

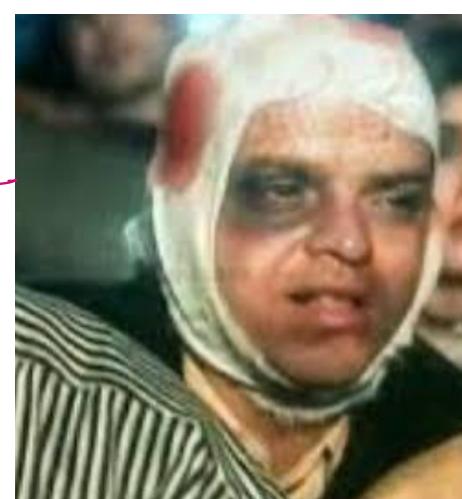
تغريغ صيدلة صناعية 1



صادر عن
الكتاب
الكتاب
تابعوا قناتي على
تعديل

لا تنسوا إضافة إعجابكم
ادخلوا بطريركم 😊

سلسلة لما نخاف
اد Chapter



عرفنا الـ **solid dosage form** على انها **tablet** يعني نسبة **water** فيها تكون ضئيلة جداً
 ممكن تكون من دوا واحد **singel dose** زي معظم الـ **analgesic** او ممكن يكونو دوائين بنفس الحبة زي ادوية **HTN** **diuratic** **multi vitamin** او ممكن توصل **30** دوا بالحبه زي الـ



Tablets

- Tablets are **solid dosage forms** containing a single dose of one or more active ingredients and are usually prepared by compressing **uniform volumes** of particles (powders or granules). الفكرة الاساسية انها تتحضر بال compressing عشان هيكل بنحكي عنها مضغوطات
- Tablets consist the most commonly used dosage form. لأنه الـ **adult** اعدادهم اكبر من الـ **children** **adult** **pediatric** بفضلـ **oral tablet**
- They are used mainly for systemic use but some times for local (e.g. Antacids, antihelmentics). غالب ادوية الـ **systemic** زي **oral tablet** تكون **antacid** او **diuratic** **HTN** **antihelminth** علاج الديدان مثلاً

1

Tablets

لأنه سهل تحطتها بالحبيبه وسهل انك تبلغ **Convenient**

الحبة مقارنه بالـ **liquid dosage injection** وبالـ **form**

- The oral route represents a convenient and safe way of drug administration
- Compared with liquid dosage forms tablets have general advantages in terms of chemical and physical stability. لأنه الـ **water** ممكن يسبب **stability** معدومة **solid dosage form** **water** **chemical and instability** فالـ **water** ممكن يعمل **microbial growth** او يعمل **جية تروها كذا دسلاها كذا**
- The preparation procedure enables accurate dosing of drug. جية تروها كذا دسلاها كذا
- Tablets are convenient to handle by patient (Identification, swallowing)
- They provide an economical and suitable method to large scale production

خلال عملية الكبس بالـ **small scale** يمكن تكبس **500** حبة لـ **1000** حبة

والـ **large** ممكن تكبس لـ **نص مليون**

فكل ما كنت اقدر اكبس مجموعه اكبر رح تكون الكلفة التصنيعيه اقل

ورح تكون سعر الدوا ارخص للمريض

2

Tablets

الآن حبة الدواما تدخل للمعدة وللامعاء وال¹² تكون **aqueous media** فالحبيبة لازم يصير لها **dissolution** وهذا يعني وعشان يمرق من جدار المعدة عشان يصير له **absorbtion** (لازم يمرق من الـ **Lipid bilayer**) لازم تكون **water soluble**

Main disadvantages:

lipid soluble يكون مارح يمرق من الـ **highly water soluble** اذا كان **dissolution** يفسر انه **lipid bilyer** عشان هيك لازم يكون في **balance between lipid and water solubility**

1. Some drugs (poorly water-soluble or poorly absorbable) have low bioavailability.
2. Some drugs may cause local irritant effects in the gastrointestinal mucosa. → *analgesic* زیست چکنہ
3. Some drugs resist compression into dense compacts.

3

الشركة لما تسجل الدوا Al guidline بتحكى انه لازم

يكون في 3 خصائص ال efficacy || equality || saftey Tablets

الـ quality وـ efficacy وـ safety حافظ على الـ

Quality attributes of tablets

1. They should contain a correct dose of the drug. **الدواء** لازم يكون فيها **الجرعة** **وهي correct dose**
2. The appearance of tablets should be elegant and its weight, size, and appearance should be consistent. **الدواء** لازم يكون **اللون** **واضح** **elegant** يعني اللون واضح **الشكل** **ونفس الوزن** **وومنافي** كسر وبكل العلبة يكون الهم نفس
3. The drug should be released from the tablets in a **controlled** and **reproducible** way. **الدواء** **ينكون** **ما** **يكون** **immediat** **or** **non immediat** **او** **ما** **يكون** **اشترى** **علبة** **ثانى** **ملهم** **يشتغلوا** **بطريقة** **reproducible** **يعنى immediat** **بضل** **control** **يضل** **control** **بصير اشتري دوا** **يكون** **immediat** **immediat** **ويبطاع** **release**
 ما **يتحدى** **غير** **الجريف**
4. The tablets should be **biocompatible**, i.e. not include excipients, contaminants, and microorganisms that cause harm to patients.

4

Tablets

لازم حبة الدوا تتحمل ال stress وما يصير فيها fracture فرضاً لما بذلت نعملها

اكيد رح نقط كميات كبيرة والحبة رح تخطي الي حواليها فلازم تتحمل coating

ويرضه في ال drying وال shipping وال backging وادا dispensing هذا كله لازم

الحبة تتحمله

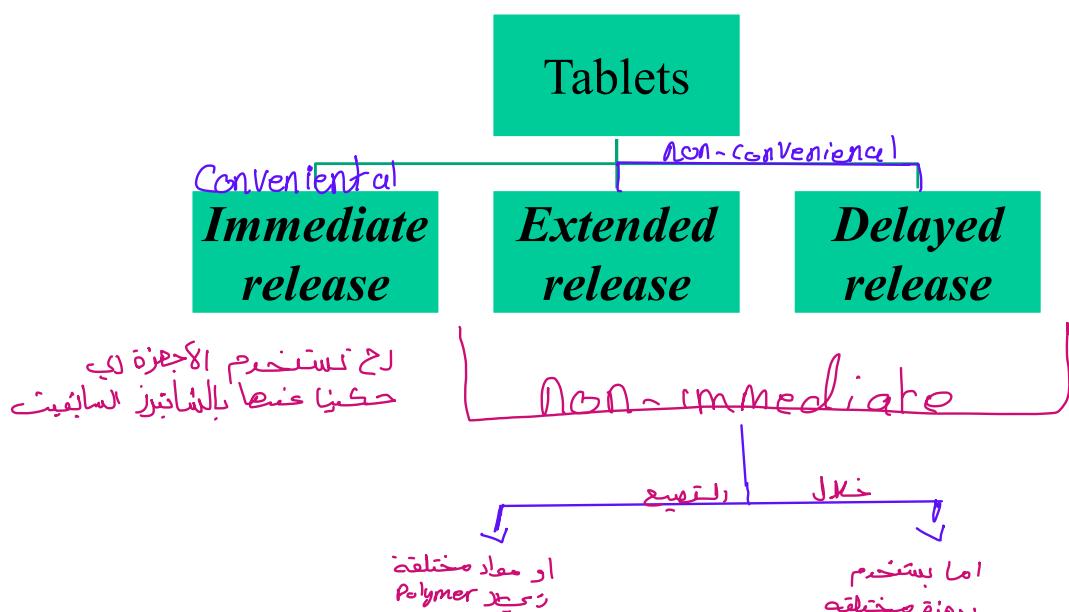
Quality attributes of tablets

5. The tablets should be of sufficient mechanical strength to withstand fracture and erosion during handling (the production, packaging, shipping and dispensing).
6. The tablets should be chemically, physically and microbiologically stable during the lifetime of the product.
7. The tablet should be acceptable by the patient.
8. The tablets should be packed in a safe manner.

