# Tablet making
# Texture of tablets

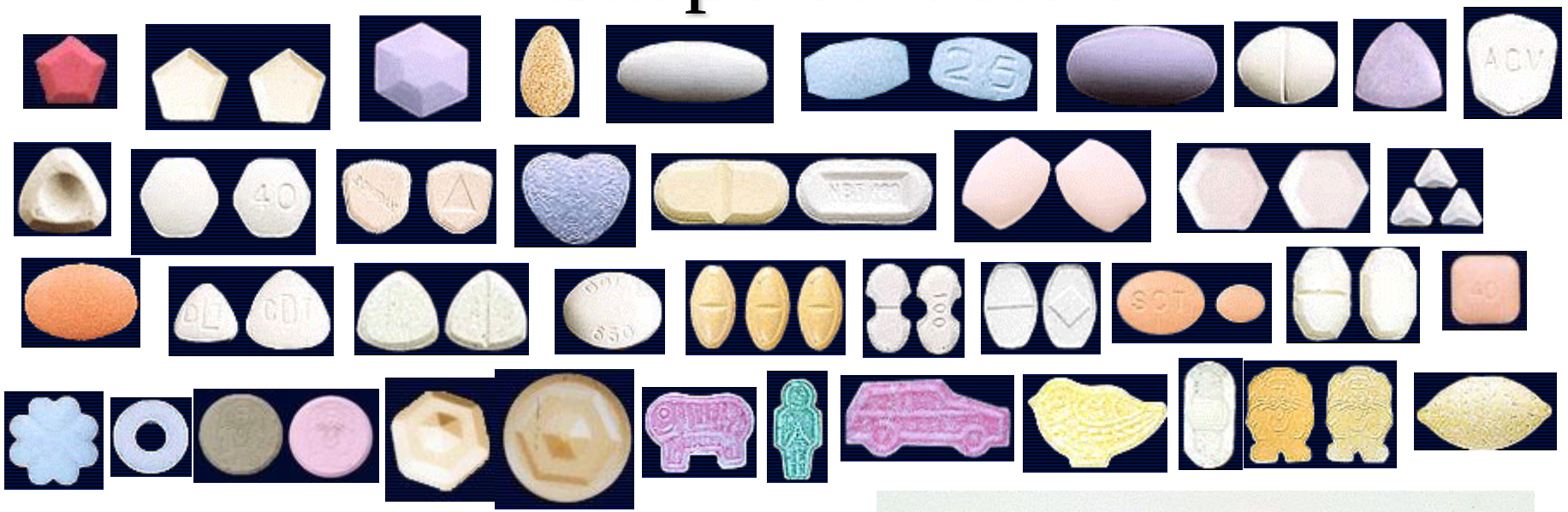
*Prof. emer. Dr. Klára Pintye-Hódi*

# Definition

- Tablets are solid preparations manufactured by compression containing definite amount of active ingredient of a single or multiple dose.

- Tablets belong to the most commonly used dosage forms due to their expansive use.

# Shape of tablets



# Some advantages of tablets

1. The active pharmaceutical ingredient (API) can be dosed exactly in little volume.
2. Tableting of the most solid drugs is solvable.
3. The APIs can be produced in large amounts by machines.
4. It is posible the protection of the API against the gastric juice, resp. enviroment.
5. The dissolution and absorption of the API are regulable.
6. Suitable storage.
7. Good taking possibility.
8. It is possible to make a difference on the base of the shape, size and colour.

# Grouping of tablets

## Oral tablets

- Uncoated tablets
- Coated tablets
- Effervescent tablets
- Dissolving tablets
- Dispensing tablets
- Modified release tablets

## Tablets in mouth

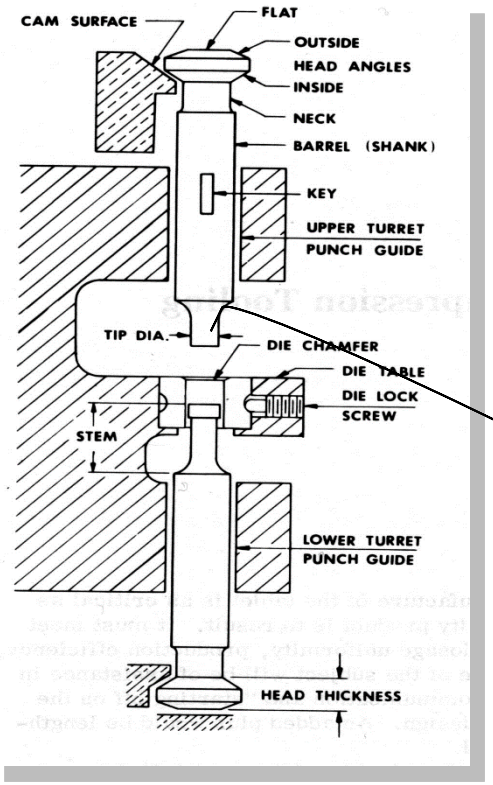
- Sublinqual tablets
- Buccal tablets
- Orodispersible tablets (ODT)
- Mucoadhesive tablets
- Chewable tablets

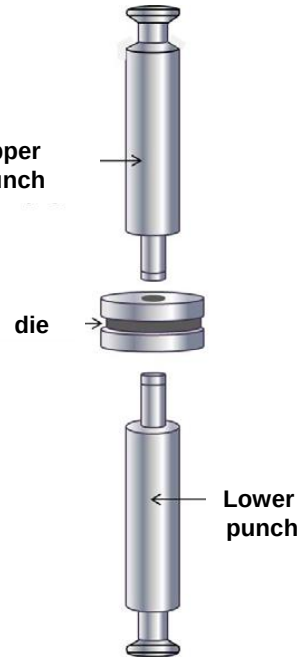
## Other tablets

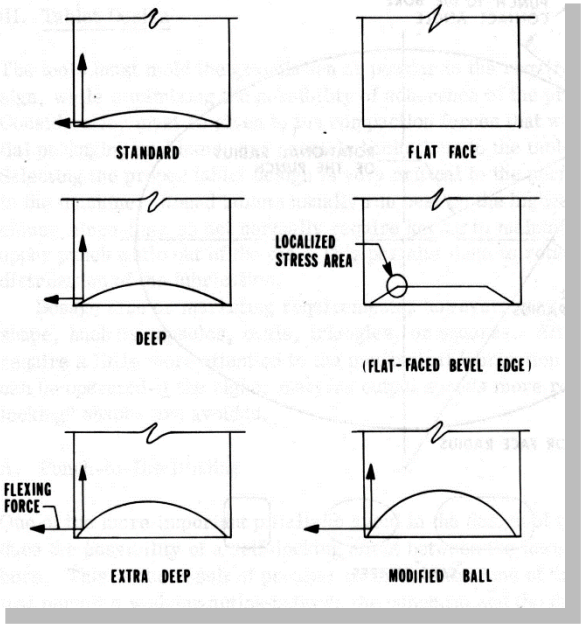
Tablets in vaginal, urethral, paradentium, etc.

