* بداية الفيديو الثالث - سلايدات 71-95

* high friction وجود لـ ممكن بسبب إنه نوعية سيئة lubricant أو كمية قليلة

Tablet excipients

Lubricants

- Besides reducing friction lubricants may cause undesirable changes in the properties of tablets:

1. The presence of a lubricant in a powder is thought to interfere negatively with the **bonding** between the particles during compaction, and thus reduce tablet strength. → بتقلل mechanical strength للتابلت

2. Because many lubricants are hydrophobic, tablet disintegration and dissolution are often retarded by the addition of a lubricant (Mixing time and mixing intensity and the amount of lubricant are important in this context)

Stearate derivatives ← Mg stearate حكينا

* أحسن واحد فيهم بوظيفة قليلة (حتى ومنه)

ما بنستغني عنه نهائياً in solid dosage forms

بيعمل كتير خاصة ejection بخطوة

هاي المشكلة بتصير بسبب إنه mixing time طويل أو عالية intensity (high speed)

* ممكن يكون في blend من أكتر من نوع lubricant (نوعين أو 3 مثلاً) لو في واحد عنده آثار سلبية فبنقلل من كميته وبنضيف واحد تاني كمان

أو حطينا منه كمية كبيرة فصار dissolution الـ hydrophobic surface فعمل

Tablet excipients

- Lubrication is achieved by mainly two mechanisms:

a) fluid lubrication

– A layer of fluid is located between and separates moving surfaces from each other.

– Fluid lubricants are **seldom** used in tablet formulation

– Example is paraffin oil.

* usually spraying بعمله

soft capsules لـ بنستعملها بال

(عالفصل التاني تفاصيلها)

Tablet excipients

b) boundary lubrication common in powder/solid lubricant

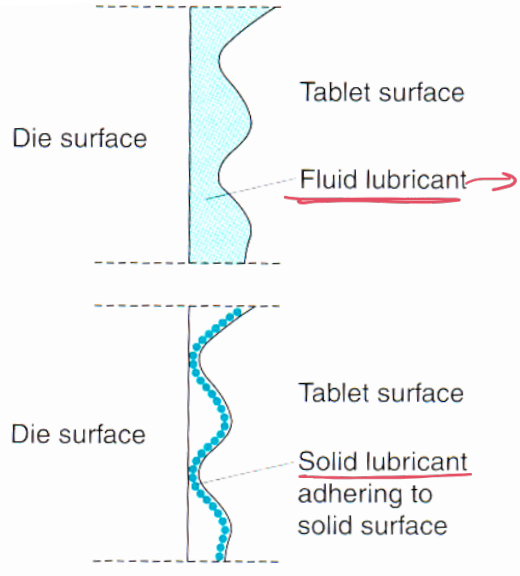
– A thin film of powder separates moving surfaces from each other.

– A number of mechanisms have been discussed including that lubricants are substances showing a low resistance towards shearing. → moving between two surfaces

shear يقلل
less friction
حركة أسرع وأسهل
ejection أسرع

- Examples: Stearic acid and its salts (e.g. Mg stearate is the most widely used lubricant), sodium lauryl sulphate, sodium stearyl fumarate. glyceryl behenate, sodium benzoate and PEG. ٧٣

surfactant



ما عادت تستخدم حالياً لـ tablets

هاد اللي بستخدم لـ tablet

Fig. 31.8 Schematic illustration of lubrication mechanisms by fluid and boundary lubrication. ٧٤

Tablet excipients

Anti-adherent

- These are materials intended to reduce sticking or adhesion of the powder to the punches or die wall.
- Many lubricants such as magnesium stearate have also anti adherent properties.
- However, other substances with limited ability to reduce friction can also act as antiadherents such as talc and starch.

used in gloves

٧٥

Tablet excipients

Sorbents

adsorption : surface phenomena

- These are substances that are capable of sorbing some quantities of fluids in apparently dry state.
- They are used for incorporation of oils or fluid extracts into the tablets.

active ingredient : liquid

زي مثلاً Vitamin E

ممكن يبجي tablet

أو fish oil

- Examples: Microcrystalline cellulose, silica, kaolin, bentonite and magnesium carbonate

زي هدول

adsorbent لكي بدنا نخزن مزيج tablet بنضيف عليه

فالمادة الـ oily (liquid) بتنضاف عهدول المواد وبتمتصها فبتكون tablets

٧٦

Tablet excipients

Colors

- Colors are added to the tablets for the following reasons:
  1 – Elegancy
  2 – To help the patient to distinguish the product
  3 – To provide control during manufacturing
  4 – To help in hiding color differences between drug and additives
- Colorants are added to uncoated tablets either as an insoluble powder or dissolved in the granulation liquid in case of wet granulation.
- Care should be taken in wet granulation as migration of soluble color may occur during drying.

Tablet excipients

Colors

- Many synthetic dyes were decertificated because of their carcinogenic effect.
- Natural vegetable colors are limited and they are often unstable.
- In the United States, FD&C numbers (which indicate that the FDA has approved the colorant for use in foods, drugs and cosmetics) are given to approved synthetic food dyes that do not exist in nature, while in the European Union, E numbers are used for all additives, both synthetic and natural, that are approved in food applications.
- Lakes are dyes that have been absorbed on a hydrous oxide and usually are employed as dry powders

* مجموعة sweeteners على شكل

Tablet excipients

chewable & effervescent tablets خاصة عند

Flavors and sweeteners → glucose, fructose, sucrose, ... etc. or synthetic (i.e: aspartam)

orange, lemon, pepperiment ↓ بتتكون من volatile oils ↓ فبتكون thermolabile (heat unstable) طبيعية

- Flavors are incorporated in a formula to give a tablet a better taste or to mask unpleasant taste.
- Flavors are often thermolabile and so cannot be added prior to operations involving heat. بنضافوا بعد drying عشان ما يتعرضوا لحرارة
- Flavors are usually used in effervescent, chewable tablets and other tablets intended to dissolve in the mouth.

٧٩

Tablet testing

لازم يتعمل عشان registeration file تتبع الدواء

official ⇒ pharmacopeial / compendial

non official ← تست في الفارماكوبيا

① *Uniformity of content of active ingredient*

- In practice, small variations between individual preparations are accepted and the limits for this variation are defined as standards in the pharmacopoeias. (حسب سنة الإصدار للفارماكوبيا) ← ممكن يكون official وممكن يطلّب لبس المصانع بتعمله
- Uniformity of dose is tested in two separate tests: uniformity of weight and uniformity of content of active ingredient.

supportive data عشان يكون أسهل تسجيل ملف الدواء

* official ← ① Content uniformity (active) ② disintegration test ③ dissolution test — دائماً لازم يتعملوا

Tablet testing

1 ***Uniformity of content of active ingredient***

- The test for uniformity of weight is carried out by collecting a sample of tablets, normally 20, from a batch and determining their individual weights.

- First: The average weight is calculated.
- Calculate average and SD
- The samples complies with the standards if the individual weights do not deviate from the mean more than is permitted in terms of percentage.
- Second: Check content uniformity

٨١

Tablet testing

Uniformity of content of active ingredient

- The test for uniformity of drug content is carried out by collecting a sample of tablets , normally 10, and determination of the amount of drug in each.