Tests and standards for some of these properties are found in the pharmacopoeias.

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Tablet Types



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كل ما استهلاك اسفي جعيده
سعر الدوا رح يرتفع

3

Tablet Types

حيه الدوا الي لما
المريض بيلعهار
يحس بتاثير
الدوا يعني بحس
onset of action
مش
زى خافض
of action
الحرارة او مثلا جه
البنادول بعد نص

Tablets can be classified into three types based on their drug release characteristics:

- **Immediate release tablets:** The tablets in which the drug is intended to be released rapidly after administration or the tablet is dissolved and administered as solution.
- This is the most common type of tablets and includes disintegrating, chewable, effervescent, sublingual and buccal tablets.



حيه تحت اللسان ، زى لا اهلا والهلا ونكت الملايين العاشر من
المعدة

دخل الفم

سرير
المعدة يسكن

ناتيرها طول
زما فى ادوية تحصل
عنت ملوك نهائى
nearly

Extended release tablets: The drug is released from these tablets slowly and at nearly constant rate (Zero order kinetics). The formulation and the used excipients are usually different from those in conventional tablets.

دورة effect+ دورة تأخير
Delayed release tablets: The drug is liberated from these tablets sometime after administration. Example is enteric tablets, for which the tablet passes the stomach and the drug is released from in the upper small intestine.

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delay \rightarrow T_{lag} \rightarrow time before drug release

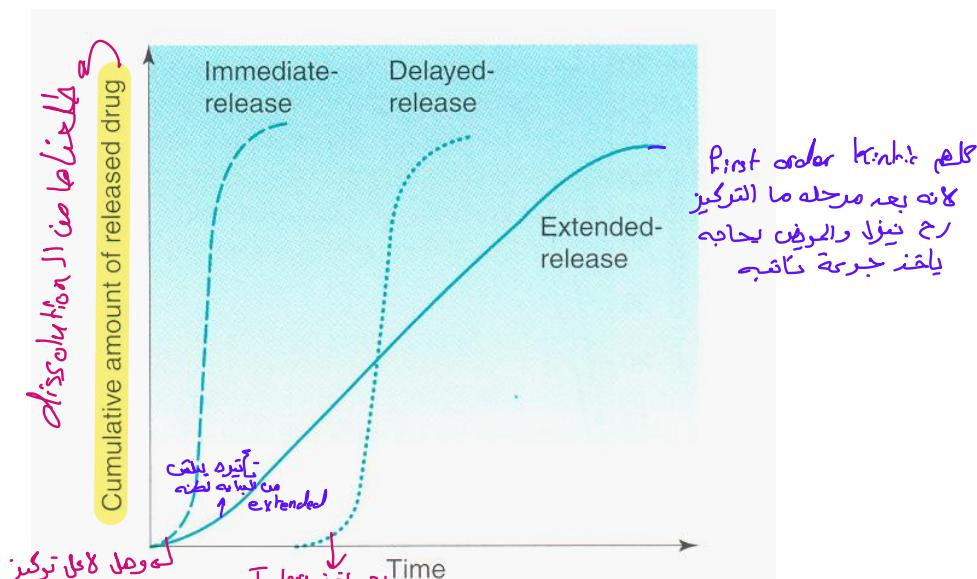


Fig. 31.10 Schematic representation of the cumulative amount of drug released from immediate-, extended- and delayed-release tablets.

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Immediate release tablets

Disintegrating tablets

حبة لازم تذبلع ولكن عمليه ال **disintegration** لها اسرع من ال **dissolution** ببليش ال **tablet** العاديه وعلى طول

- This type of tablets is intended to be swallowed and to release the drug after disintegration and dissolution.
- They are often referred to as conventional or plain tablets.
- They should include disintegrant.

كريم يذوب في الماء disintegrant لقاح disintegration tablet لقاح

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Immediate release tablets



Disintegrating tablets

- Single disintegrating tablets can be formed as multilayer tablets, i.e. the tablet consists of two or three layers cohered to each other. **multilayer** **عسان يمون عندي** **tableting machein** **فهها مادتين عشان هيك رح يكون عندي** **shield** **اللي رح يحصل او** **shielding** **تحفظ عندها ممكن تخلص** **adhesive** **وبيعدها بنضيف المادة الثانية** **وبيعدها بتصير** **final compression** **ايا لازم يكون في** **عشان يمون عندي** **multilayer**
- During the preparation of multilayer tablets the die is filled in two or three consecutive steps with different granules from **separate feed** **stations.** **لے بعضے فی** **multilayer**
- Disintegrating tablets also can be coated by different methods.

- During the preparation of multilayer tablets the die is filled in two or three consecutive steps with different granules from separate feed stations.

لہ بھٹکی multilayer

مكعبات موجدة فوراً



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هون مستخدمين اكتر من disintegrant وكمبه starch ولاحظو انه مصار اخلاق في عملية dissolution release اوون ما يلاقي aqious media release compressable starch release potato starch واللاحظو انه ال release release disintegrant اذا المقرة حسب النوع disintegrant

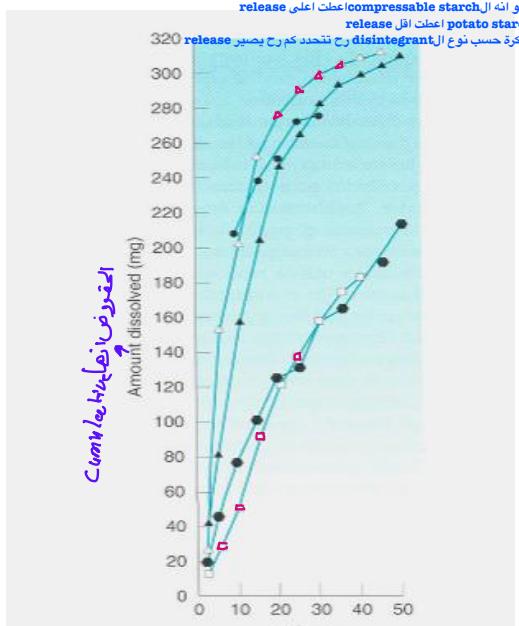


Fig. 31.11 The dissolution rate of salicylic acid, as assessed by an in vitro dissolution method based on agitated baskets, from tablets formed from mixtures of salicylic acid (325 mg) and a series of different types of starches as disintegrant: □ potato starch, ● arrowroot starch, ▲ rice starch, ▲ C12 starch, ▲ compressible starch. (From Underwood, T.W., Cadwallader, D.E. (1972) J. Pharm. Sci., 61, 239.)

Immediate release tablets

Disintegrating tablets

- The disintegration time of the tablet can be markedly affected by:
 - the choice of excipients, especially disintegrant
 - Granulation procedure wet or dry
 - Mixing conditions during the addition of lubricants and antiadherents → step آخر
 - The applied punch force
Punch force كم عص

اذا كمبه ال binder عاليه روح يكون في disintegration بكون بطيء binding عاليه وال disintegration كل ماكنت ال tablet عاليه ال force روح يكون hard processing خلال ال disintegration بكون صعب

Immediate release tablets

Disintegrating tablets

- The dissolution rate from a tablet is a function of:
 - the solubility (can be increased by salt formation).
 - the surface area (can be increased by particle size reduction and disintegration to primary particles).

solubility *disintegration* *surface area*

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Immediate release tablets

Chewable tablets

- These tablets disintegrate mechanically in the mouth by chewing it. The drug is normally swallowed and dissolves in the stomach or intestine.
- The aim of these tablets is to obtain rapid drug effect (e.g. Antacid tablets) or to facilitate the intake of the tablet (e.g. Aspirin and vitamins tablets for children).