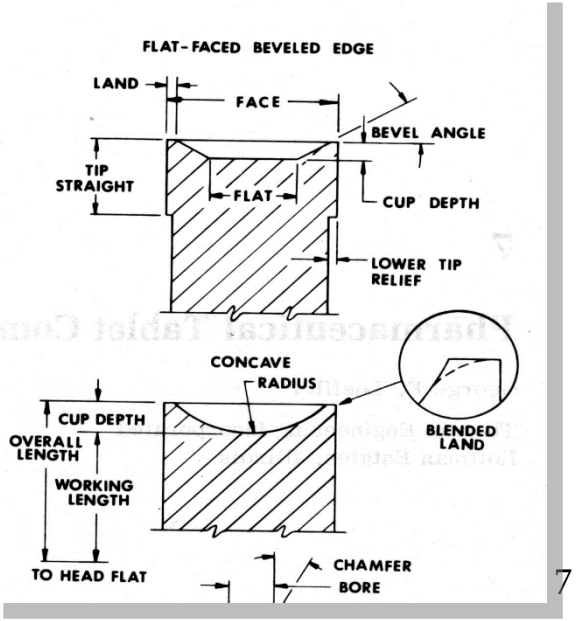
# Tableting tools, tablet machines

# Tools



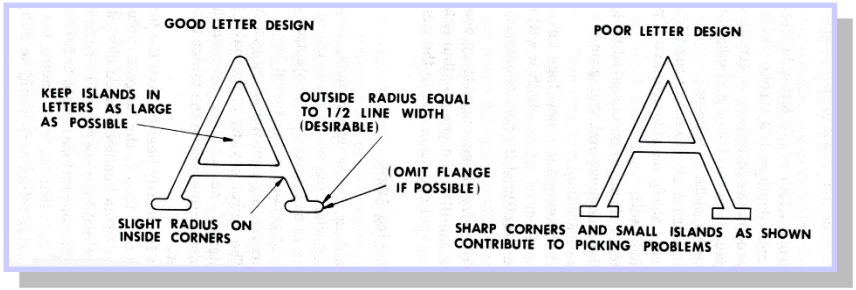



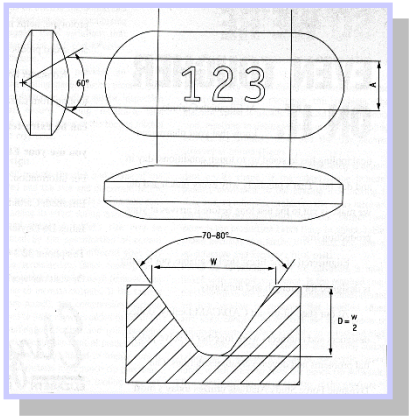

A. Dévay: The theory and practice of pharmaceutical technology, university textbook, PTE, Pécs, 2013

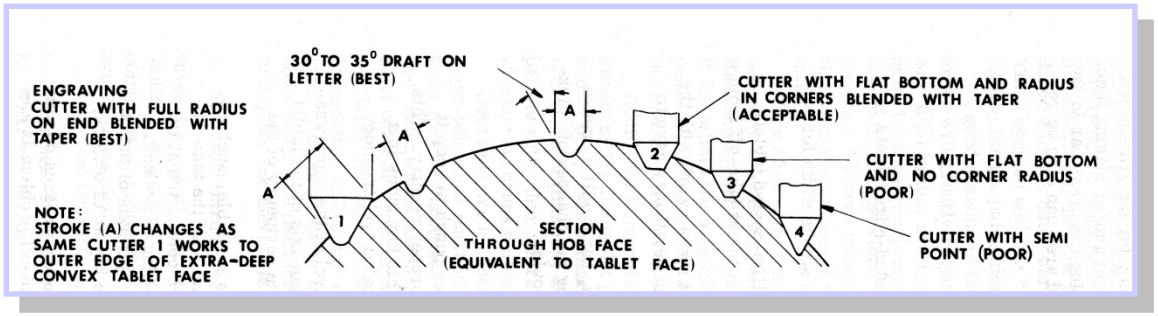
# Tools

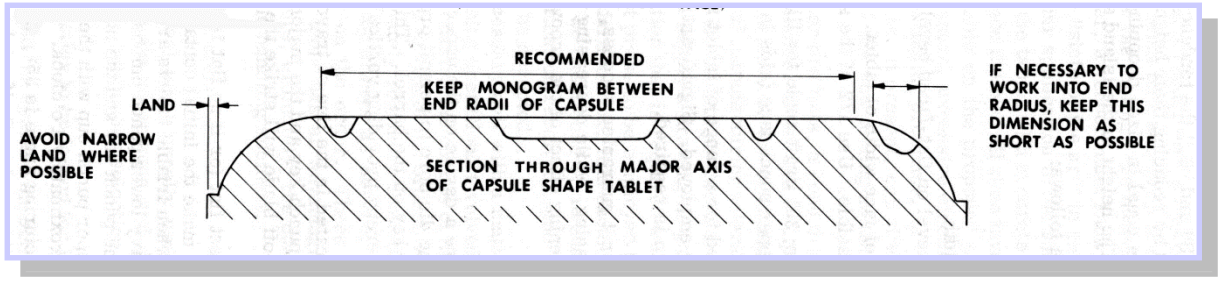
# Engraving

**Ideal area, angle and deep**

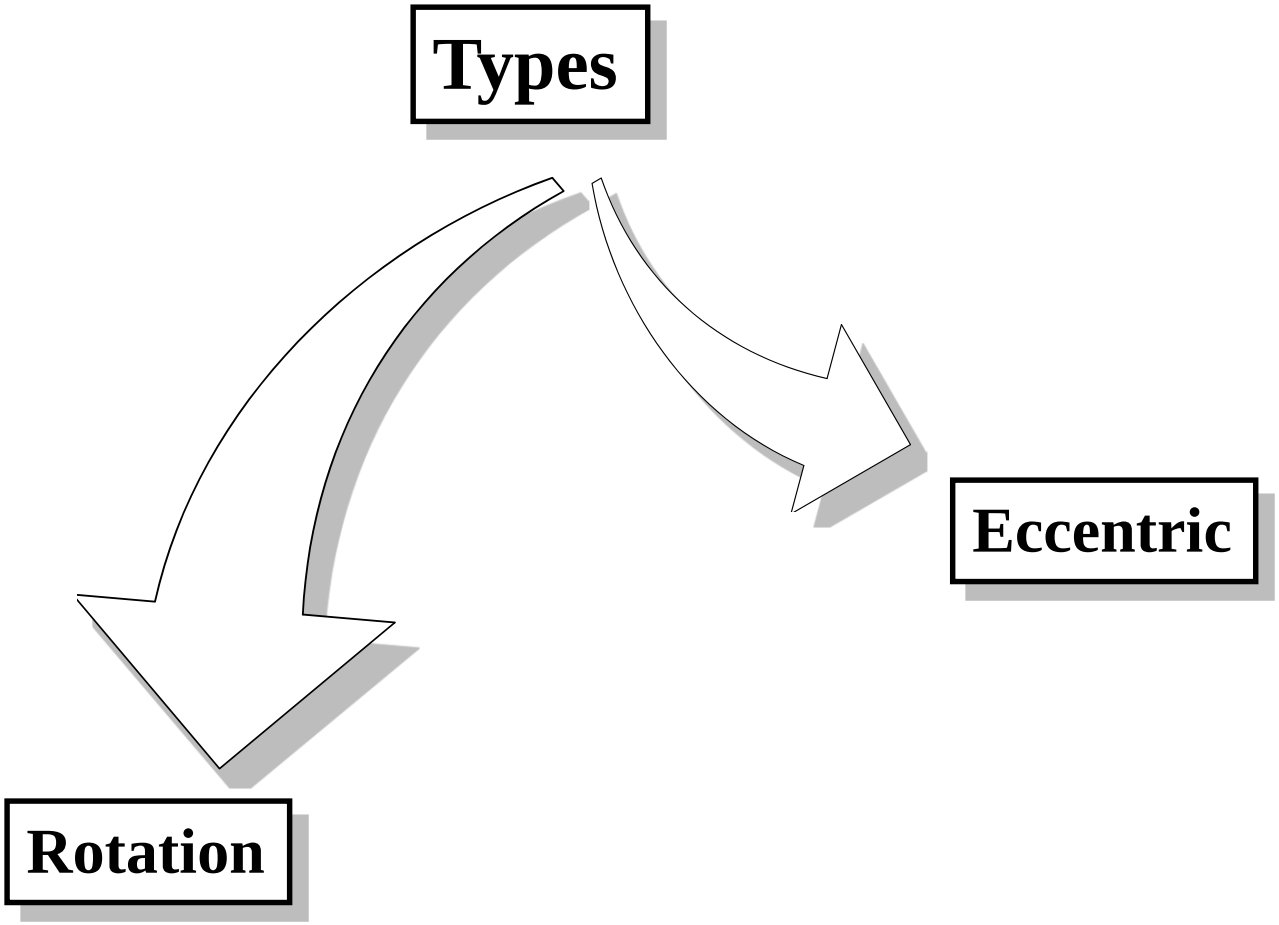


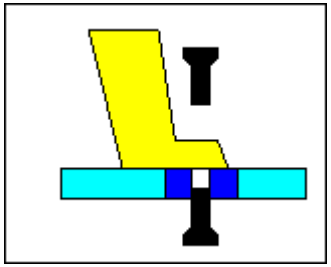



# Tablet machines

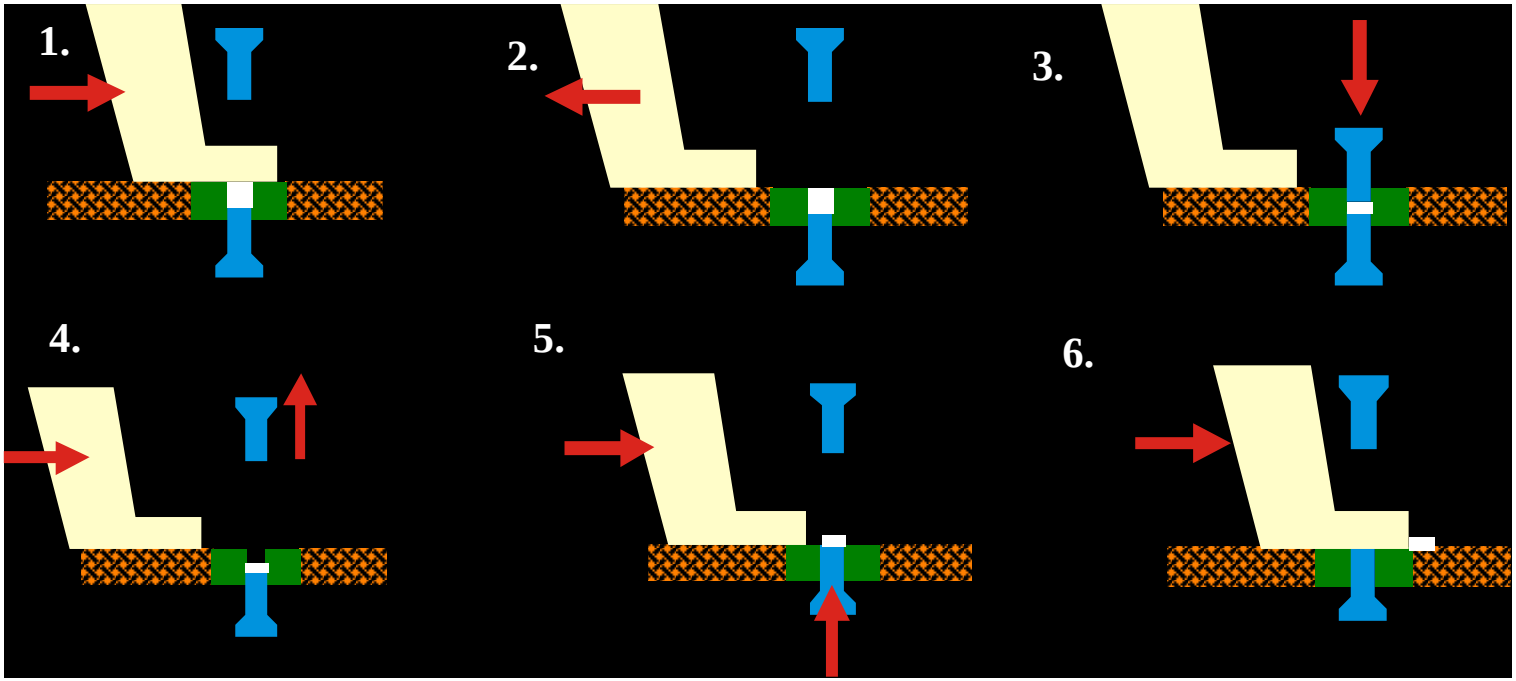


# Eccentric tablet machine

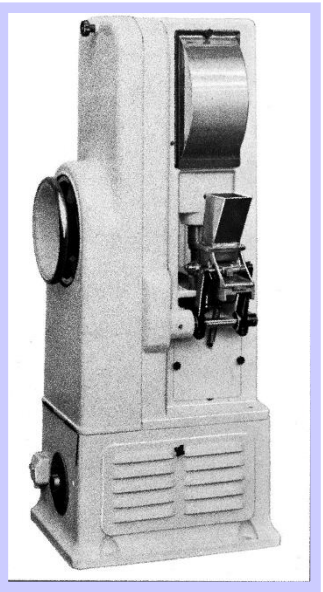


## Working scheme

**Periodic working**
**Pressure force is efforted by upper punch**
**Funnel is moving**



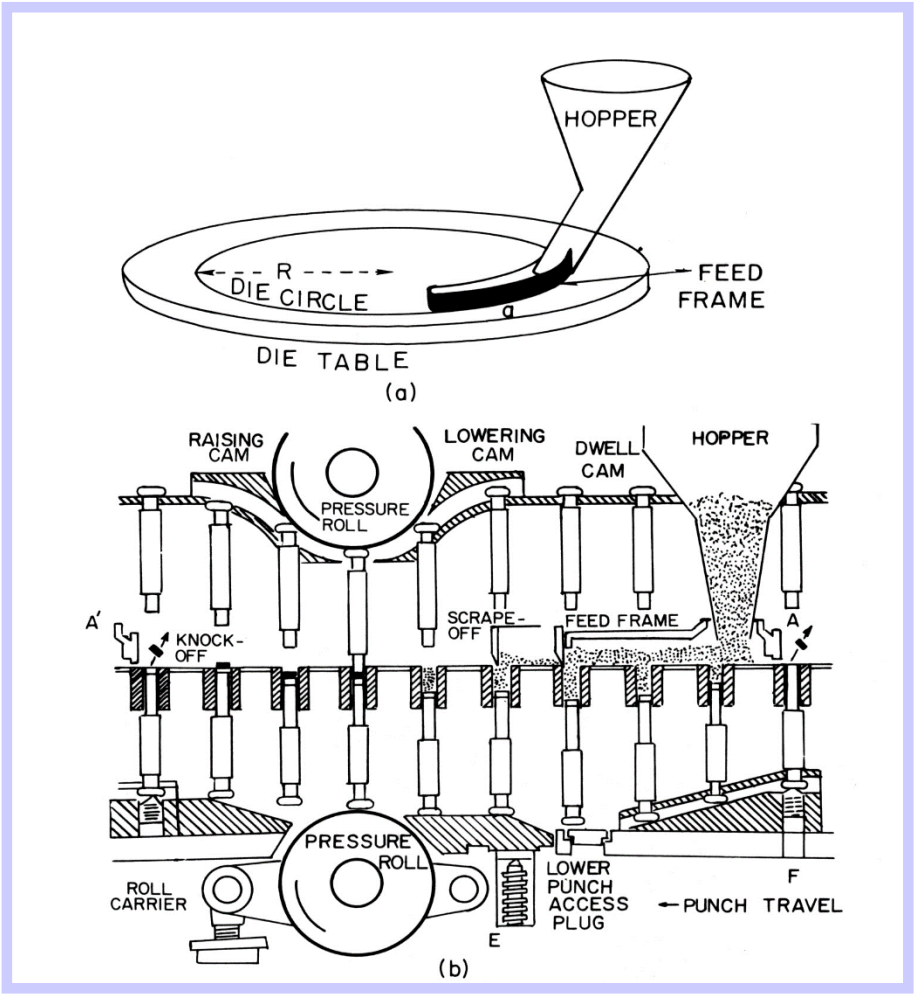

**Hanseaten Exacta 2**

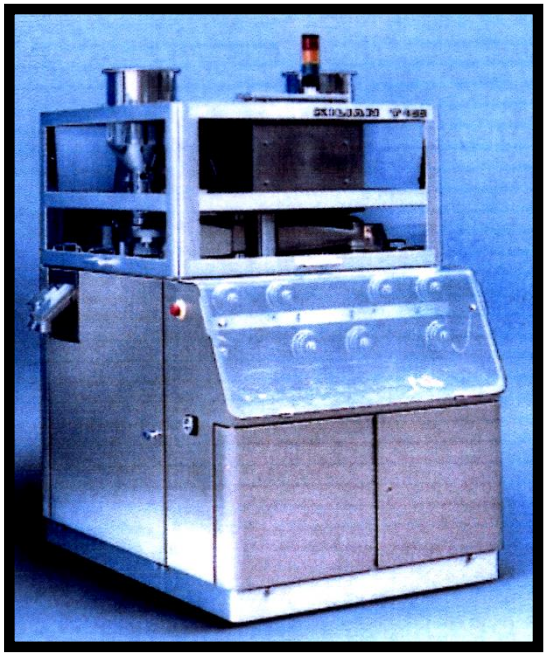


# Rotation tablet machine

## Working scheme

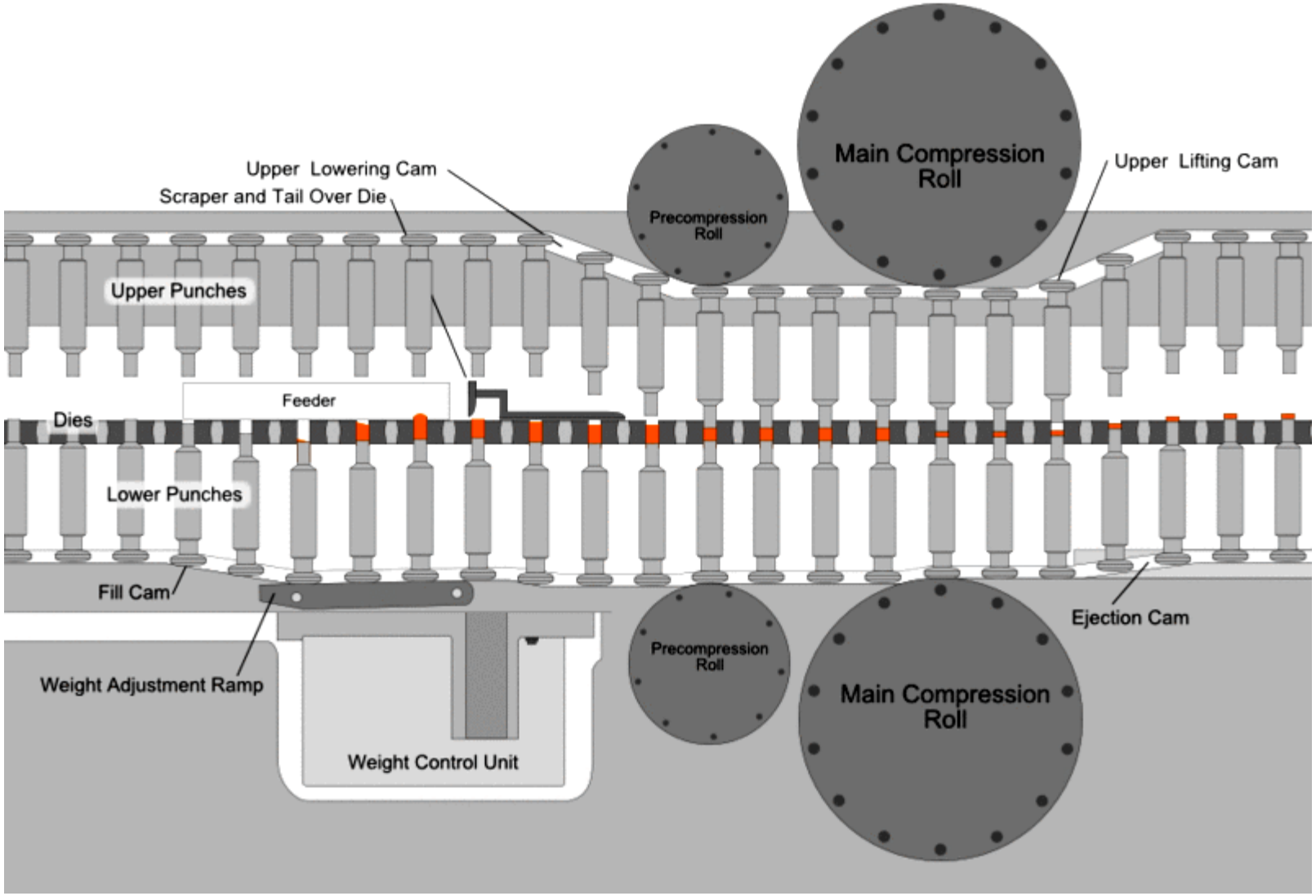