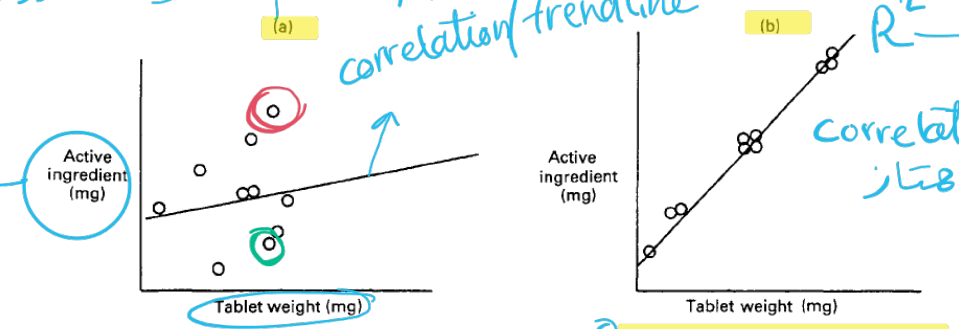
- The average drug content is calculated and the content of the individual tablets should fall within a specific limits in terms of percentage deviation from mean.

٨٢

* الوزن بالأحمر وبالأخضر تقريبًا نفسه لكن حرفة أعطاني إنه الحبة فيها كتير active ingredient وحرفة أعطاني إنه فيها كمية قليلة

عشان هيك صعب أعمل correlation بين وزن الحبة وكمية الدواء فيها لو كان دواء عيار قليل (potent drug)

افتراض إنه لو أخدت وزن content معين رح يعطيني معين من الدواء هو افتراض خاطئ



R^2 correlation/trendline

R^2 correlation ممتاز

بالحبة الوحدة

Fig. 27.18 Correlation between amount of active ingredient and tablet weight for (a) a low dose (drug content 23% of tablet weight) and (b) a high dose (drug content 90% of tablet weight) tablet. (From Airth, J.M., Bray, D.F., and Radecka, C. (1967). J. Pharm. Sci., 56, 233–235.

الرسم حفظ

antibiotic مثلاً

500 mg
750 mg
⋮

(correlation potent drug أعلى)

٨٣

linear regression ← كلما كان أعلى كلما كان أوقع

---

if dose is high ← بعمل WV: weight variation
if dose is low ← CU: content uniformity

الجدول الأخير حكت حفظ

Tablet testing

Solid oral drug products:

d) Uniformity of dosage units:

<905> UNIFORMITY OF DOSAGE UNITS (USP monograph)

Table 1. Application of Content Uniformity (CU) and Weight Variation (WV) Tests for Dosage Forms

Dosage Form	Type	Subtype	Dose & Ratio of Drug Substance: ≥25 mg and ≥25%	Dose & Ratio of Drug Substance: <25 mg or <25%
Tablets	Uncoated		WV	CU
	Coated	Film	WV	CU
		Others	CU	CU
Capsules	Hard		WV	CU
	Soft	Suspension, emulsion, or gel	CU	CU
		Solutions	WV	WV
Solids in single-unit containers	Single component		WV	WV
	Multiple components	Solution freeze-dried in final container	WV	WV
		Others	CU	CU
Solutions in unit-dose containers and into soft capsules			WV	WV
Others			CU	CU

مثلاً sugar-coated

٨٤

< 25 mg or < 25% → graph a

≥ 25 mg or ≥ 25% بتنطبق عليه graph b في السلايد السابق

Tablet testing

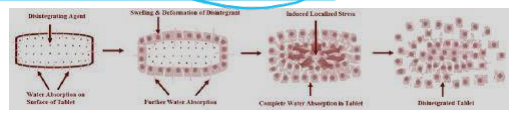
② *Disintegration* compendial test

- The drug release process from immediate release tablets often includes a step at which the tablet disintegrates into smaller fragments.
- In order to assess this, disintegration test methods have been developed and examples are described as official standards in the pharmacopeias.
- The test is carried out by agitating, in a disintegration apparatus, a given number of tablets in an aqueous medium at a defined temperature.
- Disintegration test gives an idea but does not necessarily guarantee acceptable drug release.

لو enteric بيكون disintegration في الأمعاء (بعد المعدة)

تست إجباري

والها تست كامل اللي هو dissolution



٨٥

parameters :

* speed (بطلع وبنزل)
* time
* temperature (37°C) حرارة الجسم

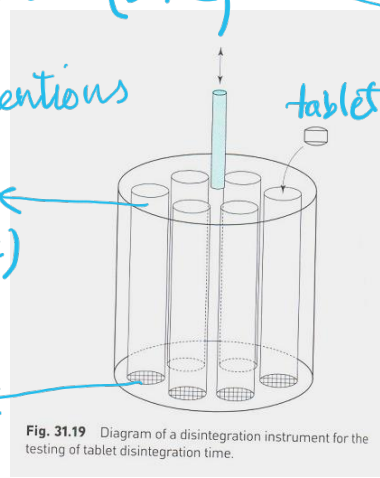


Fig. 31.19 Diagram of a disintegration instrument for the testing of tablet disintegration time.

جهاز الذراب

specific dimentions (according to pharmacopeia)

mesh/screen يسمح للسائل يدخل

(buffer: السائل)

3 vessels ممكن يتكون

بطلع وبنزل عشان يحاكي حركة peristalsis في الجسم

بنسجل الزمن متى حصل للتابلت full disintegration

حسب نوع التابلت immediate release or enteric-coated مثلاً

Tablet testing

Disintegration

- The disintegration apparatus consists normally of six tubes open at the upper end and closed by a screen at the lower.
- One tablet is placed in each and normally a plastic disc is placed on it. Then the tubes are placed in a water bath and raised and lowered at certain rate in the water in a way that the screen remains below the surface of water.
- The time to reach the end point (at which all visible parts have been eliminated from all the tubes) is recorded and the preparation complies with the test if this time is below a given limit.

Tablet testing

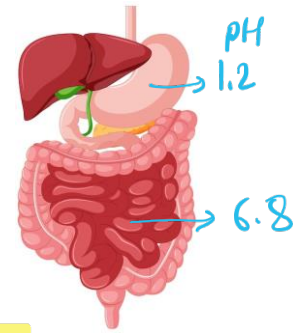
Dissolution test

- Dissolution test is the most important way to study the release of a drug from a solid dosage form under in vitro conditions.
- During the dissolution study the cumulative amount of drug that passes into solution is studied as a function of time.
- Aims of dissolution studies:
  - To indicate the performance of a formulation under in vivo conditions.
  - To evaluate the effect of formulation and process variables on the bioavailability.
  - To ensure that preparations comply with product specifications.

Tablet testing

Dissolution test

- Dissolution is accomplished by locating the tablet in a chamber containing a flowing dissolution medium. The factors affecting the dissolution process (such as composition and temperature of dissolution medium, flow or agitation rate) must be standardized.



- Normally, the concentration of the drug substance in the bulk of the dissolution medium shall not exceed 10 % of the solubility of the drug to be near to sink conditions.

٨٩

Tablet testing

Dissolution test

- The amount of drug dissolved is analyzed once or at a series of consecutive times.

- The composition and pH of the dissolution medium may vary between different test situations.

- A number of official and nonofficial methods exist for dissolution testing, which can be applied for both drug substances and formulated preparations.