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Immediate release tablets

Chewable tablets

- They normally do not contain disintegrant. → مافي داعي لاستر هو Chewing chewing mechanical effect effect
- Flavors and colors are common → بالنسبة للون لازم يكون متواافق مع النكهة
- Mannitol and sorbitol are common examples of fillers. → حسليون

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Immediate release tablets

Effervescent tablets → acid + base + الدواء

- These tablets are dropped into a glass of water before administration, during which carbon dioxide is liberated facilitating tablet disintegration and drug dissolution.
اسنة وفيها الـ **bubbling**
- The effervescent carbon dioxide is created by a reaction in water between a carbonate or bicarbonate and a weak acid such as citric or tartaric acid. **or ascorbic acid**

لازم ال patient يشرب الكاسة وفيها ال **bubbling** يصب سترن CO₂ بطلع

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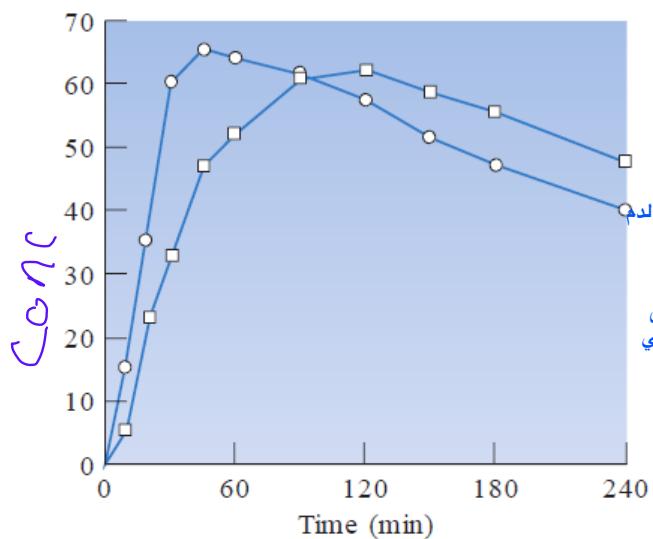


Fig. 30.12 • Concentration of salicylates in plasma after administration of acetylsalicylic acid tablets (1 g). Circles, effervescent tablet; squares, conventional tablet.
(Courtesy of Ekenved et al, 1975, with permission.)

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Immediate release tablets

Effervescent tablets

- Effervescent tablets are used to obtain rapid drug action (e.g. analgesics) or to facilitate the intake of drug (e.g. vitamins).
- They often include a color and a flavor and do not contain a binder.  لأنه مابدئي يصبر
- Water soluble lubricants are preferred in order to avoid formation of a hydrophobic lubricant layer on the surface of the water after tablet dissolution.

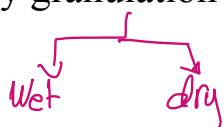
افضل انواع lubricant هو ال **magnesium sterate** بس هو **hydrophobic fatty acid** لانه عبارة عن عشان هيك رح اختار يكون **hydrophilic lubricant** عشان ما **dissolution** بيات عملية ||

Immediate release tablets

Effervescent tablets

ما يصير يكون في رطوبة بالمصنع او خلال عملية التصنيع
لأنه مابدئ الـ effervescent يعمل الا لما المريض يفتح
الحبه فخلال التصنيع لازم ما يكون في رطوبة ولا حتى
بعملية الـ packaging

- Humidity should be controlled during manufacturing.
- They should be packaged in a way that they are protected against moisture.
الغلب الـ effervescent مغلقة تغليفين
غالبا تكون في plastec او metal containir بس الـ closure
very tight
- Effervescent tablets are prepared by either direct compaction or by granulation (by fusion or using ethanol).



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تاتشرها اهها بالفم او
باتحلق

زعي الملاس \rightarrow Lozenges

Immediate release tablets

التهاب الحلق

- Lozenges are tablets that dissolve slowly and used for local treatment in the mouth.
- They are usually used to treat sore throat or to control coughing in the common cold.
- They may contain antiseptics, antibiotics, local anesthetics, demulcents, astringents and antitussives.
- They are normally prepared by compression under high pressure to have high mechanical strength and low porosity in order to dissolve slowly in the mouth.

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بكسها على ضغط عالي جدا لتعطيني high mechanical strength
(السبب الي رح يخلوي الـ dissolve بطيء) و low porosity (لأنه الثقوب
رح تزيد الذئبية وانا مابدئ يصير هيك)

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Immediate release tablets

Lozenges

- They do not contain disintegrants. لأنه مابدئ الحبة تطسر وتتفتت
- The filler and binder should be water soluble. بالماء قويم ليمتص الحبة وتذبل عليه وذالم بكون ماء ماء soluble عذان زذوب بالائم
- They often contain color, flavor and excipients which contribute to a pleasant taste or feeling during tablet dissolution. مابدئ الحبة يغير (release) الدوا جوا افم فيعزز رح اسنان الفم عذان حبيبة تذبل في الماء (ن้ำ)
- Common examples of fillers are glucose, sorbitol and mannitol. السكريات
- Common binder is gelatin. الجلاتين

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Immediate release tablets

Buccal and sublingual tablets

الدوا رح يدخل للدم مباشرة بدون ما يفوت على الـ GI

- These tablets are intended to be held between the cheek and teeth (buccal) or under the tongue (sublingual) and to release their drug content for absorption directly through the oral mucosa (i.e. systemic drug effect).
- Advantages →
 - More rapid onset of action (vasodilators) دوس دا
 - Avoidance of gastric environment which cause decomposition for certain steroids and hormones. بعضها يهانط الطرفة لأنه صحت تذبل في الماء
 - Avoidance of first pass metabolism جاف مجا
 - Avoidance of nausea produced by swallowing certain drugs (e.g. methyltestosterone) رحة انجين مجا المعدة الى ما رحة كثير تذبل لا nausea

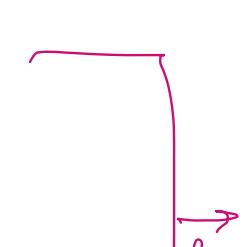
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Immediate release tablets

حبه لما تحطها بالفم رح يصير الها **disintegration** وتصير سائله بالفم وما

Fast dissolving tablets في داعي ابلغه لانه رح يصير ال absorption بالفم وما بحتاج اشرب معها

- These tablets that dissolve or disintegrate quickly in the oral cavity, resulting in solution or suspension without the need for the administration of water.
- Rapidly dissolving tablets are also known as:
 - Melt in Mouth tablets
 - Mouth dissolving tablets (MDT)
 - Quick dissolving tablets
 - **Rapid disintegrating tablets (RDT)**
 - **Fast disintegrating tablets (FDT)**
 - Orally disintegrating tablets
 - Oro dispersible tablets (ODT)



fast dissolving

slow tablet

Immediate release tablets

Fast dissolving tablets

Advantages

- Administration to patients who:

الحالات التي لا تستطيع \
swallow, such as: the elderly, stroke victims, bedridden patients;