**Continuous working**
**Pressure force is efferted by both punches**
**Funnel is fix**



**Kilian T400**
**900 000 tabl/hour**
**73 punches**

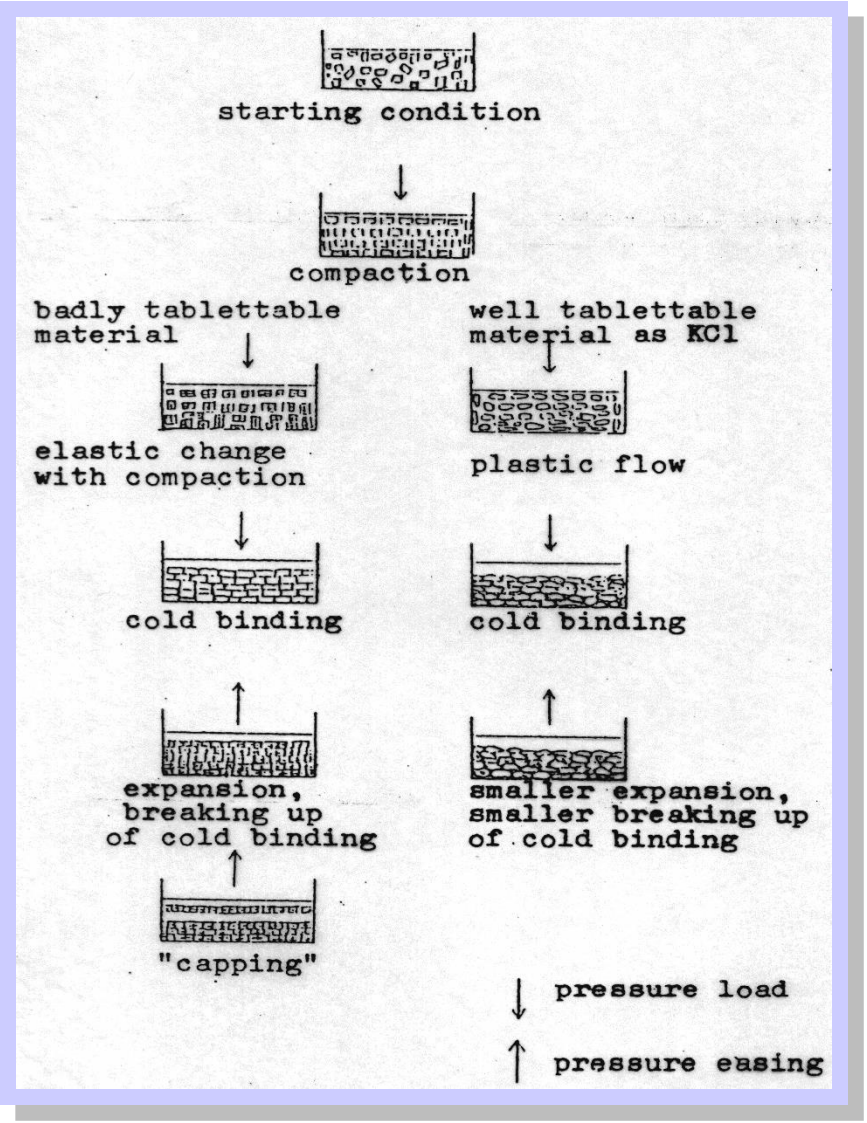
# Working mechanism of rotary tablet machine



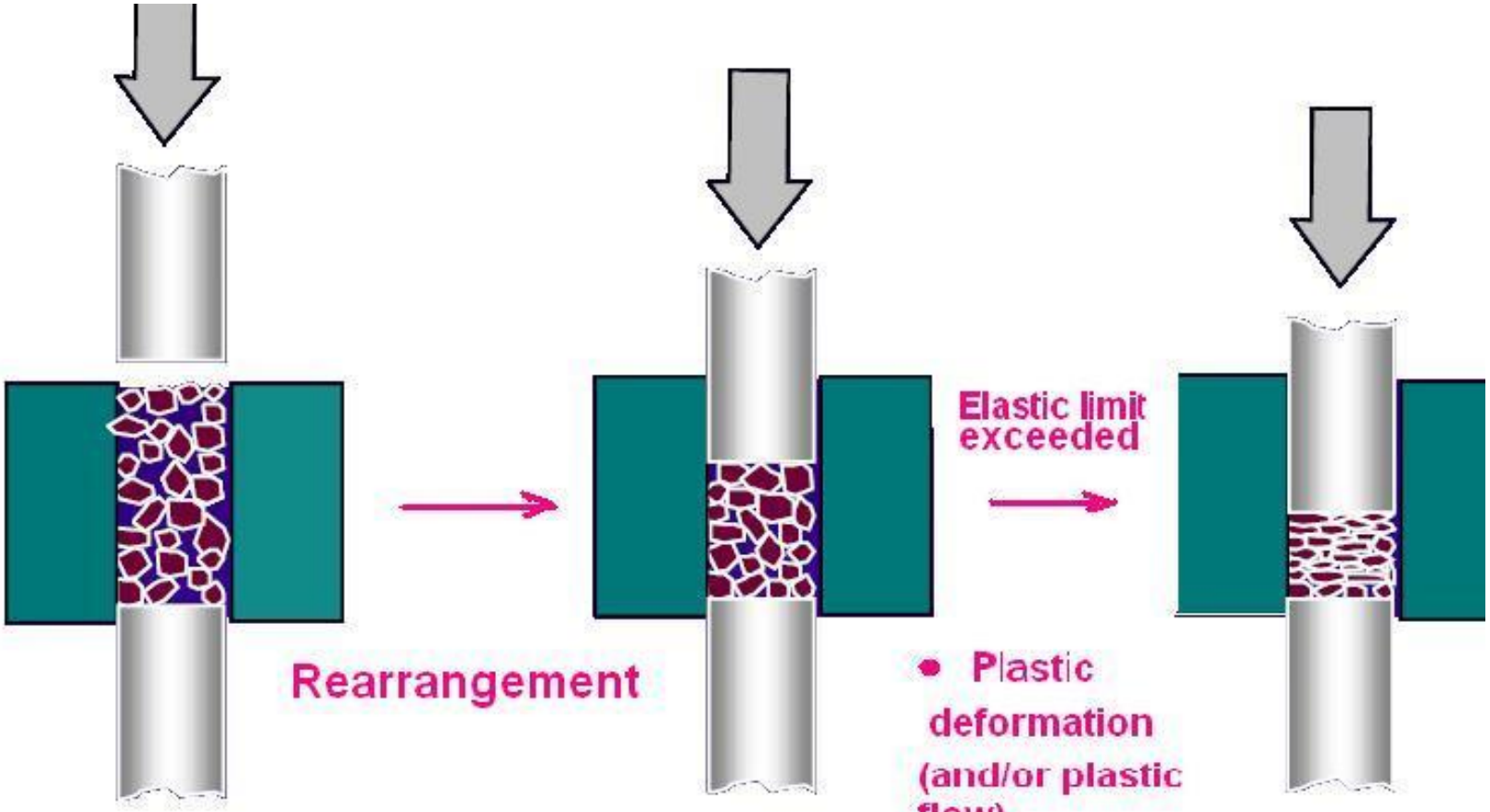
# RONCHI

# Tablet manufacturing

# Deformation during loading



# Stages of compression



# Behaviour of materials

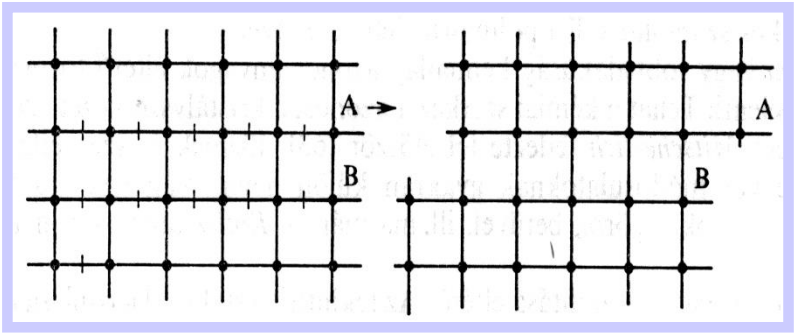
***Plastic materials:*** **when materials are ductile they deform by changing shape (plastic flow).**

**They are two elemetary processes:**

**KCl-comprimate, 5kN**

**1. <u>Mechanical translation</u>:**

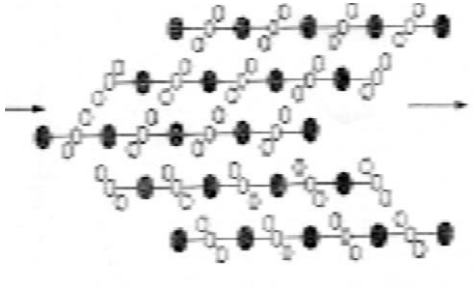
**The parts of the crystals move in parallel in response to external forces, but the connection between the parts of the lattice does not cease.**

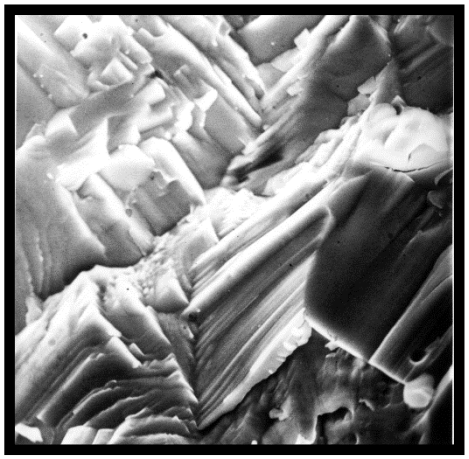


# Behaviour of materials

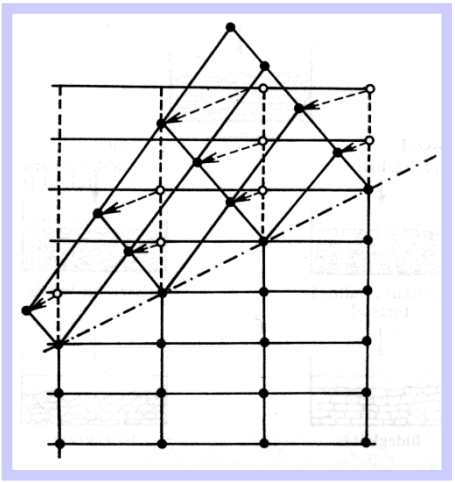
## 2. Twin formation

**The moving of the crystal particles is not parallel, but one part of the crystal jumps into a twin position to another.**



