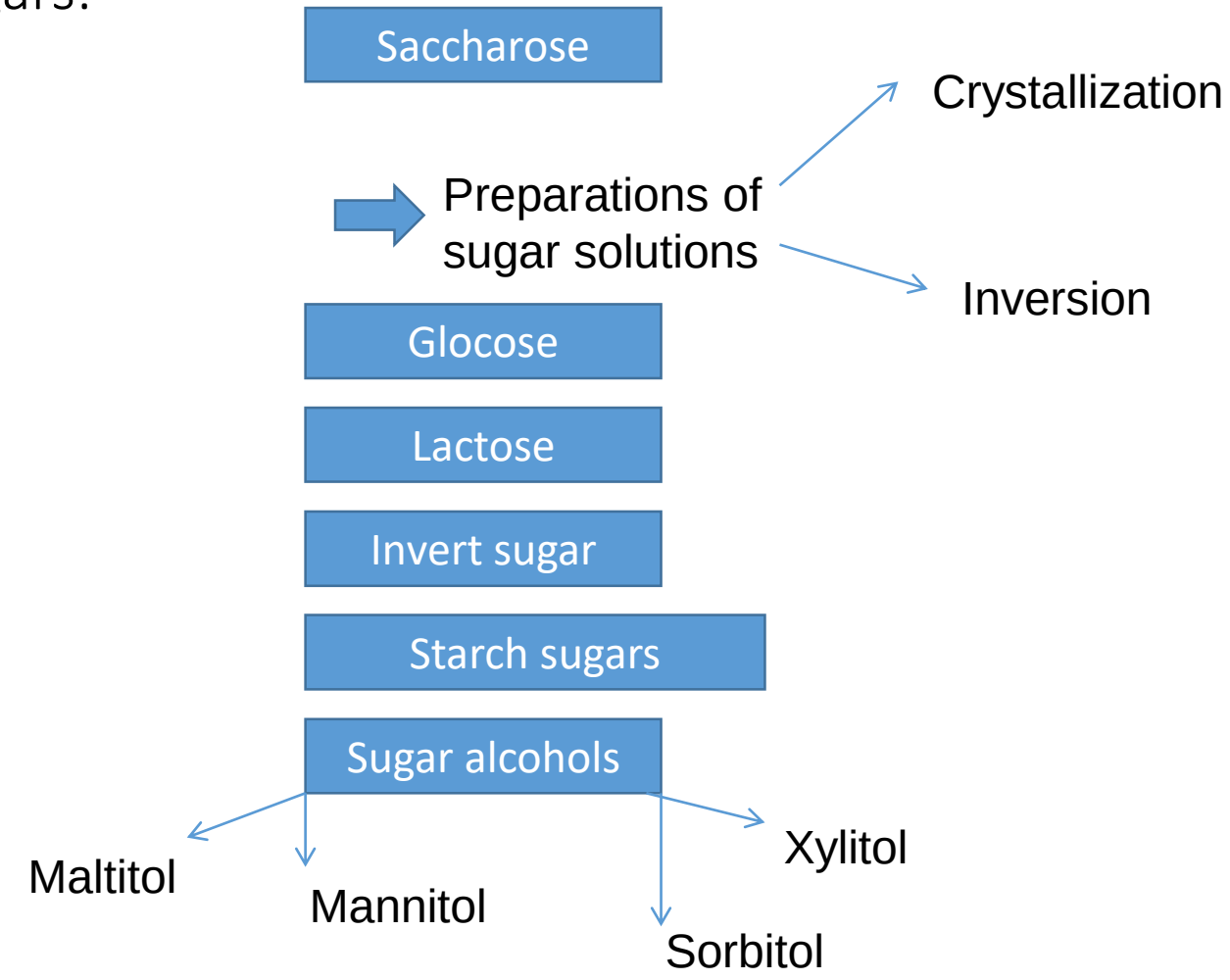
- Form/shape and size
- Mechanicel strength and friability
- Formulation
- Sensitivity to heat and moisture
- Interactions with coating

There are some drawbacks of sugar coating.

- Due to the increase in diameter and weight (about 2 times or 30-100 % increase), packaging and transfer-handling fees have increased.
- There is a possibility of damage due to the fragility of the coating.
- Specialized personnel for coating process are required to achieve high aesthetic quality.
- There is a polishing process that makes coding difficult to print.
- There is a complex application which makes the transition to automation difficult: Various operations and functions are used.

Excipients used in the formulations of sugar coating

- Sugars:



Other excipients used in the sugar coating formulation

Coating agents:

Gum acacia, agar-agar, carboxymethyl starch, cellulose ethers, dextrins, gelatin, PVA, PVP, sodium alginate

Fillers:

Calcium carbonate, talc, titanium dioxide, calcium sulfate, calcium hydrogen phosphate, calcium lactate

Coloring agents:

Soluble organic dyes, pigments, lakes

- Flavors

  Fruit essences, methyl salicylate, vanilla, cocoa, chocolate, condensed milk, caramel

- Lubricants

  Talc

- Polishing agents

  Waxes, oils, resins

- Suspending agents

  Surfactants

Coating process and coating layers

Coating layers:

1. Sealing (protective coating)
2. Subcoating
3. Corrective coating (rossing/smoothing)
4. Color coating
5. Polishing

Uniform coating

Priming coat

Rounding layer

Finishing layer

Process steps applied for each layer:

- Application of coating formulation
- Mixing for homogeneous distribution of formulation
- Drying