يُطْلَبُ تَذَكِّرُ أَنَّ الْجِبَهَ هُمْ يَرَى رَجَعَهُمْ مُنْتَهِيَّهُمْ لِيَلْجُوَوْهُمْ رَجَعَهُمْ
 renal failure patients should not swallow, such as those affected by renal failure;
 refuse to swallow, such as pediatric, geriatric and psychiatric patients

- Rapid drug therapy intervention and more rapid drug absorption
- Convenience and patient compliance
- New business opportunities and patent-life extension

پس انت بنت همید احیاوه گانعله
tablets dissolving²⁴ سکل ل
tablet

الحادي tableت دى تدعى

Immediate release tablets

Vaginal tablets

- Vaginal tablets, also called *vaginal inserts*, are uncoated, bullet-shaped or ovoid tablets inserted into the vagina for local effects.
- normal vaginal pH ranges **between 3.8 and 5.0** أعماق الرحم تدبر pH 3.8-5.0
- They are prepared by compression and shaped to fit snugly on plastic inserter devices that accompany the product. plasticic insert
- They contain antibacterials for the treatment of nonspecific vaginitis caused by *Haemophilus vaginalis* or antifungals for the treatment of vulvovaginitis candidiasis caused by *Candida albicans* and related species

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dispensing

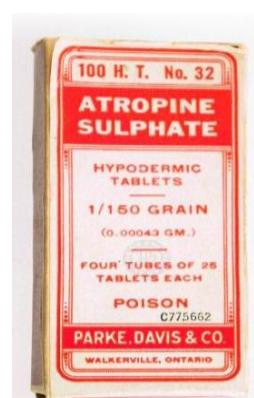
Immediate release tablets

Dispensing tablets XXX

- Dispensing tablets are intended to be added to a given volume of water by the pharmacist or the consumer.

Hypodermic tablets XXX

- Hypodermic tablets are no longer available.
- They were originally used by physicians in extemporaneous preparation of parenteral solutions.



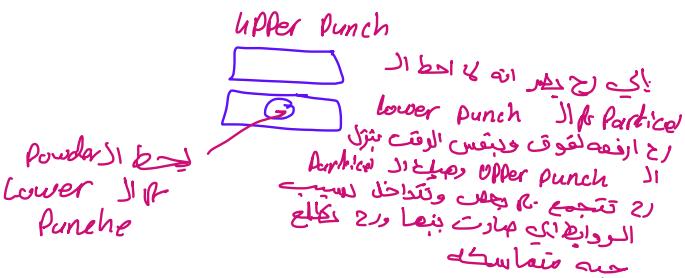
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Tablet Manufacturing

Tablets are prepared by forcing particles into close proximity to each other by powder compression, which enables powders to cohere into a porous, solid specimen of defined geometry.

The compression takes place in a **die** by the action of two **punches**, the lower and the upper.

مبدأ الاجهزه های يعتمد انه تكبس الـ **particels** على بعض واخلي بينهم مساحات قليله (clos) تسمح انه يكون في بين الـ **particels** مساحات قليله ور تكون السبب انه يصير روابط بينهم ور يطلع عندي ما فيها فراغات وتمون صلبه والها شكل معين



الـ compression رح يصير بقالب (die) وهو الي رح يعطي شكل الـ tablet طيب مين الي رح يضغطه؟ الـ lower punches حيث تكون عندي upper والثاني

Tablet Manufacturing

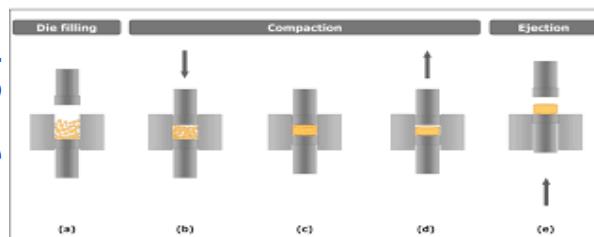
Compression is defined as the reduction in volume of a powder owing to the application of pressure.

Because of the increased proximity of particle surfaces accomplished during compression, bonds are formed between particles which provides coherence to the powder, i. e. a compact is formed.

عن طريق ال圧縮 compression رح

Compaction is defined as the formation of a porous intact specimen of defined geometry by powder compression.

الـ **reduction in volume** يعني رح يعمل حجمها رح يقل لما اسلط عليها الضغط واقل المسافات بينها ونتيجه زياده مساحة الاسطح الناتجه الي هي اسطح التلاصق بين الـ **particels** الي رح يخللي في مساحة تلاصق اكتر بين الـ **particels** لانه الروابط رح تزيد بينهم



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الثلاسيف بضم Com pression
فتح لـ (C) بفتحه واحدة
فتح (C) بفتحه بضم
فتح (C) بفتحه بضم

Tablet Manufacturing

Compaction cycle:

1. Die filling

بكون عندي **hopper** هو ورح يدخل الـ**particels** على الـ**lower**

وهو الـ**punch** يكون ارضيه المفالي

- This is normally accomplished by gravitational flow of the powder from a hopper via die table into the die.
- The die is closed at its lower end by the lower punch.

الـ**upper punch** ينزل عشان يكبس

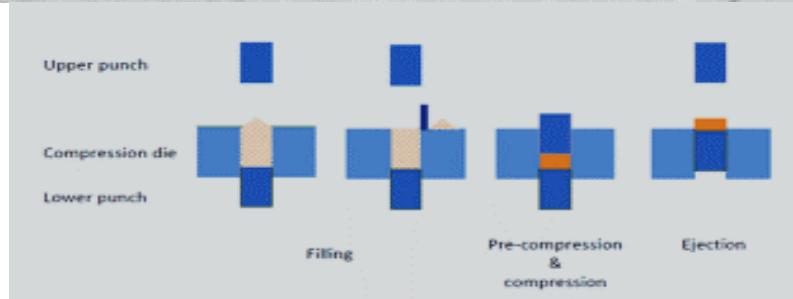
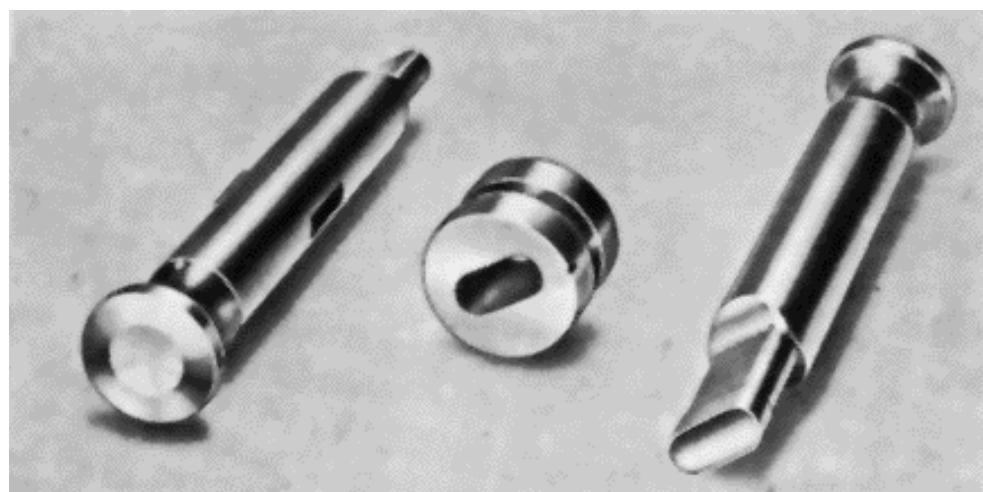
2. Tablet formation

- The upper punch descends and enters the die and the powder is compressed until a tablet is formed.