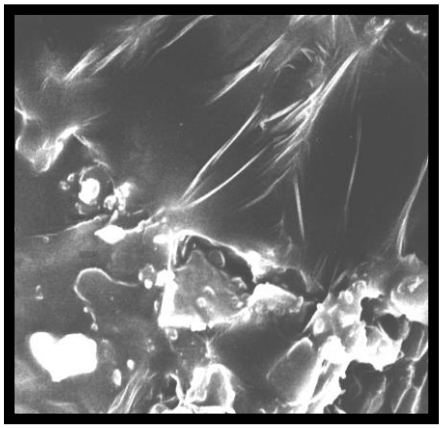


**KCl-comprimate, 10 kN**



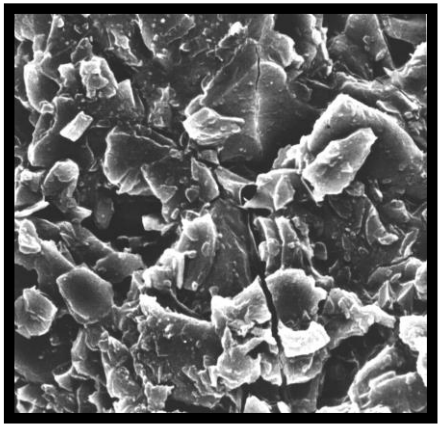
# Behaviour of materials

**Crimping:**
**the common form of plastic deformation.**



*Sulphacetamide sodium compr., 15 kN*

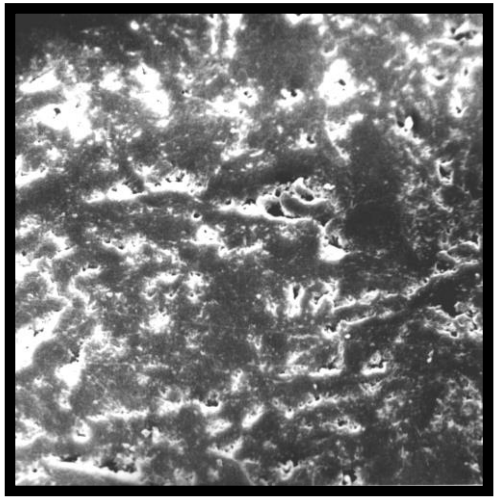
**Breaking:**
**response to mechanical effects, after both plastic and elastic deformation.**



*Sulphathiazole comprimate, 5 kN*

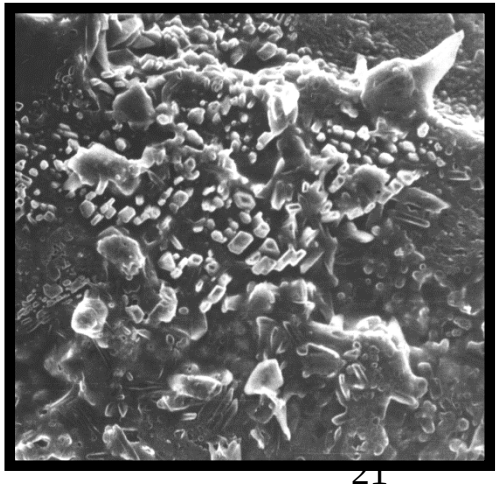
# Behaviour of materials

**Sintering:**
**the thermal properties of the crystal axes are different, orientation with the axis having larger heat conductivity (“hot spots”).**



**Theobromine comprimate, 25 kN**

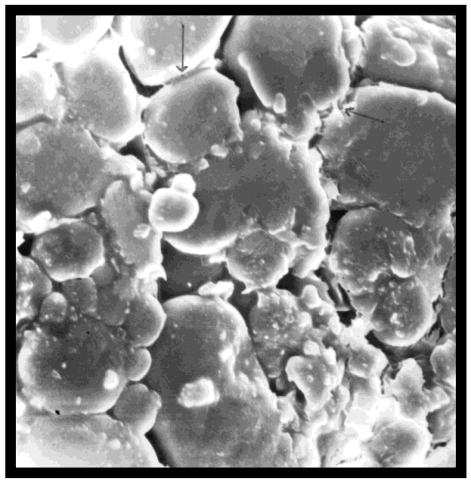
**Recrystallization:**
**very small crystals can formed during elastic recovery after compression maximum.**



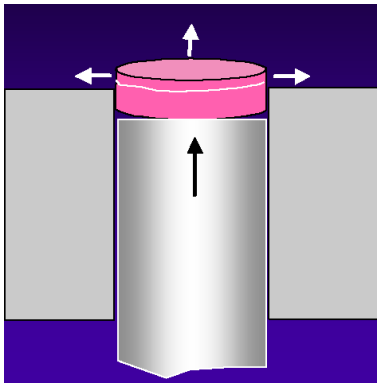
**Barbitone comprimate, 20kN**

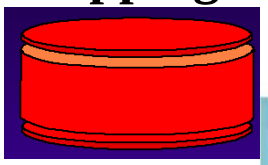
# Behaviour of materials

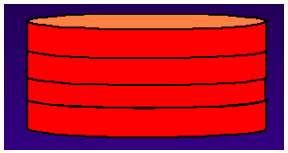
**Elastic behaviour:**
**the deformed crystals strive to regain their original form after pressing. This behaviour causes large internal strain, leading to breaking inside the tablets (lamination or capping).**

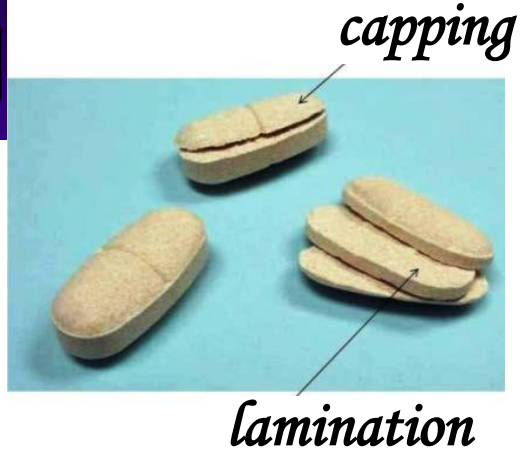


**Placebo tablet, 10 kN**






**Elastic recovery combination with poor bonding**

# *Measurement of compressional force*

- **Compactibility**
- **Instrumentation of tablet machines (strain gauges, displacement transducer)**

  **-Force-curves (Force-time, force-displacement diagrams)**
- **Evaluation of force curves**

  **- Energy distribution**

  **- Deformability, plasticity**

  **- Elastic recovery**

  **- Compressional work**

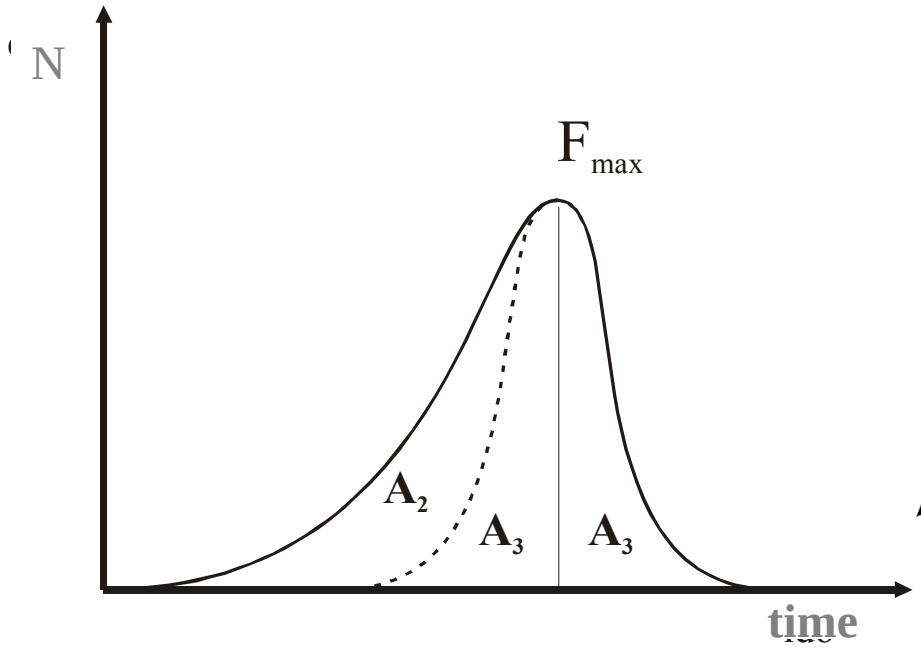
  **- Friction work**

  **- Protocol**
- **Compressibility**

# Possibility of measurement of pressure force

| Force | Tablet machine | |
|---|---|---|
| | eccentric | rotation |
| upper punch force |  |  |
| lower punch force |  |  |
| ejection force |  |  |
| residual force |  |  |
| force on die wall |  |  |
| pushing force |  |  |