٩٠

Tablet testing

Dissolution test

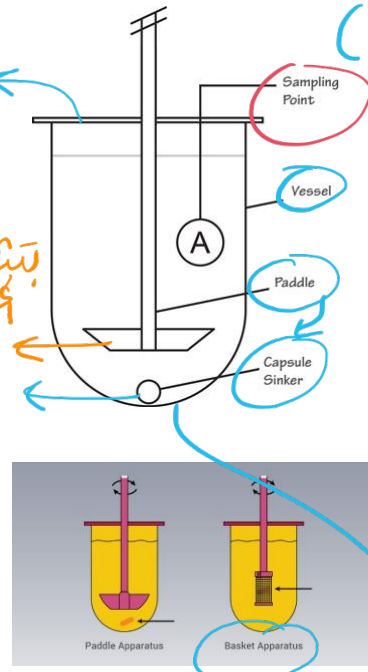
Stirred vessel methods

- The most important stirred vessel methods are the *rotating-basket* and the *paddle* methods.

- Both use the same type of vessel, which is filled with certain volume of a dissolution medium of certain temperature.

- In the paddle method, the tablet is placed in the vessel and the dissolution medium is agitated by rotating the paddle.

- In the basket method, the tablet is placed in a small basket formed from a screen, which is then inserted in the dissolution medium and rotated.



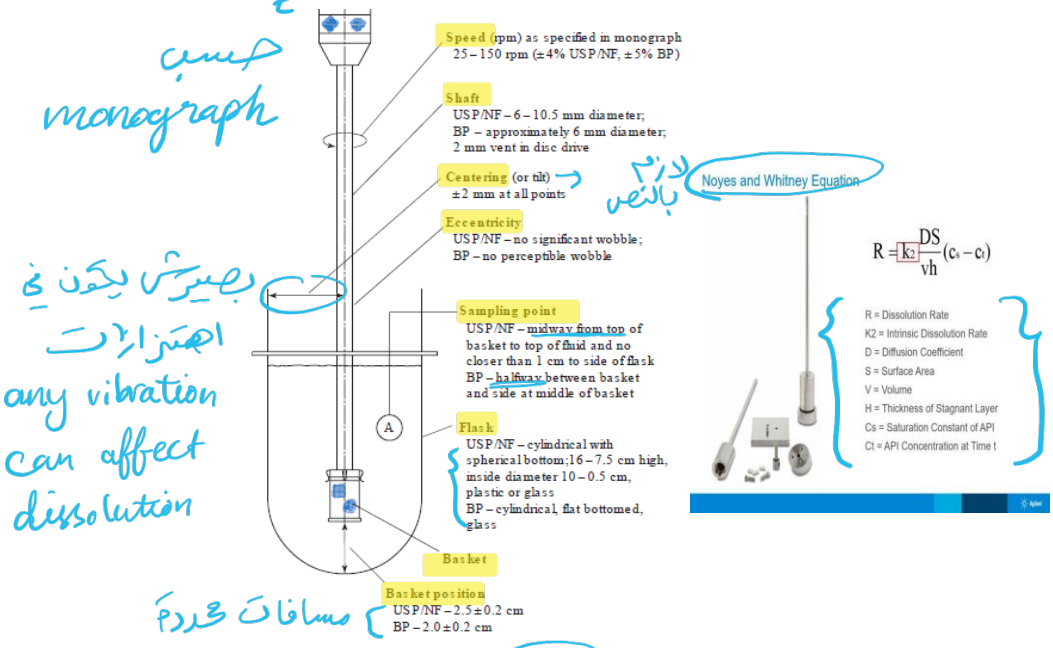


Fig. 30.20 • Diagram of a dissolution instrument based on the rotating-basket method for the testing of tablet dissolution rate. (Courtesy of Banakar, 1992, with permission.)

٩٣

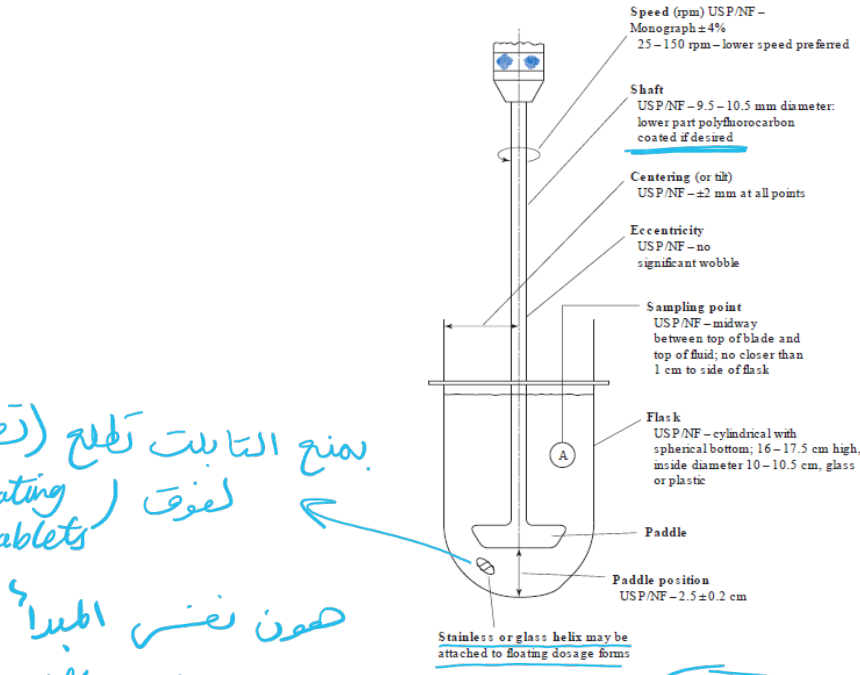


Fig. 30.21 • Diagram of a dissolution instrument based on the rotating paddle method for the testing of tablet dissolution rate. (Courtesy of Banakar, 1992, with permission.)

٩٤

Tablet testing

Dissolution test

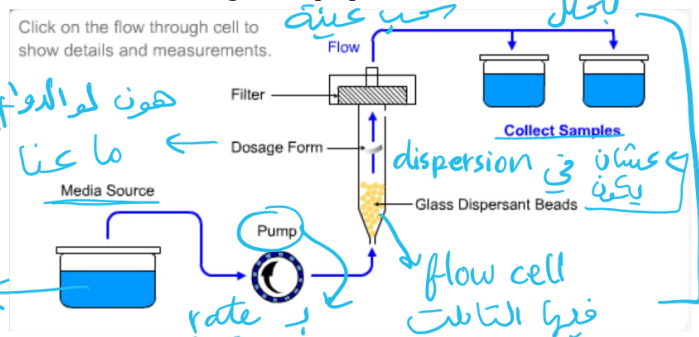
هاد نوع مختلف عن التقليدي

Continuous flow method

- In the Continuous flow method the preparation is held within a flow cell, through which the dissolution medium is pumped at a controlled rate from a large reservoir.

- The liquid which has passed the flow cell is collected for analysis of drug content.

- Advantages
  - Maintain sink conditions throughout the experiment
  - Avoid floating of the preparation.



٩٥

Tablet testing

Mechanical strength

- An acceptable tablet must remain intact during handling between production and administration.

- An integrated part of the formulation and production of tablets is the assessing of their mechanical strength.

- Aims of mechanical strength testing:
  1. To assess the effect of formulation and production variables on their resistance towards fracturing and attrition.
  2. To characterize the fundamental mechanical properties of materials used in tablet formulation.
  3. To control the quality of tablets during production (in-process control).