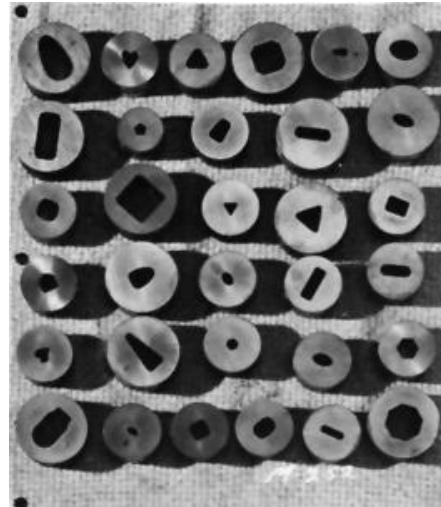
3. Tablet ejection

- During this phase the lower punch rises until its tip reaches the level of the top of the die.

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نجلاند لاجچارہ

Tablet presses

① single punch press (eccentric press)

- A single-punch press possesses one die and one pair of punches.
- The output of tablets is about 200 tablets per min.

عندہ **upper punch** واحد و **lower punch** واحد یعنی رح یطلعلی حبہ واحدہ فقط زی الی شفناہ باللاب بس بستغل بسرعہ تریث بطلع بالدقيقة 200 حبہ بس مع هیک العدد یعتبر قلیل بنسخدمہ باللابات او بالادویہ الی ما بدنہ کمیات کبیرہ منها

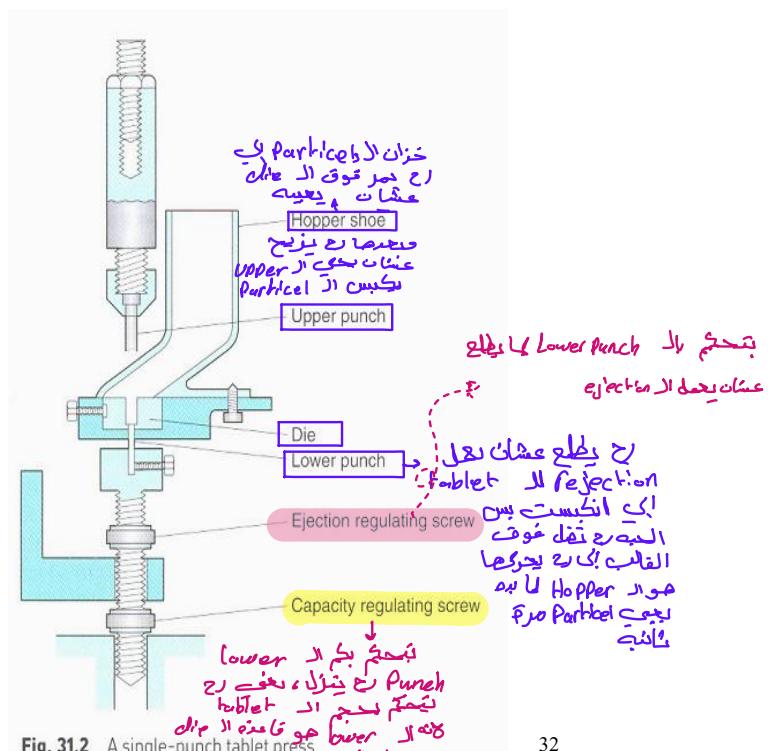


Fig. 31.2 A single-punch tablet press.

Tablet presses

Single punch press (eccentric press)

Steps of compaction

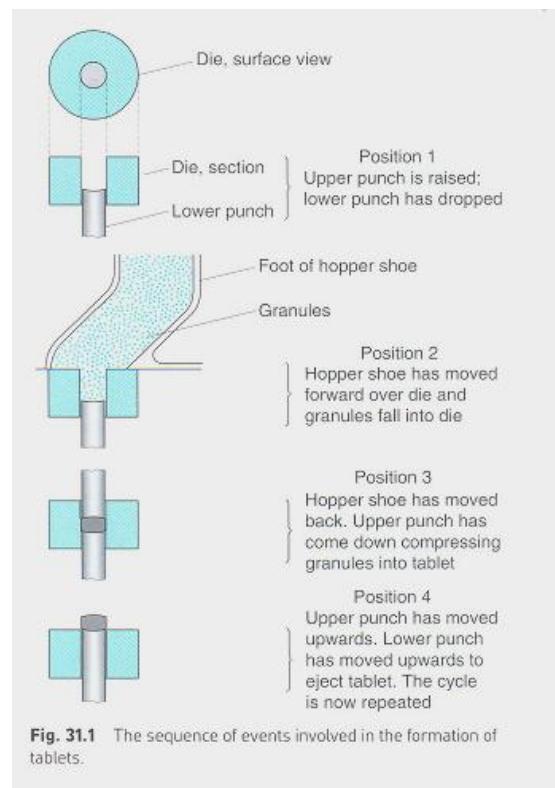
On turning the driving wheel: *لما اسعد الجهاز*

لتنبض الحجارة

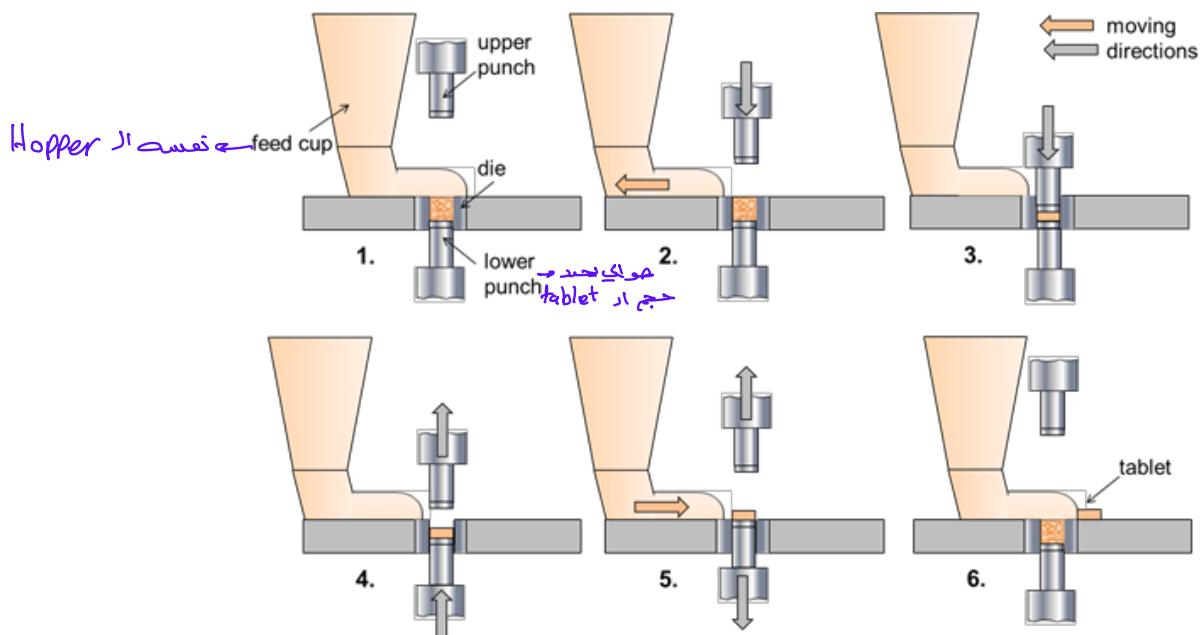
على الرسالة

1. Upper punch rises.
2. Feeder (hopper shoe) moves until becomes over the die.
3. The lower punch drops to a position controlled by the capacity regulating screw.
4. The hopper shoe moves aside leaving the die filled with powder.
5. Lower punch ^{بابت} *remains stationary* while upper punch comes down *هو المصنف من المطبخ* compressing the powders into a tablet.
6. The upper punch rises out of the die and the lower punch rises also to eject the tablet.