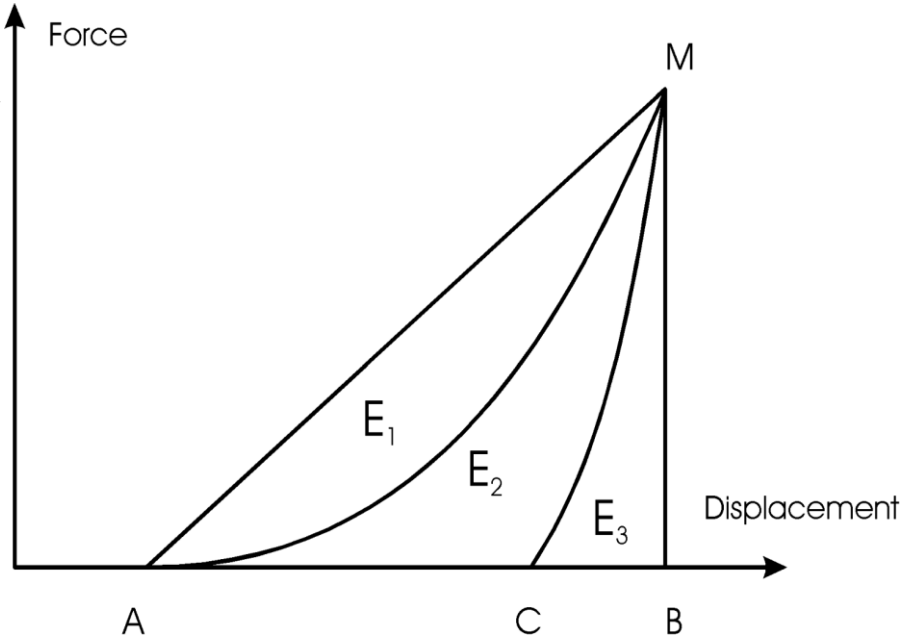
# Compressional curves




*Plasticity (Stamm-Mathis)*

$$Pl_{S-M} = \frac{E_2}{E_2 + E_3} * 100$$

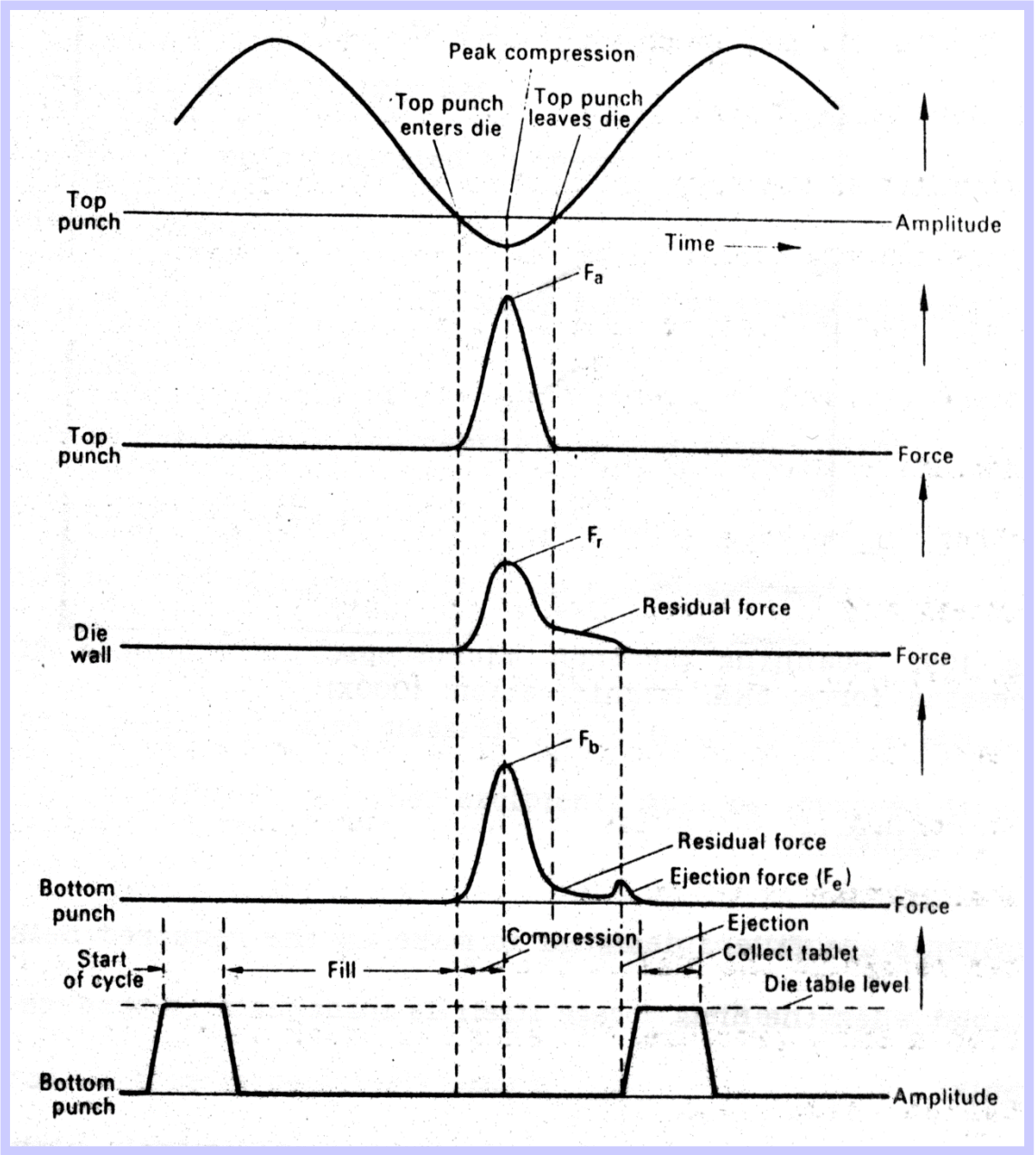
Force-displacement diagram




$$Pl_E = \frac{A_3}{A_2 + A_3}$$

*Plasticity (Emschermann)*

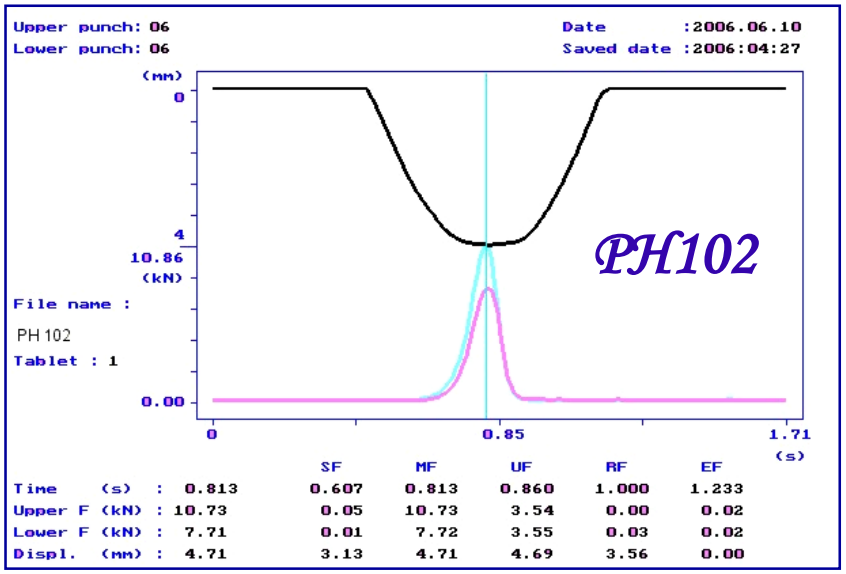
# Force-time diagrams

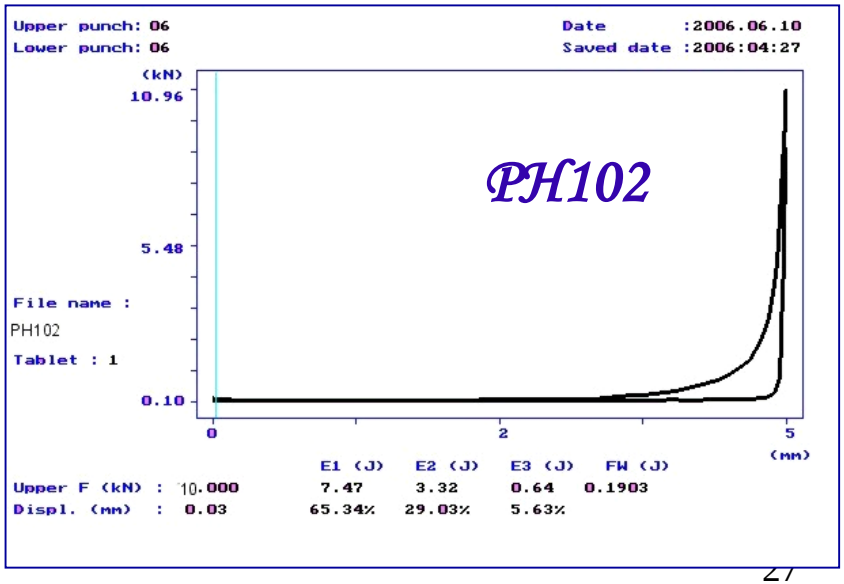


# Excipients

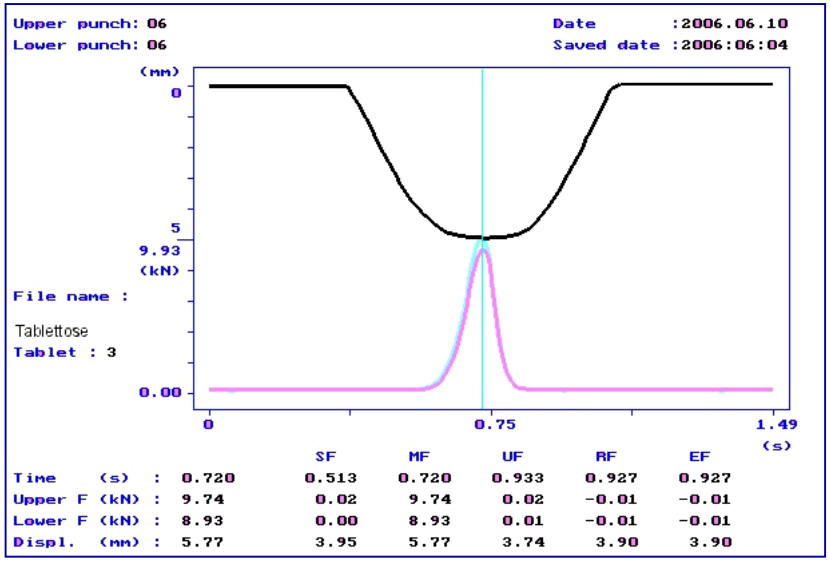
**Microcrystalline cellulose**

**Avicel PH102**

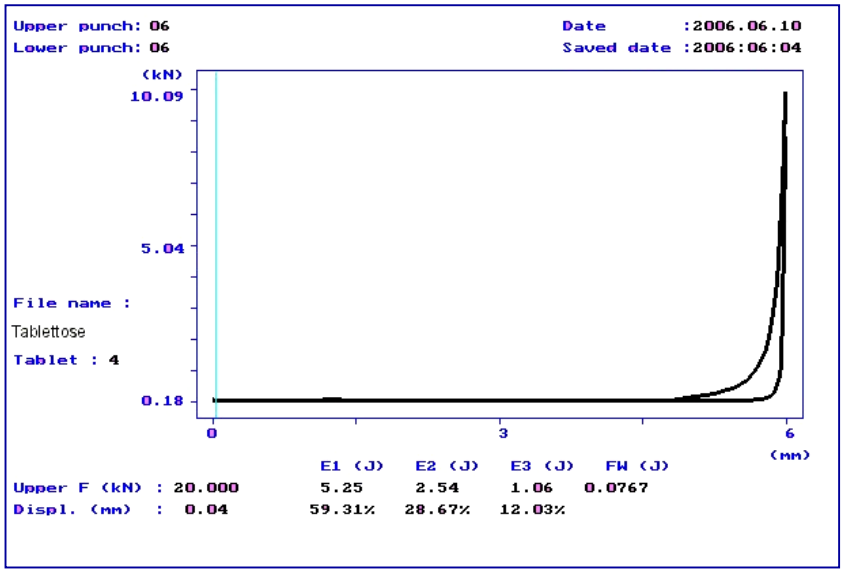


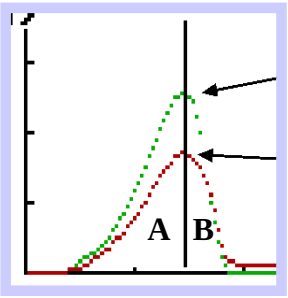
# Excipients




## Tablettose

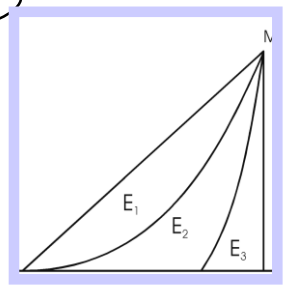


# Calculations




## Distribution of energy

$$ED = \frac{E_2(\%)}{E_1(\%) * E_3(\%)}$$




## Plasticity

$$Pl_2 = \frac{E_2}{E_2 + E_3} * 100$$

**Stamm-Mathis**

$$Pl_1 = \frac{B}{A}$$

**Emschermann**

## Friction work

$$FW = \int_{s_0}^{s_m} \left\{ F_{up} - \left[ \left( F_{up} - F_{lo} \right) / ln \frac{F_{up}}{F_{lo}} \right] \right\} * ds$$

## Usefull work

$$W_{use} = W_{eff} - W_{fw}$$

## Lubrication coefficient

$$R = \frac{F_{lo}}{F_{up}}$$

$$U_1 = \frac{F_{up} - F_{lo}}{F_{die\ wall}}$$ (static)

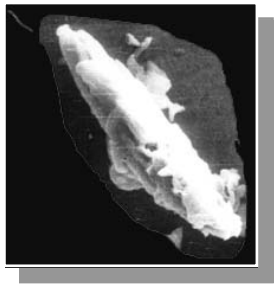
$$U_2 = \frac{\text{ejection force}}{\text{residual force on die wall}}$$ (kinetic)

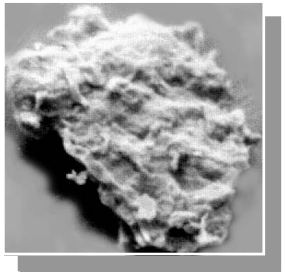
# *Compressibility value*

$$\mathrm{Pr}_{(mass)} = \frac{\sigma_x}{W_{spec}} = \frac{\sigma_x}{E_2 / m} \left[ \frac{\mathrm{Pa}}{\mathrm{J \cdot kg^{-1}}} \right]$$

$$\sigma_x = \frac{2H}{\pi \cdot d \cdot h}$$

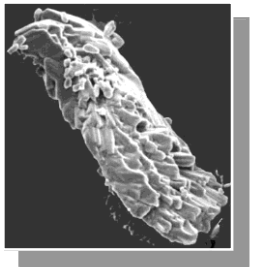
# *Compressibility value*

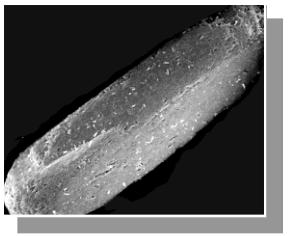


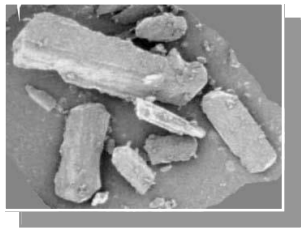


| *Celluloses* | | *Pl (%)* | *$Pr_{(mass)}$ ($Pa/Jkg^{-1}$)* |
|---|---|---|---|
| *Avicel PH101* | | *95.08* | *144.30* |
| *Avicel PH301* | | *98.28* | *93.76* |
| *Avicel PH302* | | *97.80* | *93.99* |
| *Vivapur 101* | | *94.64* | *>> 406.30* |
| *Vivapur 102* | | *93.17* | *378.32* |
| *Vitacel M80* | } microfine | *82.98* | *84.21* |
| *Vitacel A300* | | *80.09* | *32.54* |