٩٦

Tablet testing

Mechanical strength

- The most commonly used methods for strength testing are the resistance to abrasion test (friability test) and the crushing strength (fracture resistance). → hardness test

Attrition- resistance methods

- The most common method to determine attrition (abrasion) resistance involves the rotation of tablets in a cylinder followed by the determination of weight loss after a given number of rotations.

rotation per minute (rpm)

$W_1 - W_2$

- Normally, weight loss of less than 1% of tablet weight is required.

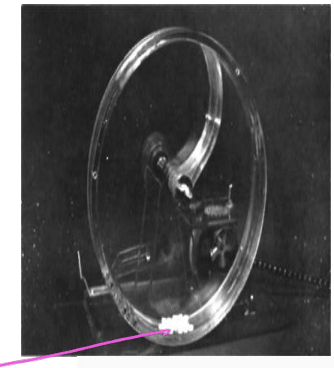
$\frac{W_1 - W_2}{W_1} \times 100$

٩٧

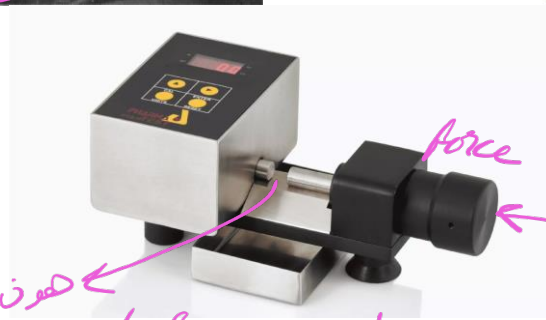
جهاز استخدمناه في اللاب

friability tester

plastic



ثابت (حدد تعيينه حسب monograph)



force

صمون بخط الحبة وبتكسر مع الـforce

hardness tester (crushing)

automated

not automated

ممكن يكون جهاز بسيط زي هيك بيستخدم لـ thickness & hardness

Tablet testing

Mechanical strength

Crushing (Fracture) resistance methods

- In this test, the tablet is usually placed against a platen and the load is applied along its diameter by a movable platen. The force needed to fracture the tablet is recorded.

- The force needed to fracture a tablet depends on the tablets dimensions.

flat-faced tablet
الصورة من الفيديو

Tablet testing

Mechanical strength

Crushing (Fracture) resistance methods

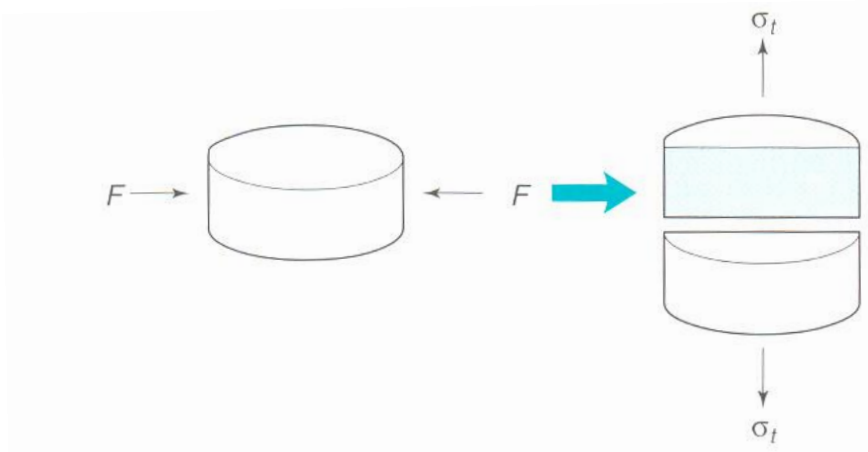
- An ideal test, however, should allow comparison of tablets of different sizes or even shapes.
- This can be accomplished by assessing the strength of the tablet, i.e. the force needed to fracture the tablet per unit fracture area.
- For a cylindrical flat-faced tablet the tensile strength can be calculated by the following Eqn provided that the tablet fails in a tensile fracture mode:

tensile strength

$$\sigma_t = 2F/\pi Dt$$

- F: the force needed to fracture the tablet, D and t are the diameter and thickness of tablet

يقاس عن طريق Calibar أو الجهاز البسيط اللي بالصور فوق



two equal halfs

Fig. 31.22 Illustration of the tensile failure of a tablet during diametral compression.

how much force is needed to fracture the tablet into

Fundamental aspects of compression of powders

Compressibility: the tendency propensity of a powder to reduce in volume while loaded.

- The compression of a powder bed is started by rearrangement of particles in the die, resulting in reduced porosity (closer packing).
- At a certain load the reduced space and friction between particles prevent further movement of particles.
- The subsequent decrease in tablet volume is therefore associated with changes in the dimensions of particles (fragmentation or deformation).
  - 2 – Elastic deformation: reversible on removal of the load
  - 1 – Plastic deformation: Irreversible
  - B – Fragmentation: particles are fractured to smaller size

تحت في الرسمة

- Sometimes the degree of deformation is time-dependent and is referred to as viscous deformation and viscoelastic deformation.

liquid بتتصرف ك

elastic or plastic من ناحية

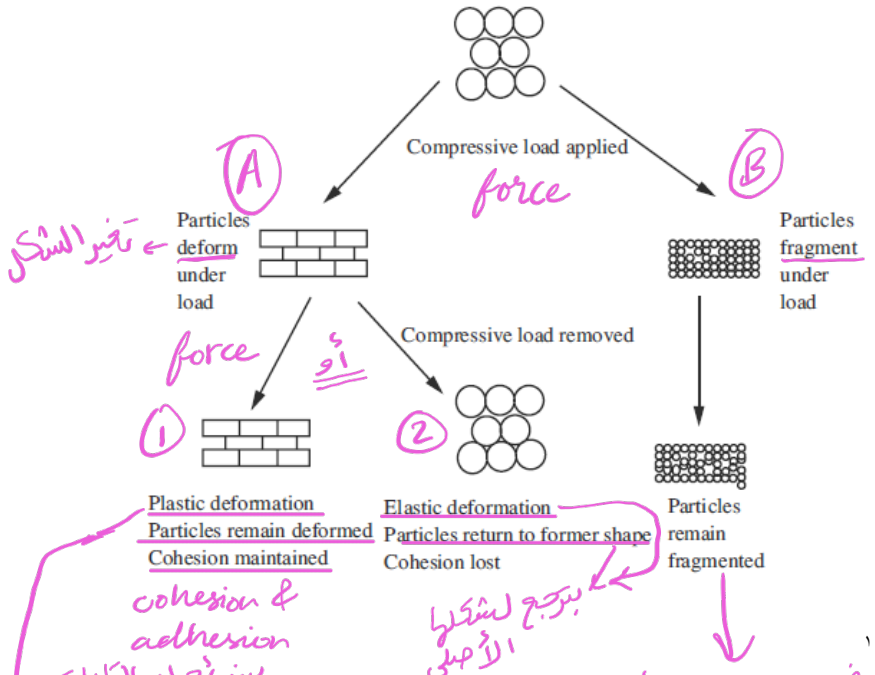
between solid and liquid depending on how much time is allowed