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Tablet presses

هذا الجهاز المستخدم بالمصانع حيث رح ينتج
كميات اكبر من الـ tablet ويتكون من اكثور من die

2- Rotary press (multistation press)

- The rotary tablet machine consists of three parts:
 - An upper part carrying the upper punches
 - Lower part carrying the lower punches
 - Central part carrying the dies
- Both the die table and punches rotate together during operation
- It can press tablets in a rate higher than 10 000 tablet/min.
- Number of dies and sets of punches can vary considerably from 3 to 60.

عدد الـ die والـ punches يتراوح بين الـ 3-60

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Tablet presses

Rotary press (multistation press)

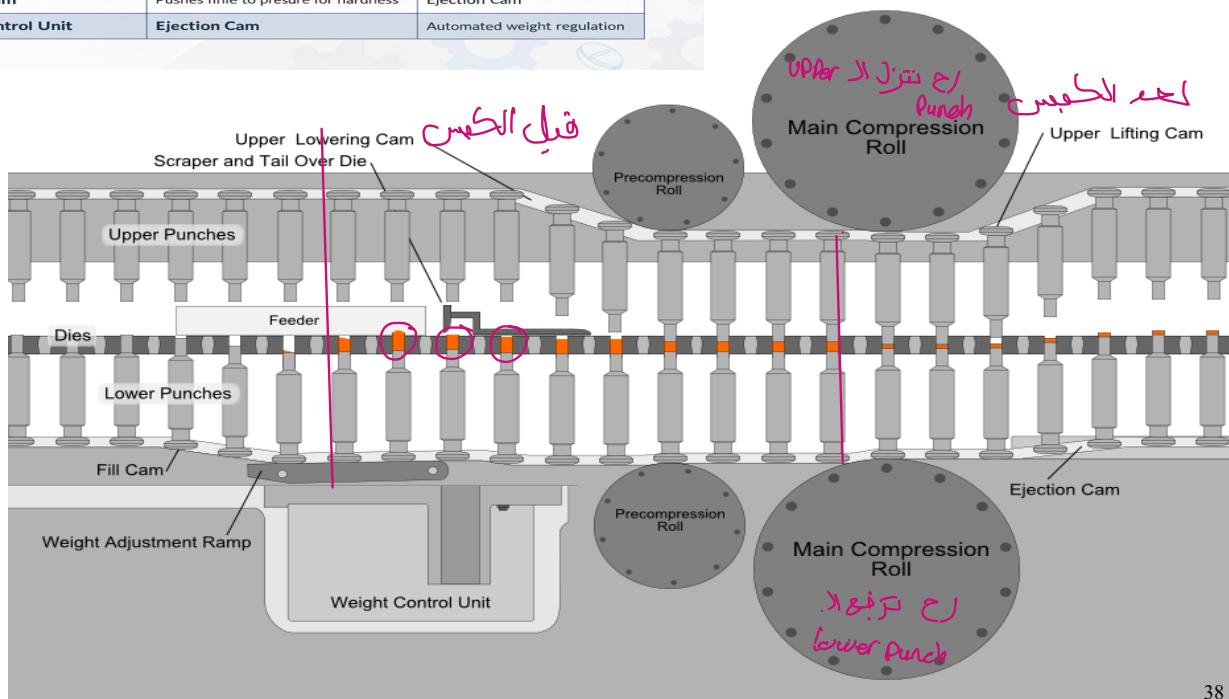
The process can be summarized by the following steps:

- When the lower punches pass below the feed frame they will be in their lowest point.
- The powder from the hopper is fed continuously to the feed frame so the dies will be filled with powder. الما في الما يمرق من فوقه الما **lower punch** يكون باقل نقطة الما عشان يعبي **hopper** الما **feed fram** (زي الما **die**)
- Then the dies will pass over the powder volume adjuster to expel the excess of the powder. الما اعبي الما **die** رح يطلع في **volum** زنادة فهذا الجهاز عنده زي الفرشاشية بشيل الما **volum adjuster** وهذا اول فرق بينه وبين الما **particels** الما **upper punch** رح يطلع في **volum** مارح يساهم بعملية الكبس حيث الما **upper particels** ويكبس الما **lower punch** بينما بالما **rotary** رح ينزل والما **lower punch** رح يطلع وهيد الاثنين اشتغلوا بعملية الكبس
- The lower and upper punches move towards each other to compress the powder. الفرق الثاني انه بالما **single punch** مارح يساهم بعملية الكبس حيث الما **upper punch** رح ينزل والما **lower punch** رح يطلع وهيد الاثنين اشتغلوا بعملية الكبس
- Both the upper and lower punches rise to eject the tablet.

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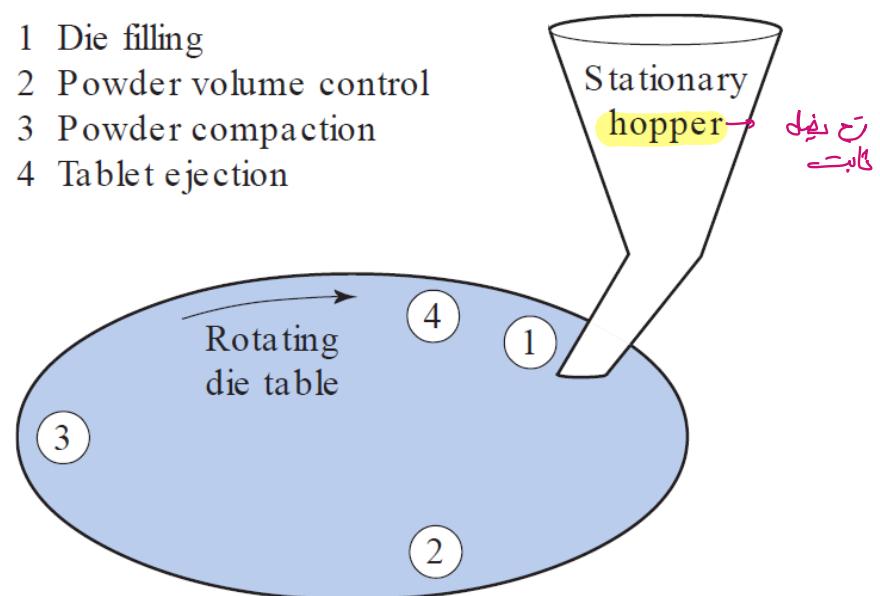
Rotary Tablet Press Components

Term		Function
Upper Punches	Move down to compress weight and or ejects and retract	Move downward Regulates weight with the tablet retract
Dies		Defines tablet shape and size
Dies	Distributes powder or into size	Lowers punch for filling
Feeder	Fill Cam	Fine-tunes tablet weight
Fill Cam	Fill Cam	Lowers punch for filling
Scraper	Removes excess powder	Applies final prevent capping
Precompression Roll	Scraper	
Main Compression Roll	Lifts upper punch after compression after compression	Upper Lifting punch after
Ejection Cam	Pushes finis to pressure for hardness	Ejection Cam
Weight Control Unit	Ejection Cam	Automated weight regulation