# *Compressibility value*

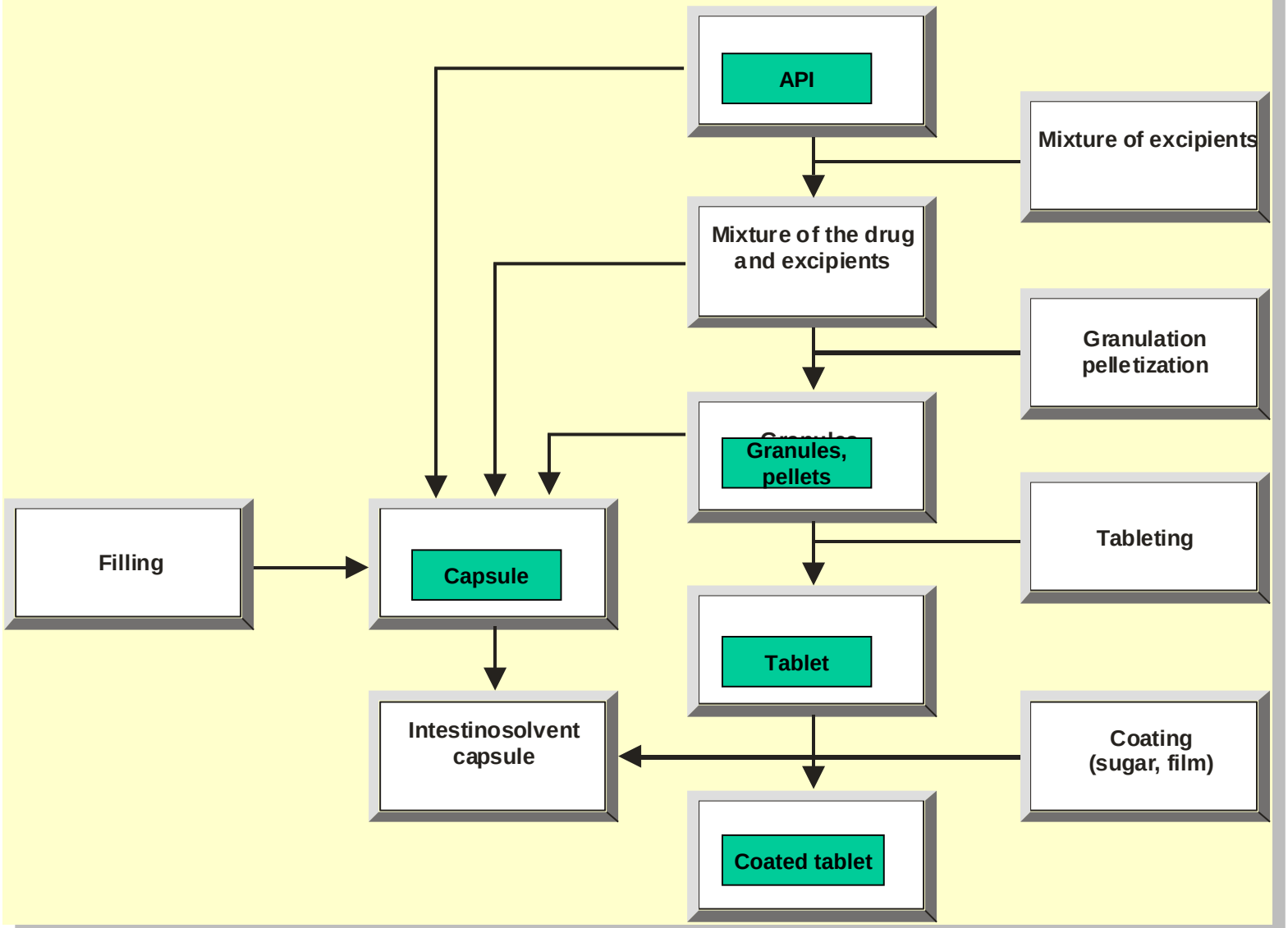


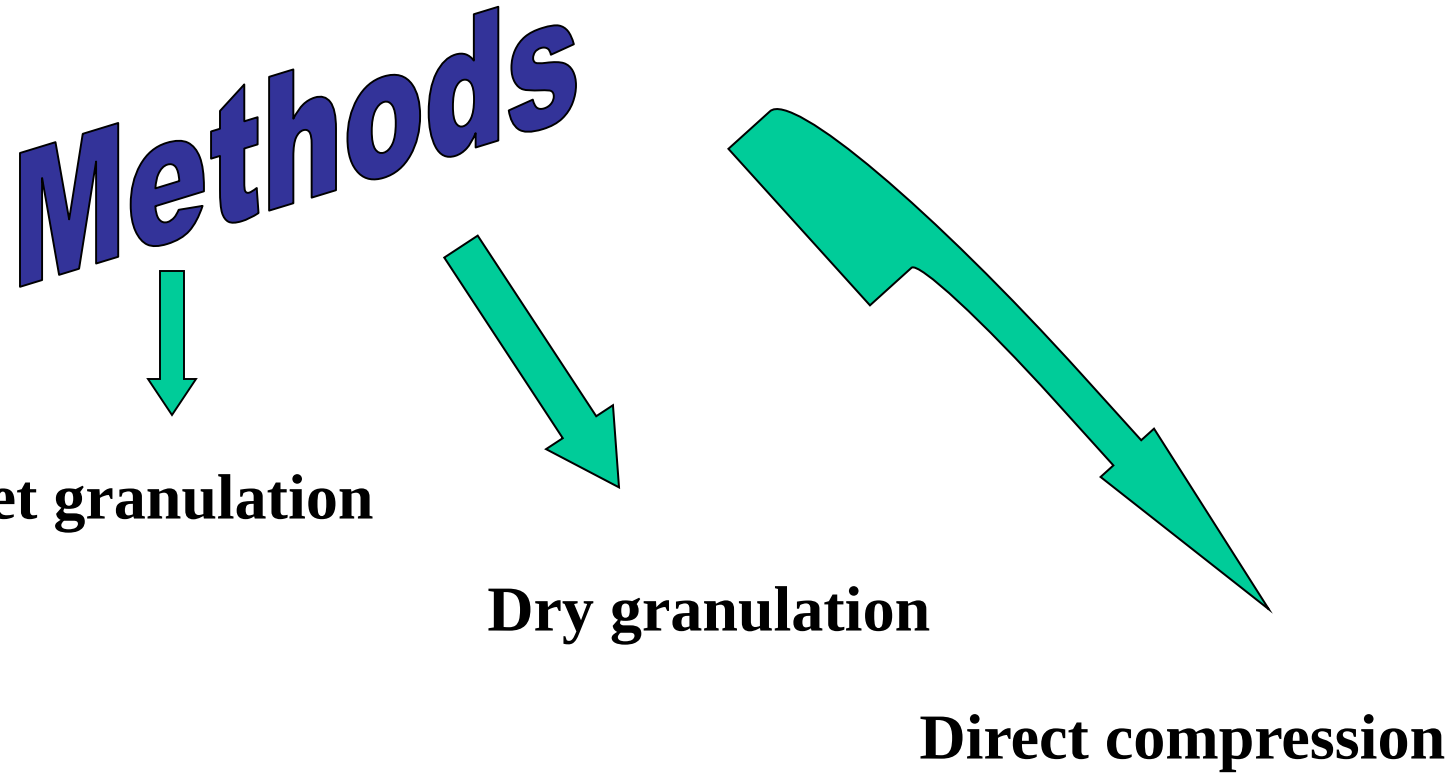




| *APIs* | *$Pr_{(mass)}$ ($Pa/Jkg^{-1}$)* |
|---|---|
| *Phenobarbitone* | *47.71* |
| *Pyridinolcarbamate* | *129.13* |
| *Acetylsalicylic acid (ASA)* | *76.94* |
| *$\alpha$ – methyldopa* | *n.m.* |
| *Dimenhydrinate* | *n.m.* |

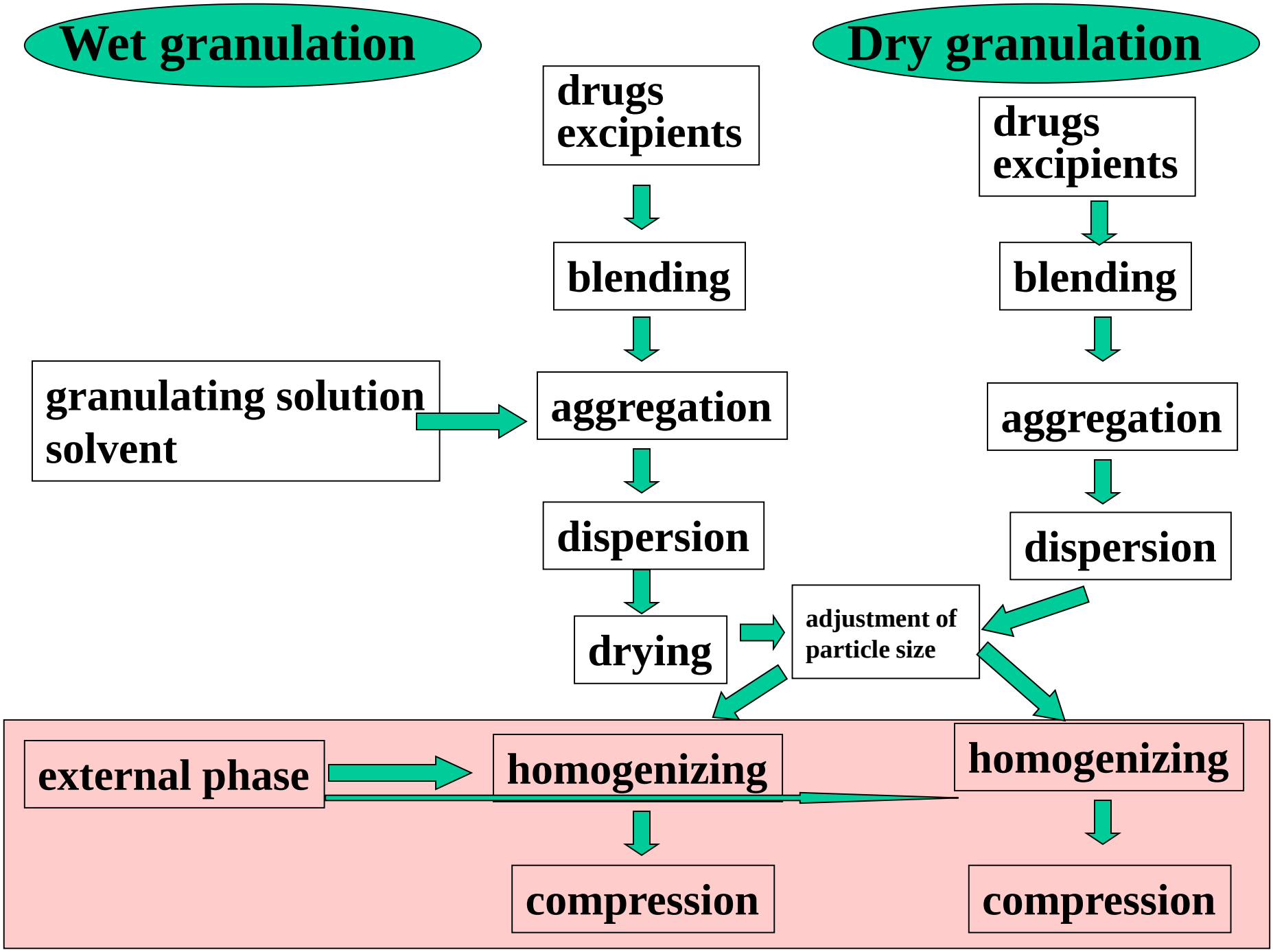
# Development of a solid dosage form






**Preparing methods**

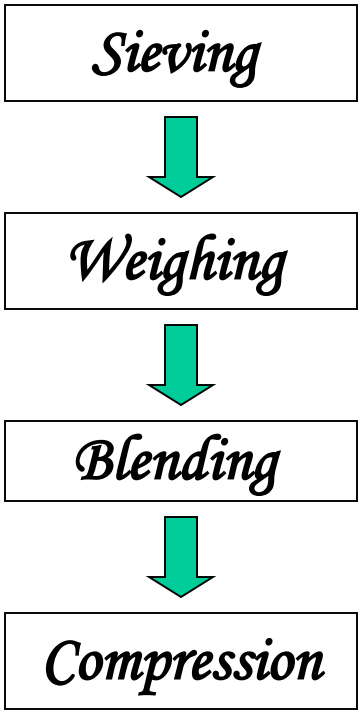
- **Grinding**
- **Sieving**
- **Blending**


Wet granulation
drugs excipients
blending
granulating solution solvent
aggregation
dispersion
drying
Dry granulation
drugs excipients
blending
aggregation
dispersion
adjustment of particle size
external phase
homogenizing
compression
homogenizing
compression

# Direct compression

*"The most obvious advantage of direct compression is economy"*

*Prof. Shangraw*




- *reduced processing time*
- *reduced labor costs*
- *fewer manufacturing steps*
- *fewer pieces of equipment*
- *less process validation*