تصيرفيزيا

زي شكل ① في الصورة تحت

بترجع لشكلها الأصلي

movable



force

تغير الشكل

أو

نوع ② صعب يعيدلها Compression فغالبًا بنعطيها Capsule

cohesion & adhesion بين أجزاء التابلت

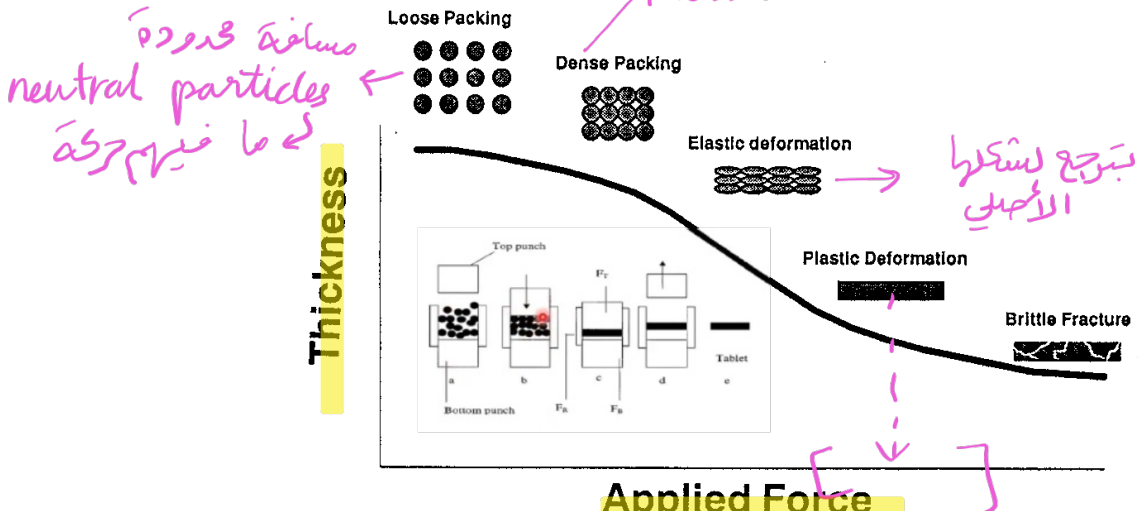
permanent deformation

بترجع لشكلها الأصلي

Change in shape صار في لكن مش الـ compression المطلوب

١٠٣

لحل المواد same mass, less volume



مسافة محدودة neutral particles كما فيها حركة

بترجع لشكلها الأصلي

لو شلنا الـ force الأنها لسة elastic

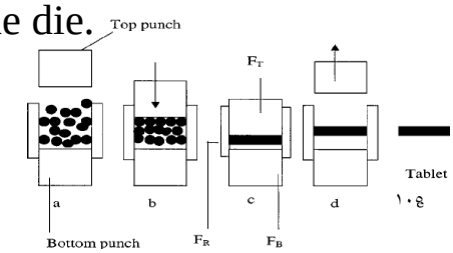
excessive force

avarage force needed

١٠٤

Fundamental aspects of compression of granules

- For granules processes involved in their compaction can be classified into two groups:
  - Physical changes in the granules
  - Physical changes in the primary particles from which the granules are formed
- At low compression forces the reduction in volume of the bed of granules can occur by a rearrangement within the die.



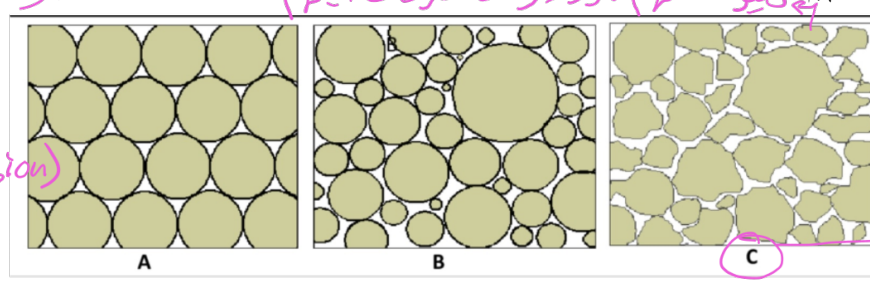
لما نوصل الـ volume النهائي بيبش يصير cohesion & adhesion ← وبتتكون التابلت

Fundamental aspects of compression of granules

- With increased loading the granules can:
  1. – Deform elastically → (شلناها) لو رفعنا الـ force رح ترجع للشكل الأصلي
  2. – Deform plastically → permanent, irreversible
  3. – Densify (i.e. reduce their intragranular porosity)
  4. – Broken into smaller units by different mechanisms
     - Primary particles might be removed from the surface of granules when they slide against each other or against the die wall (granule attrition).
     - Granules can fracture into a number of smaller ones (granule fragmentation)

ما بتغير ↑ $D = mass/volume$ ← بقل ↓ بالتالي D بتزيد

الـ granule اذا بتكسر فقط بتكسر أو البارتكلز المكونة لـ granules هي اللي تتكسر بحيث تتجنب الفراغات (cohesion & adhesion) dense mass ← tablet



١٠٦ تضغط بشكل التدريجي وقلت الفراغات بينهم

densify

Fundamental aspects of compaction of powders

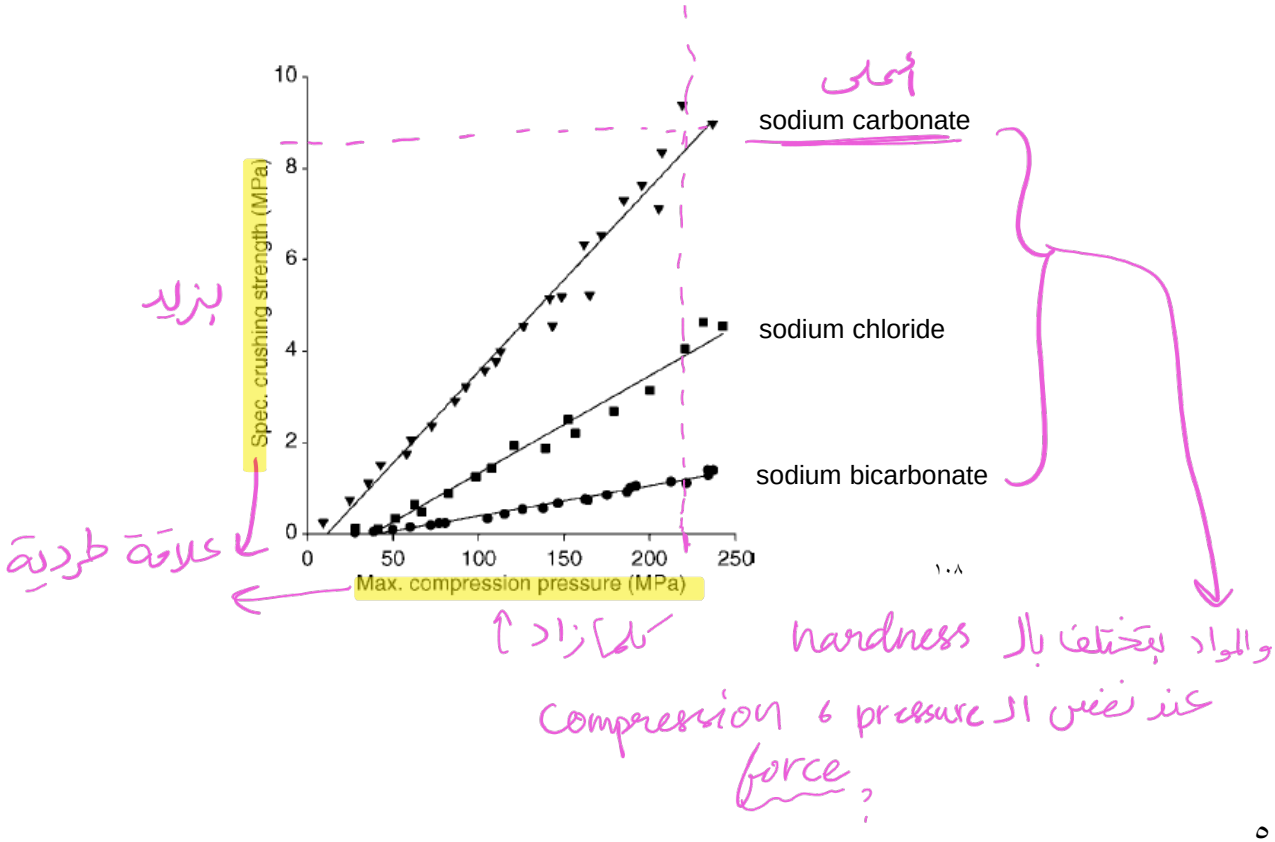
Compactability: The propensity of powder to form a coherent tablet.