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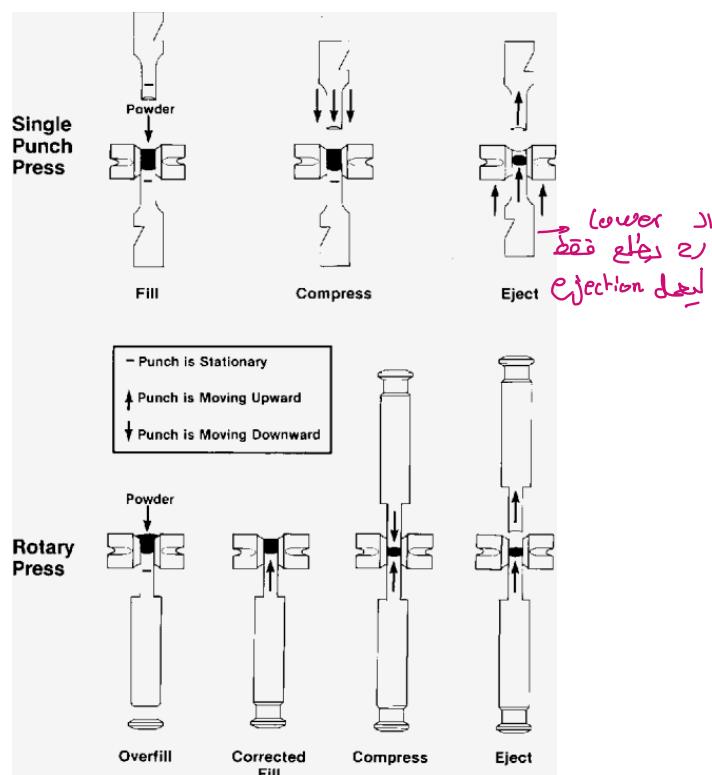
- 1 Die filling
- 2 Powder volume control
- 3 Powder compaction
- 4 Tablet ejection



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Tablet presses



Computerized hydraulic press (simulators)

هذا الجهاز يحاكي (simulate) الحركة للجهاز الذي يستخدمها بالانتاج زي rotary وال singl لاده هاي الاجهزه تعتمد على كثير parameter بالثر على جودة tablet الي رج تنتج زي قديه اضل ضاغط على ال tablet خلال عملية الكبس سجوسرعة الكبس... الخ حيث هذا الجهاز رح يساعدني اعرف كيف اتحكم بهاي ال parameter

- For computerized hydraulic presses the movement of the punches can be controlled and varied considerably. نقدر نتحكم بحركة ال punch وكيف رح يكبسو ال tablet في القالب عشان يحاكي حركة ال lower and upper parameter ويشوفو شو احسن اقدر
- Tablets can be prepared under controlled conditions with respect to the loading pattern and loading rate. → **هندل من لا اكي لبي Parameter التحكم فيه**
- Possible applications are the investigation of the sensitivity of a drug to such variations or to mimic the loading pattern of production presses to predict scale-up problems. بتطلع عندي حبه مش متamasكة بدبي اعرف شو السبب هل سرعة التعبئة هي السبب ولا ال punch ما يكبسو بقوة كافية او ما معهم وقت يكبسو مني فبنستخدم هذا الجهاز لهذا الغرض

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حکایتیں قبل جسائیں
granulation ہے

Tablet production via granulation

The main aims of granulation before tabletting are:

خال عملیہ ال granulation ورح تزید ال bulk density

1. to increase bulk density of the powder mixture and thus ensure that the required volume of powder can be filled into the die.
2. to improve mixing homogeneity and reduce segregation.
3. to improve the flowability of powder to ensure complete and uniform filling of dies and therefore less weight and dose variation in the tablets.

برزید ال powder ورح تقلل الفراغات بینہم

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Tablet production via granulation

The main aims of granulation before tableting are:

4. to improve the compactability of powder by adding a **solution binder**, which is effectively distributed on the particle surfaces.

5. to ensure a homogenous color in a tablet by adding the color so that it is distributed effectively over the tablet surface.

تخیل تکبس مادہ **hydrophobic** المی مارح نقدر تفوت بینہم
عشنان ہیک خال ال **granulation** ورح اخلي المادہ
ال **hydrophobic** محاطہ بسادوہ **hydrophilic** وھیک المی رح تدخل
بینہم وتحسن ال **solubility**

6. to affect the dissolution process for hydrophobic poorly soluble particles by using fine particles and mixing them with a hydrophilic filler and a hydrophilic binder.

- Granulation methods are either **dry** or **wet**

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wet granulation حشيشة granulation حشيشة

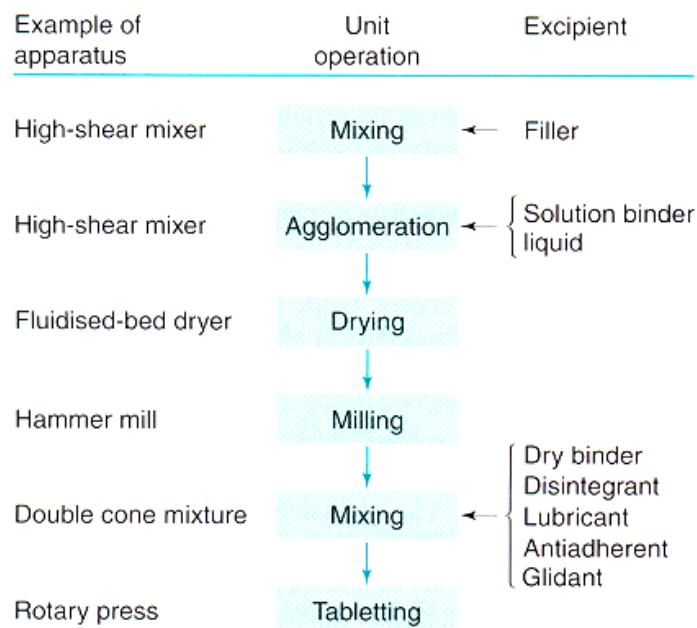


Fig. 31.5 Overview of the sequence of unit operations used in the production of tablets with precompaction treatment by granulation.

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Tablet production by direct compaction

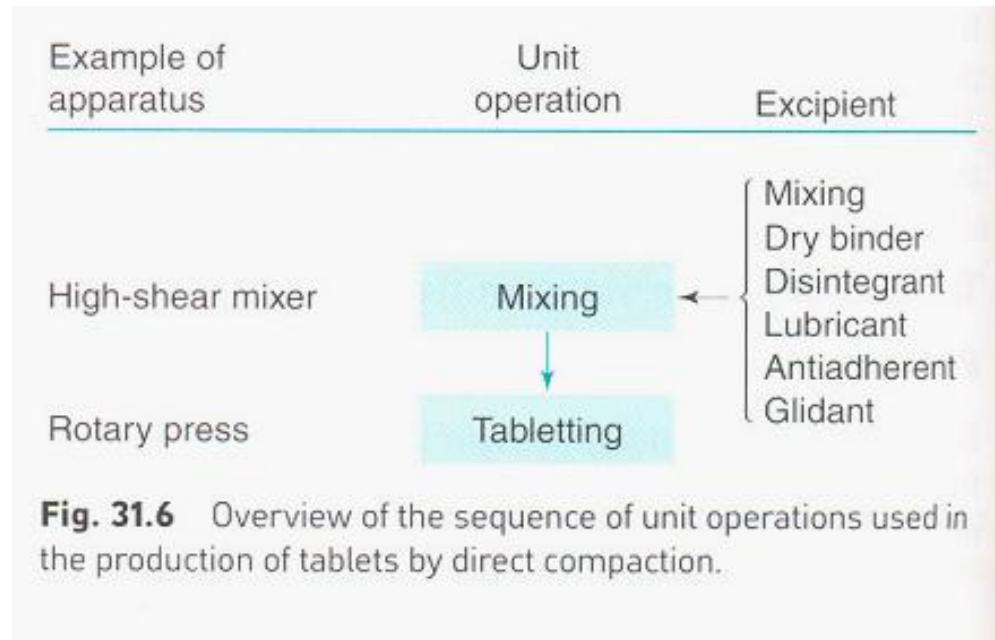
- This process involves mixing of the active ingredients and additives and compression directly in the tabletting machine.

active ingredient
الله mixing
الهم ecepiant
وال 2 بكونو solid
عمل مباشره

Advantages:

- Simple process
- Reduced production time and operation cost
- Improved product stability by avoidance of moisture and heat.