# Excipients

## Requirements

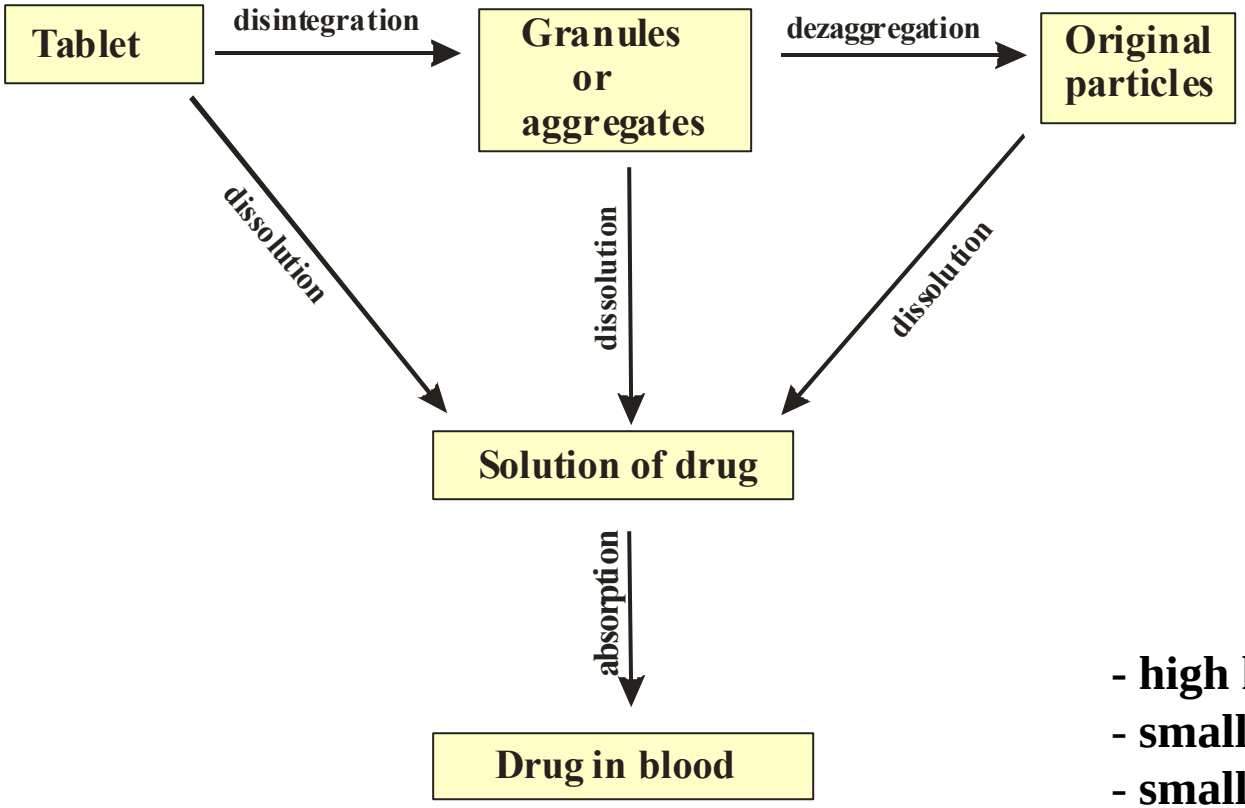
- **nontoxic, physiological inert**
- **free of any unacceptable microbiologic “load”**
- **physically and chemically stable**
- **colourless, odourless, tasteless**
- **obtainable, acceptable cost**

# Excipients

## Grouping

**Diluents*** **(amount of API is very small)**
**Disintegrants*** **(the tablets should disintegrant to small particles)**
**Binders***
**Adsorbents**
**Humectants**
**Hydrophilizing materials**
**Agents retarding dissolution**
**Glident***
**Lubricants***
**Antiadhesive materials***
**Antistatics***
**Colours, flavours, sweeteners**

# Role of disintegrants



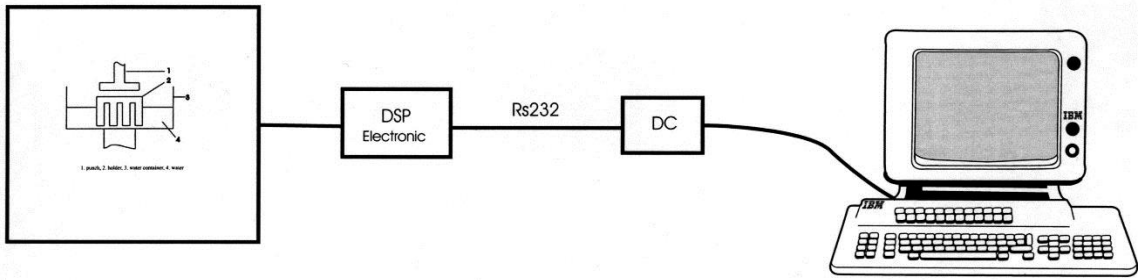

**Requirement**

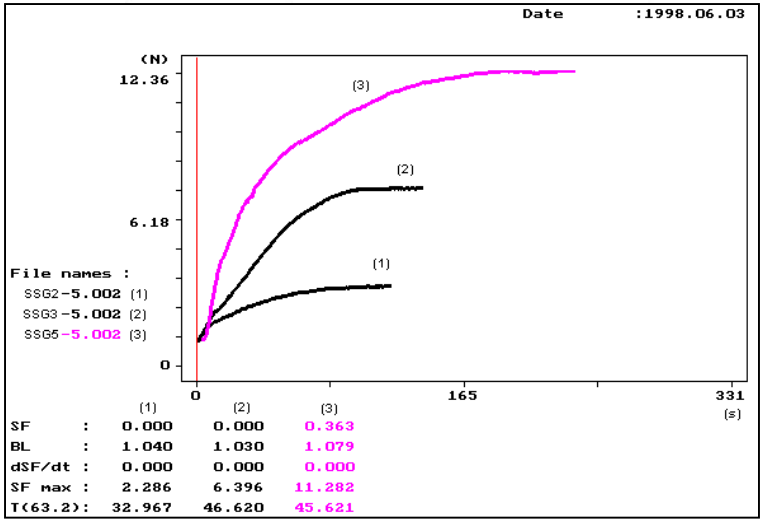
- **high hydratation into the tablet**
- **small solubility**
- **small geling properties**
- **high binding in tablet**
- **good flowability**
- **good compressibility**

# Mechanism of disintegration

- swelling force
- wicking effect
- adsorption heat during wetting
- gas forming

# Measurement of swelling force



# Excipients

## Grouping

**Diluents***

**Disintegrants***

**Binders*(facilitate the compression, support of good hardness)**

**Adsorbents**

**Humectants**

**Hydrophilizing materials**

**Agents retarding dissolution**

**Glident***

**Lubricants***

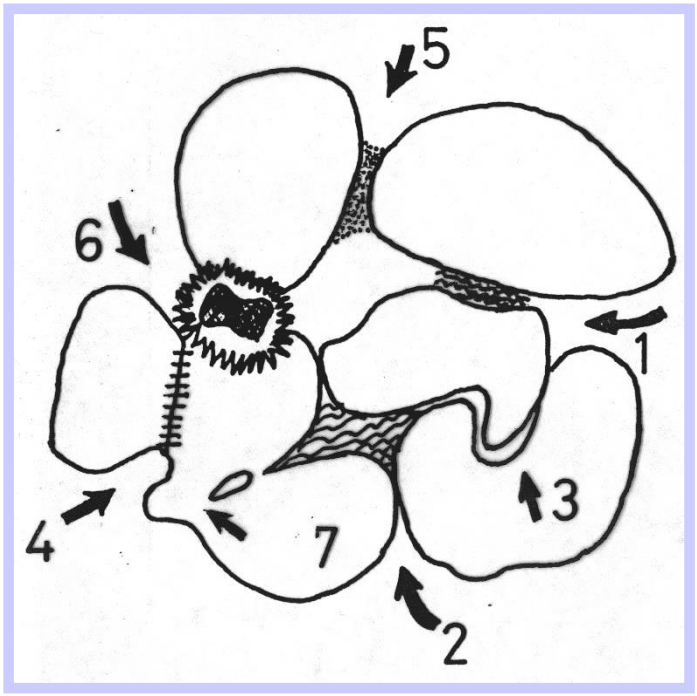
**Antiadhesive materials***

**Antistatics***

**Colours, flavours, sweeteners**

# Pressing of Solid Particles Compressibility and Process

## *Binding mechanisms*




1. Liquid bridges
2. Capillary forces in the cavities full with liquid
3. Structure-closing linkages
4. Dispersion forces
5. Hardening binders
6. Crystallization of dissolved material
7. Sinter-bridges, cold binding

# Texture of tablets

- solid coherent system
- fixed solid particles
- pores among them

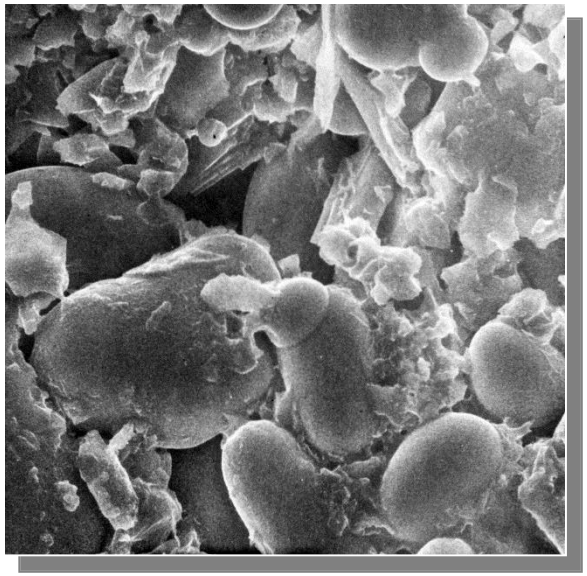
**Characteristic of texture:**

- surface area
- porosity, distribution of pores

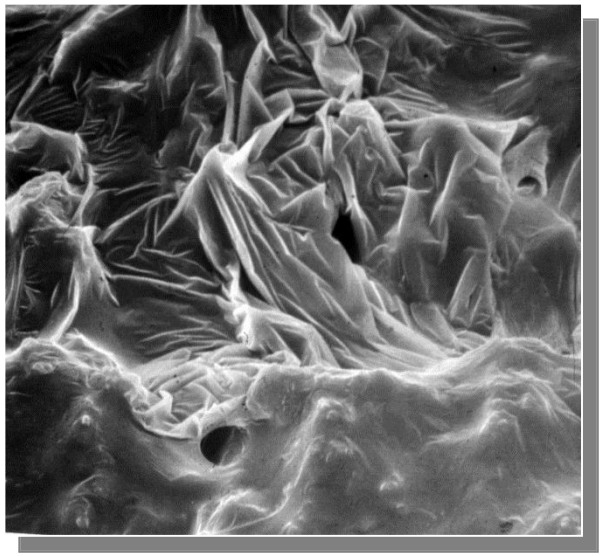
# Hardening binders

Surface

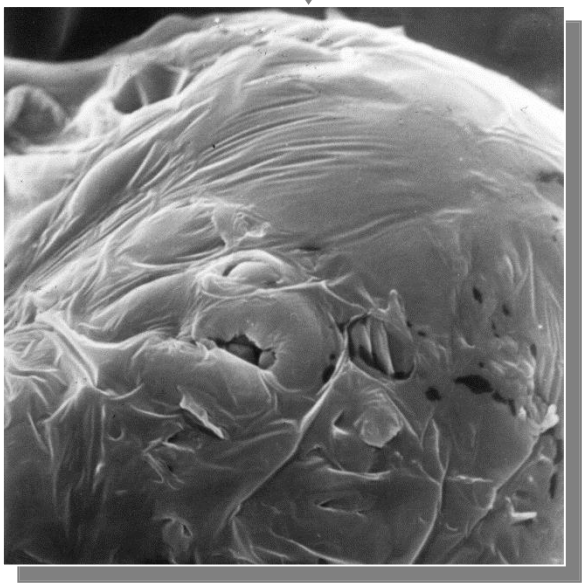
Breaking surface



**Szulfacetamid sodium tablet**
**Binder: Polyvidon**
**Pressure force: 10 kN**



**Furosemid tablet**
**Binder: Klucel MF**
**Pressure force: 10 kN**

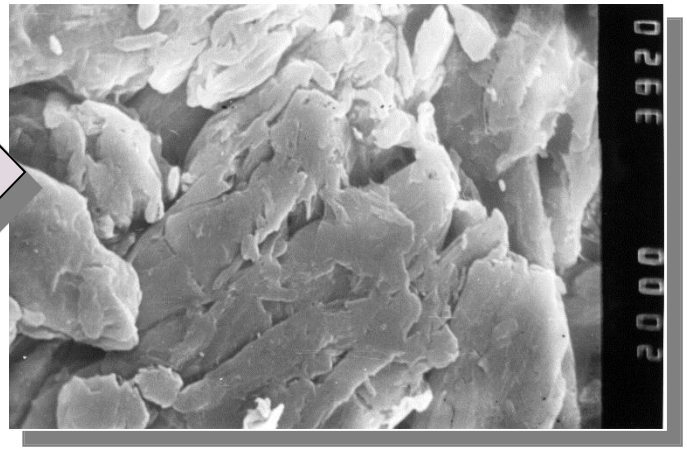


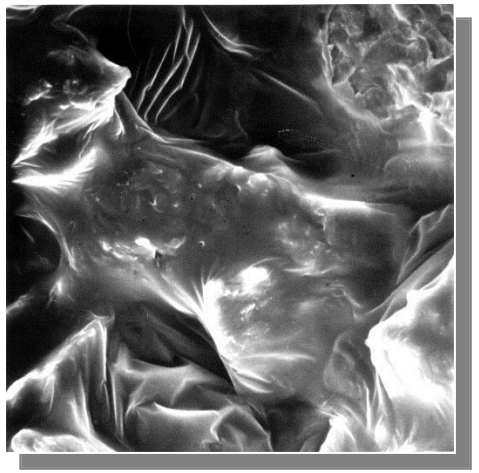
**Szulfacetamid sodium tablet**
**Binder: Modocoll**
**Pressure force: 10 kN**