- Factors affecting compactability could be related to material and formulation or processing conditions or environmental conditions.

- In practice, the most common way to assess powder compactability is to study the effect of compaction pressure on the strength of resulting tablet.

١٠٧

Fundamental aspects of compaction of powders



١٠٨

Fundamental aspects of compaction of powders

- Mechanisms of bonding in tablets include:

1 – Solid bridges
2 – Bonding by liquid (surface tension forces)
3 – Binder bridges
4 – Intermolecular and electrostatic bonding
5 – Mechanical interlocking

١٠٩

* tablet isn't 0% moisture

Relationships between material properties and tablet strength

Role of moisture

- Small percentage of moisture in tablet formulas can dramatically affect the behavior of these feed materials and that of finished products.

- Moisture is also important in wet granulation process.

- Water may be squeezed out during compaction and the expelled moisture may act as lubricant at the die wall but it can also cause sticking to the punch faces.

Relationships between material properties and tablet strength

The compaction of granules

- The compactability of granules is affected by:
  1. – the mechanical properties of the primary components (i.e. particles before granulation)
  2. – the design of the granulation process
- Granules may deform or fragment into smaller components during compression.

active/inactive

plastic/elastic

بدنا plastic عشان تكون تابلت

زي شكل B في الرسمة في السلايدات السابقة

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Relationships between material properties and tablet strength

Post compaction tablet strength changes

- The mechanical strength of powder can change with time. (aging)
- The underlying mechanisms for such change are complex.

starch, cellulose derivatives, alginate, ... زي

polymer

تغيير خصائص المادة مع الزمن وغالبًا مرتبط بوجود

2-3 years ← expiry date

الـ age اللي بدنا اياه اللي هو حسب طبيعة الدواء

حكينا الأساس المادة الفعالة إذا في polymer بيقل مشكلة بالصلاحية بتبدله

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Problems and difficulties in tableting

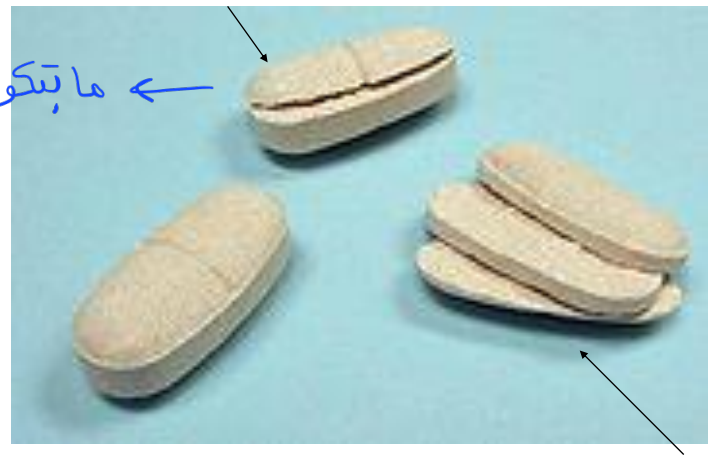
- A number of technical problems can arise during the tabletting procedure.
- Such problems are related to:
  1. – the properties of the powder intended to be formed into tablets, and
  2. – the design and conditions of the press.

Problems and difficulties in tableting

Capping and lamination

- Capping: Partial or complete separation of the top or bottom of a tablet from the main body
- Lamination: The separation of the tablet into two or more distinct layers
- Usually these problems appear immediately after compression but may occur after hours or days.
- Causes of capping and lamination:
  1. – Rapid speed of compression: air is not given enough time to escape.
  2. – Presence of excessive fines
  3. – Over drying of granules → 0% moisture
  4. – Incorrect setup at the press

Capping ← من فوق أو من تحت



ما بتكون flat الحبة ←

Lamination ← بتنقسم بطريقة عرضية طبقتين أو 3 مثلاً

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Problems and difficulties in tableting

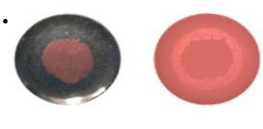
Picking and sticking

- Picking: The removal of the surface material of tablet by sticking to punches.
- Picking is of particular concern in case of engraved punches, especially with letters of small enclosed areas like "B" and "A", which are difficult to manufacture cleanly.
- Sticking: The adhesion of tablet material to the die walls.
- Sticking can cause chipping of edges of tablet and does not allow free movement of lower punch (may cause machine damages).

محفور

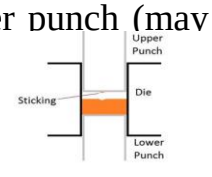
حرف الـ B بيكون محفور ← هون بيكون مبين بروز عالحبة

الهون الأعم ← picking لـ



Sticking

Picking



Sticking to punch and picking from tablet

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impose: تتوات
depose: حفر

جزء من التابلت علق

الأحرف والأرقام هاي لحفرها الـ punch نفسه مرا لازم تكون simple & large

لو كانت fine details

منلاً بالـ picking هاي التفاصيل ما رح تبين هيك ، رح يوخد الـ punch جزء معه

punch لما يطلع الـ picking يوخد معه فتافيت من التابلت

Problems and difficulties in tableting

Picking and sticking

- Solving of picking and sticking:
  1 – Engraved letters should be designed as large as possible
  2 – Addition of lubricants and anti-adherents.
  3 – Additional binder or change of binder may may the granules more cohesive and therefore less adhesive to the punches and die.
  4 – Low melting materials (such as stearic acid and PEG) which may soften from the heat of compression causing sticking may be replaced by higher melting point additives.
  5 – High moisture content may cause sticking and this is solved by further drying

Problems and difficulties in tableting

Mottling

- It is unequal distribution of color on tablets

- Reasons:
  1 – Difference in color between drug and excipients
  2 – Colored degradation products
  3 – Migration of color during drying of granules (May be solved by changing solvent system, changing the binder system, reducing temperature or grinding granules to smaller particle size).
  4 – In direct compression formulations, uneven distribution of dye or large particle size may cause mottling

* tableting machines in factories are heavy-duty
فلازم تتحمل وحافظ عليها من سوء الاستخدام على سنين طويلة

Problems and difficulties in tableting

Weight variation

- Reasons
  1. – bad flowability of powder
  2. – Variation in size and size distribution of granules
  3. – Poor mixing with glidants and lubricants.
  4. – Punch variation (lower punches are unequal in lengths)

Hardness variation

- It has the same causes as weight variation because hardness depends on the weight of material forming the tablet

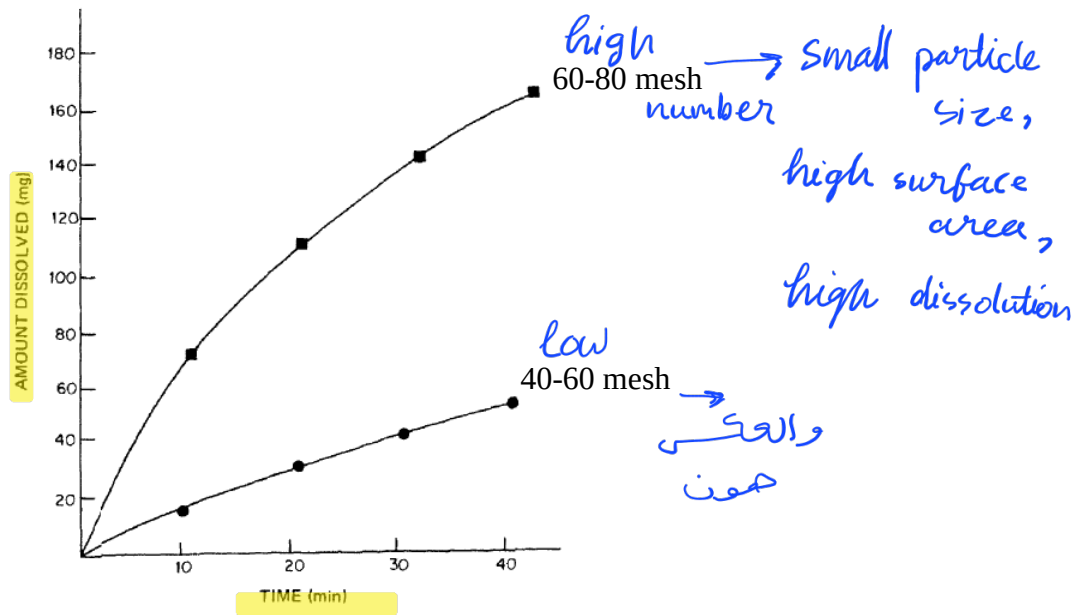
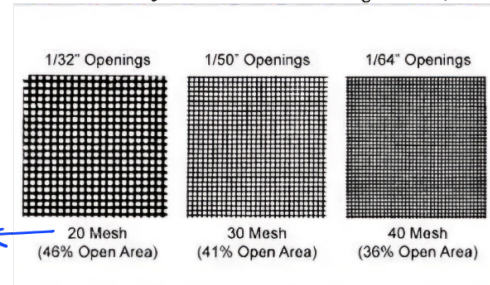


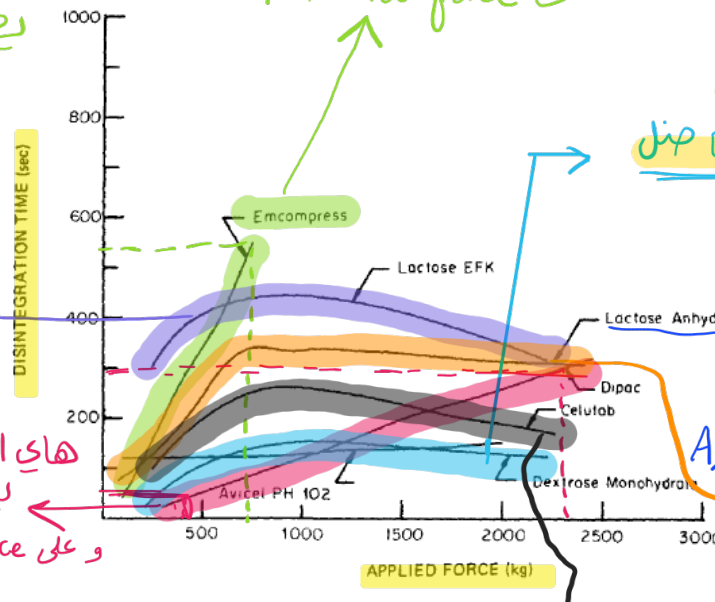
Figure 2 Effect of granule size on the dissolution rate of salicylic acid contained in compressed tablets. Key: ● 40- to 60-mesh granules; ■ 60- to 80-mesh granules.



(زيادة الـforce بتزيد الوقت)

بتحتاج وقت طويل low compression force هاي المادة على

عشان more time احتجنا low force على عشان يصير disintegration



هاي المادة مع زيادة الـforce زاد الزمن قليلاً لكنه تقريبًا ضل ثابت

مع زيادة الـforce بتزيد الزمن ثم برجع بقل

لو اجت الرسمة في الامكان الأسماء هاي مش معلولة رح يكون في A, B, C...

low force هاي المادة على بتحتاج زمن طويل و على force أعلى زاد الزمن لكنه لا يزال محمول ضمن المحتمل (مش عالي كتير)

زاد الزمن ثم ثبت

بتزيد الزمن بحدين بقل

(مادة تعتبر fair)

زيادة الـforce بتزيد الوقت gradually

Figure 4 Disintegration time versus applied force for compacts of various materials.

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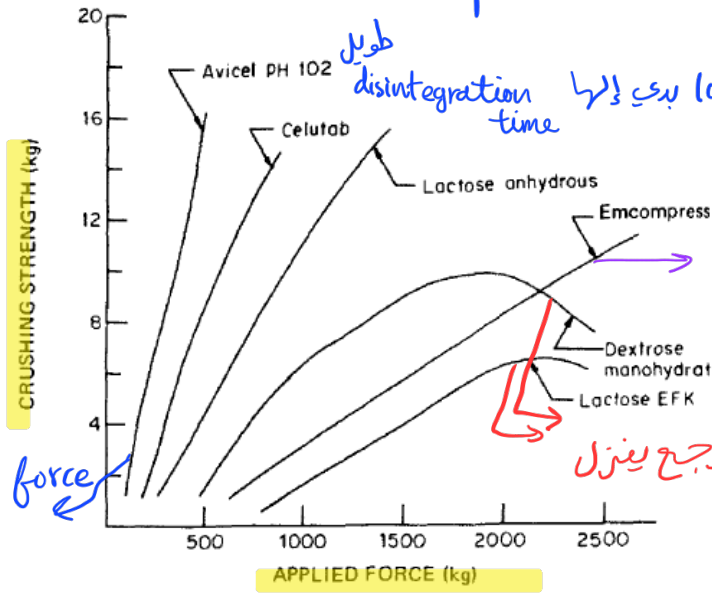
* الفكرة إنه نشوف optimum force عشان نعطيني optimum disintegration time



* زي ما حكينا قبل مثلاً lozenges بدي إلها طويل disintegration time فبتحتاج high force.

gradul increase نلاحظ لكن له hardness أقل من باقي المواد

بزيد وبرجع ينزل

hardness عندها ← low force عالي بدها) crushing strength عالية)

Figure 5 Crushing strength versus applied force for compacts of various materials.