# Structure-closing linkages

Mechanical interconnection: form-closing bindings

Avicel PH 102
2 kN

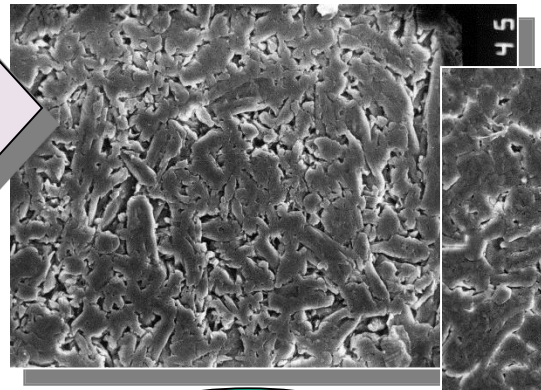




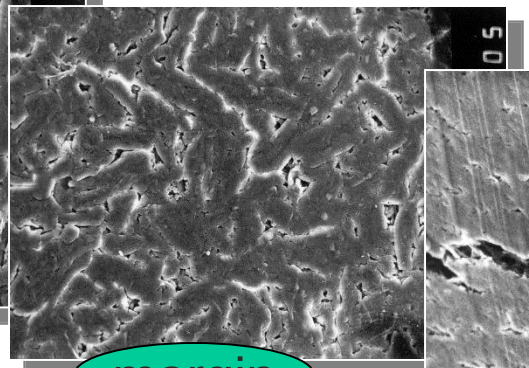
KCl + Avicel PH 101
10 kN

Avicel PH 101
25 kN

surface

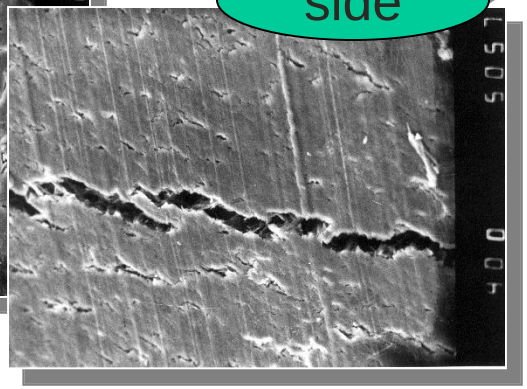


middle



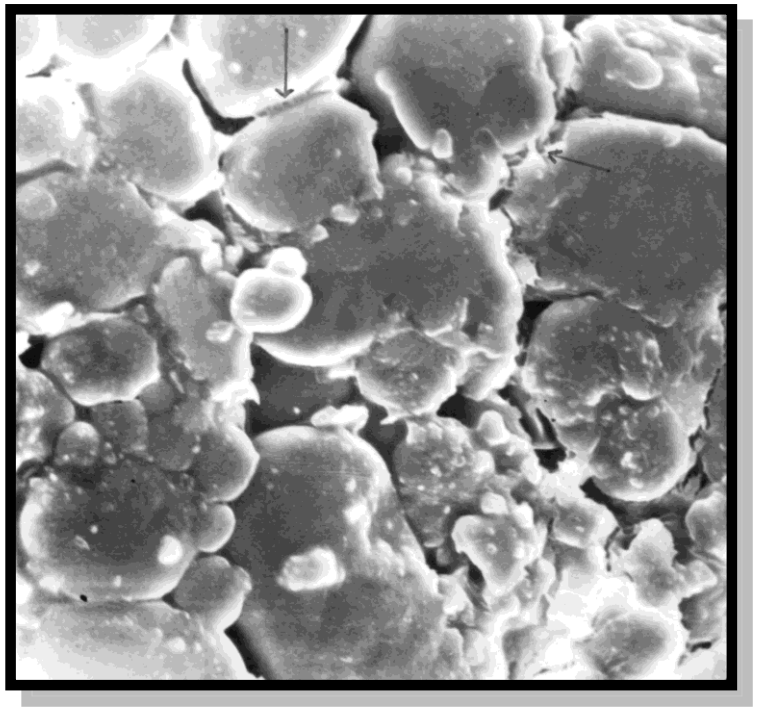
margin

side

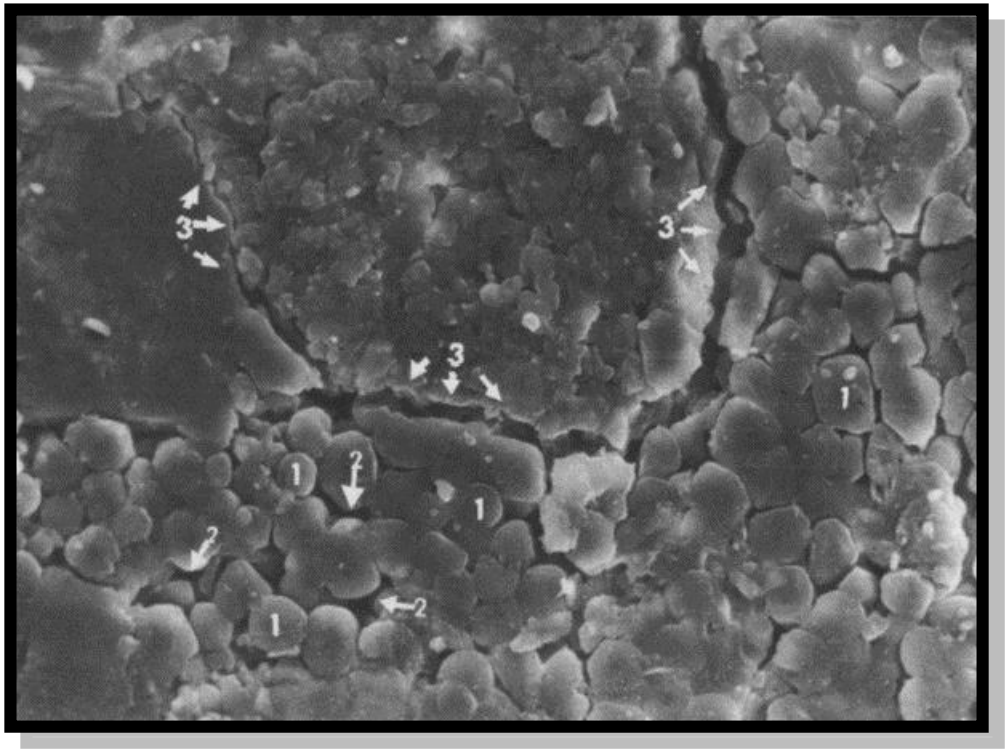


# Type of pores

## Primer pores



## Secunder pores




*1, 2 = primer pores*
*3= secunder pores*

# Excipients

## Grouping

**Diluents***
**Disintegrants***
**Binders***
**Adsorbents** (e.g. API is fluid, or eutectic is forming)
**Humectants** (to insure the suitable moisture content)
**Hydrophilizing materials** (to increase the wettability of the tablet)
**Agents retarding dissolution** (e.g. buccal or sustained release tablets)
**Glident*** (to increase the flowability)
**Lubricants*** (to decrease the friction and sticking)
**Antiadhesive materials*** (to decrease the adhesion to the punches)
**Antistatics*** (to decrease the static charge)
**Colours, flavours, sweeteners** (to correct the unpleasant taste or smell, or distinction the tablets)

# Influencing factors on the physical parameters

*CTD (Common Technical Documentation)*

**Material factors:** quality of substances
shape parameters of particles
particle size

**Machine factors:** compressional force
compressional speed
type of tablet machine
condition of punches

**Preparation condition:** composition
technology
storage condition

# Influence of some important factors on the compression

1. Crystal structure
2. Morphology
3. Flow properties
4. Quality and quantity of binder
5. High pressure force
6. Speed of pressing
7. Mechanism of compression
8. Moisture of material
9. Relative air humidity
10. Condition of punches and dies

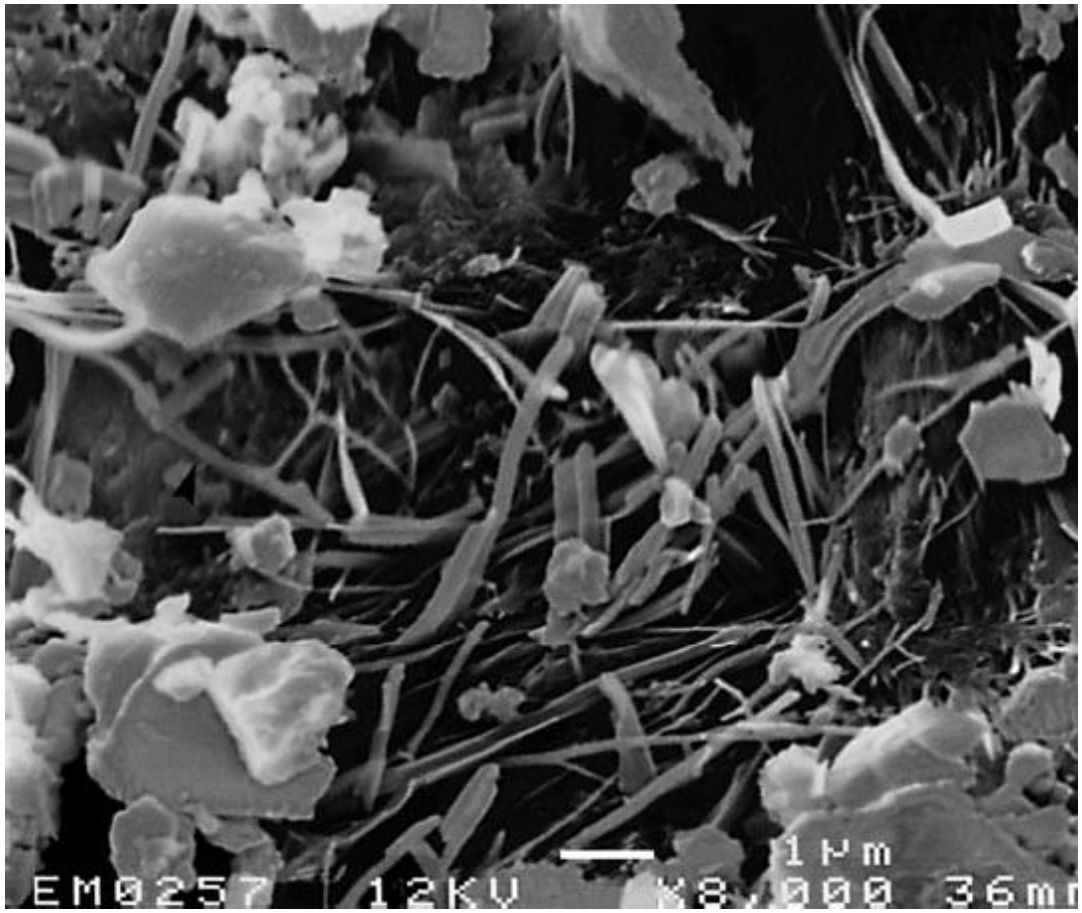
# Problems during tableting

1. Abnormal noises in the tableting press
2. Sticking and adhesion to the punches
3. Capping and lamination
   - crystal system
   - too lot of fine powders
   - little amount of binder
   - too little moisture
   - too high or shock pressing
   - worn surface of punches
   - air
4. Small mechanical hardness
5. Long disintegration time
6. High mass deviation

# In process control (IPC)

| Product (intermedier) | Critical parameters |
|---|---|
| Drug | Particle size (distribution) |
| Powder mixture | Homogeneity, moisture content |
| Granule | Particle size, moisture content, content uniformity, homogeneity, density (loose, tapped), flowing time |
| Tablet | Mass uniformity, strength (breaking , friability), height, disintegration time, assay, content uniformity, dissolution, microbiological purity (E. coli, Staphylococcus aureus, Pseudomonas aeruginosa, mushroom, pathogen mikroorg.) |

# *Thank you for your attention!*




**Fungi threads on the surface of vitamin C tablets**