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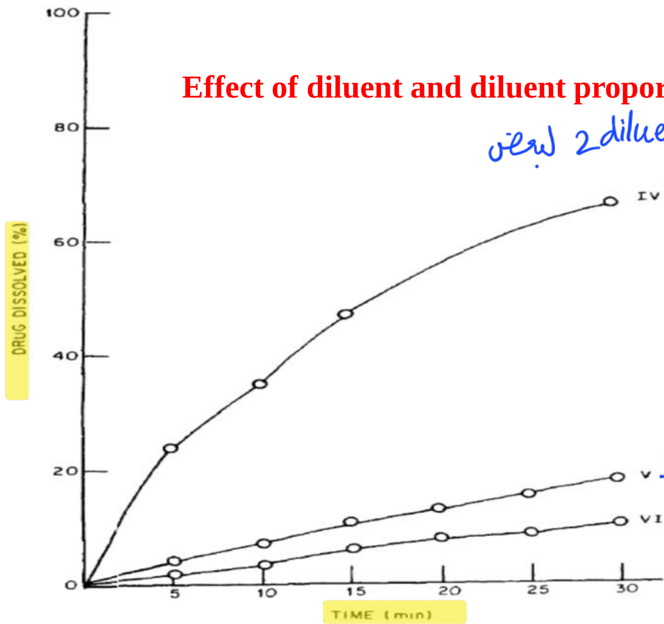
** الأسماء في هذا الشكل أسماء تجارية ليست للحفظ *

* هاي الشغلات لازم ندرسها أثناء عملية optimization للتابلت Conditions

Effect of diluent and diluent proportions

نسبة 2 diluents لبعض



قل ال dissolution

قل لما كان

Figure 7 Drug release of an insoluble drug from direct-compression diluents (see text). IV = microcrystalline cellulose N.F./dibasic calcium phosphate N.F., 50:50. V = microcrystalline cellulose N.F./dibasic calcium phosphate N.F., 30:70. VI = microcrystalline cellulose N.F./dibasic calcium phosphate N.F., 16:84.

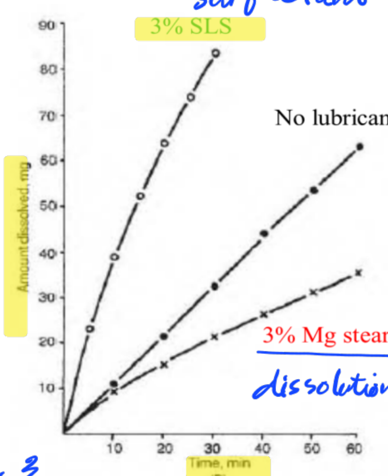
→ water insoluble

* لازم ندرس نوعية diluent المناسبة والنسب المناسبة
* كلما زادت نسبة diluent insoluble رح يقل dissolution للتابلت
والعكس كلما كان ← hydrophilic أكثر رح يتحسن dissolution

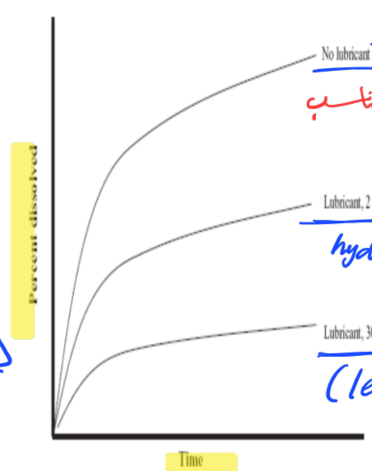
water soluble ممكن الدواء
∴ high dissolution
وحتى لو الدواء insoluble
لازم نختار mixing time مناسب

good lubricant in good percantage

surfactant



قل dissolution



mixing 2 min
less dissolution
لأنه مثلاً hydrophobic lubricant

overmixing (less dissolution)

stearate مجموعة
Na/Mg خاصة

Effect of lubricant type on dissolution of salicylic acid from compressed tablets

Effect of lubricant and its mixing time on dissolution rate of drugs

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حكينا قبل أحسن lubricant هو ← ...
لكن النسبة الأفضل optimum
منهم هي 1% إذا زادت
بصير overlubrication ← يعني بصير الدواء hydrophobic
وذائبيته تبقل
(fatty acid وهي بتغلف الحبة بتغلفها)

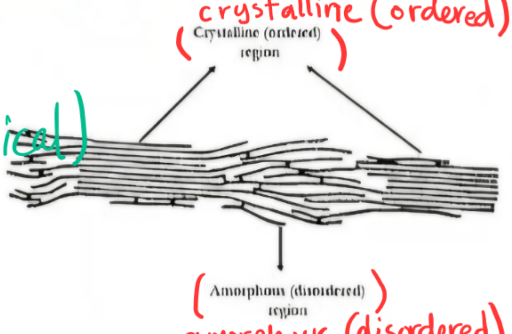
* تذكير: لما بدنا يصير complete dissolution
زي حالة effervescent tablet
لازم نستخدم hydrophilic lubricant

Microcrystalline cellulose (MCC)

is pure partially depolymerized cellulose synthesized from α-cellulose precursor.[6]

The MCC can be synthesized by different processes such

1. reactive extrusion,
2. enzyme mediated,
3. mechanical grinding,
4. ultrasonication,
5. steam explosion and
6. acid hydrolysis.



The acid hydrolysis. process can be done using mineral acids such as H_2SO_4, HCl and HBr as well as ionic liquids. The role of these reagents is to destroy the amorphous regions leaving the crystalline domains.

The MCC particles with size lower than 5 μm must not be more than 10%.

Tablet formulation example for a quantity of 100000 tablets

Item code	%	Composition	Unit wt. mg	Batch wt. Kg	Application
	12.50	Diclofenac Sodium Powder(BP)	25.00	2.50	Active ingredient
	1.50	Aerosil-200 (Colloidal Silicon Dioxide)(USP-NF)	3.00	0.30	Glidant
	22.50	Avicel (MCC) (BP)	45.00	4.50	Diluent
	26.00	Lactose M.H. Fine Powder(USP-NF)	52.00	5.20	Diluent
	33.00	Maize Starch Fine Powder(BP)	66.00	6.60	Diluent
	1.50	Povidone (P.V.P. - K 25)(USP)	3.00	0.30	Binder
	2.00	Na Starch glyconate (Primojel) Powder (USP-NF)	4.00	0.40	Disintegrant
	1.00	Magnesium Stearate M.F. Powder (USP-NF)	2.00	0.20	Lubricant
	XXXXX	Ethanol 96% w/v (USP)	XXXXX qs		Kneading solution
Total	100		200	20 Kg	

* ال formula إذا اجت في الامتحان خرجي لـ tablet

إذا في أنواع

↓ immediate release → direct compression

↳ granulation → إذا wet بتكون في Kneading solution / binder ، وال solvent ممكن يكون موجود أو لا

* إذا العضيرة direct compression غالباً بتكون very simple
لكن بتعتمد عالدواء جرعة عالية أم قليلة

← في المثال السابق diclofenac is not a potent drug
لكن جرعته هنا قليلة فبترتب عليه إنه العضيرة غالبا diluent

* أعقد الحالات تكون كل أنواع excipients موجودة

* ممكن يكون في antioxidant إذا الدواء بحيرله أكسدة

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* Wearing: الجهاز بحيرله تلف مع الزمن، مثلاً تغيّر صوته حتى، كشط مع كثرة أو سوء الاستعمال
with time or due to poor storage

* Ageing of polymers: chain of monomers
في أشياء زي: linear/nonlinear, branched, crystalline ..

* الفكرة إنه الـ polymer على الـ shelf-life بحير فيه تغيّر (عالستين مثلاً)

ممكن تؤثر عليه بكتيريا مثلاً ← natural polymer
polymer ← degradation ← physical/chemical
يعني ممكن الثابلت تتلف بسبب

* مش معتاد إنه excipients يعني خلص ما بتخرب