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Tablet production by direct compaction

Limitations: → direct compaction → gives

- Relatively large particle size must be used to have acceptable flowability and bulk density which:
 - may affect degree of mixing
 - Segregation may occur.
- It needs specially **designed fillers** which are usually more expensive than traditional ones.
- If the drug is the major component the application of direct compression depends mainly on the properties of drug.

موجة قدرجية

Molded Tablets

- Molded tablets are usually prepared from soluble ingredients so that the tablets are completely and rapidly soluble.
- After the excipient is blended with the drug, the powder mix is dampened with solutions containing high percentages of alcohol.
- The dampened powders are pressed into molds, removed, and allowed to dry.

1. المكونات وسرعة الذوبان

"Molded tablets are usually prepared from soluble ingredients so that the tablets are completely and rapidly soluble."

الشرح: يتم تصنيع هذه الأقراص من مواد قابلة للذوبان بالكامل في الماء أو الملعاب. الهدف الأساسي منها هو أن تذوب بسرعة ويشكل كاملاً مجرد وضعها في الفم أو خلطها مع القليل من الماء. لهذا السبب، غالباً ما تُستخدم للأدوية التي تحتاجها لتفطير مفعولاً سريعاً.

2. عملية الترطيب (الذوبان)

"After the excipient is blended with the drug, the powder mix is dampened with solutions containing high percentages of alcohol."

الشرح: بعد خلط المادة الفعالة (الدواء) مع المواد المضافة (المكونات) أو السكر مثلاً، يتم ترطيب هذا المسحوق الجاف.

لماذا الكحول؟ يستخدم محلول يحتوي على نسبة عالية من الكحول بدلاً من الماء الصرف، لأن الكحول يساعد في جعل الخليط رطباً بما يكفي للتشثيل، ولكنه يبخر بسرعة لافقة، كما أنه يمنع ذوبان المكونات السكرية تماماً أثناء التصنيع، مما يحافظ على نكهة القرص.

3. التشكيل والتجفيف

"The dampened powders are pressed into molds, removed, and allowed to dry."

الشرح: يتم ضغط هذا المسحوق "الميلل" (Molds) تطهيرها شكل القرص. بعد ذلك، تُخرج من القوالب وتُترك لتجفف. عندما يتبخّر الكحول، تُنفق أقراص ملنة لكنها "جافة" قليلاً وهذا ما يسمح لها بالذوبان فوراً عند الاستخدام.

باختصار، هذه الأقراص تعتمد على "الصب في قوالب" وهي رطبة تم تجفيفها، بدلاً من "الكبس القوي" لمساحيق الحافة، والهدف هو المساعدة القصوى في الذوبان.

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العاديَةِ زِيَ الْتَّبَلْتِ الْمَوْلَدِيَّةِ الْمَوْلَدِيَّةِ الْمَوْلَدِيَّةِ الْمَوْلَدِيَّةِ

Molded Tablets

- Solidification depends upon crystal bridges built up during the subsequent drying process and not upon the compaction force.
- They can be prepared in small or large scale.
- They are not common nowadays.

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Tablet excipients

عبارة عن حشوات يستخدمها لـ أكبر حجم tablet

Diluents (Fillers)

- Materials used to increase the bulk volume of powder and hence the size of the tablet.
- Tablets weigh at least 50 mg. اصغر tablet ممكن تلقيتها حجمها رح يكون 50mg ، طيب مرات الـapi بتكون 5mg او 10mg عشان رح استخدم الـ diluent عشان امبر حجمها
- They are not necessary if the dose of drug per tablet is high. اذا كانت الـapi كميتها كبيرة مارح احتاج الـ

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Tablet excipients

هذول الخصائص لكل ال excipient مش

Diluents (Fillers)

- The ideal diluent should fulfill a series of requirements such as:

معد خاصلة،) تفاعل
1. be chemically inert →
2. be non-hygroscopic → ما يتمتع بروبوس
3. be biocompatible
4. be color compatible → لون مماثل (كافئ
5. possess good biopharmaceutical properties
6. possess good technical properties (su
7. no chemical or physical changes on a
8. acceptable taste → لحم مقبول
9. be cheap → خفيف

8. acceptable taste → مقبول
9. be cheap → رخيص

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Tablet excipients

Examples on diluents:

• Lactose

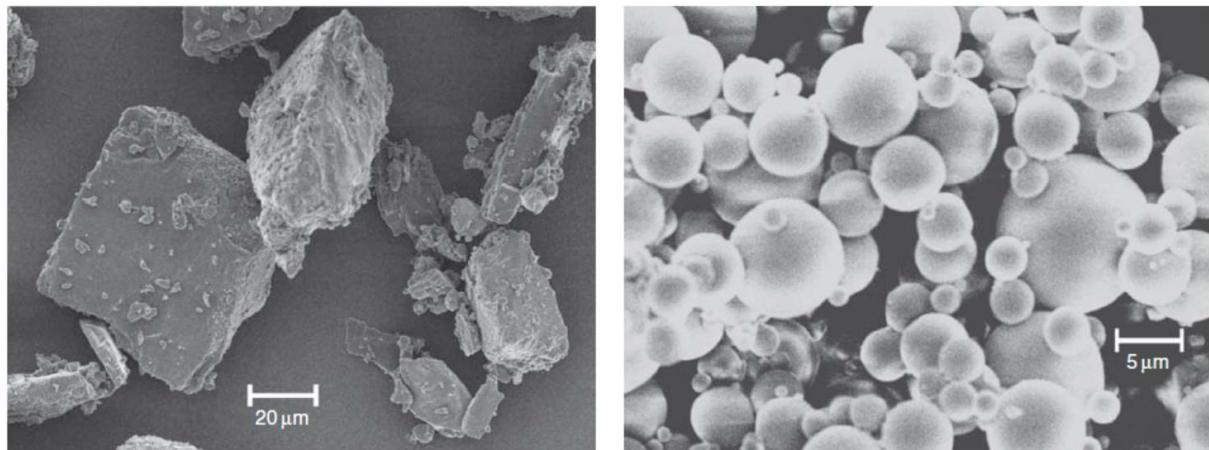
- The most commonly used because of good properties (dissolves readily in water, has a pleasant taste, non-reactive, non-hygroscopic, has good compactability) لactose مانقدرات علیه دواعیه filler می باشد
- Its main limitation is that some people have **intolerance to lactose**.
- In the solid state, lactose appears as various isomeric forms, depending on the crystallization and drying conditions. It is found as:

Lactose حالتان
Solid form بار

- monohydrate $\xrightarrow{\text{Water}} \text{Lactose molecule}$ ماء \rightarrow مolecule لكتوز
- anhydrous $\xrightarrow{\text{Water}} \text{Lactose}$ ماء \rightarrow لكتوز
- amorphous (spray dried lactose)

العنصر الثالث **solid form** **lactose** **عنده 3 أشكال** **بالطبيه** **وحده** **يحدد** **الشكل الناتج**؟ **drying** **وال** **crystallization** **وال** **condition**

high surface area \rightarrow high flowability



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Tablet excipients

Examples on diluents:

• **Celluloses** organic

احنا بنستخدم مشتقات cellulose عشان هيكل
كتب celluloses

- Advantages
 - Biocompatible
 - Chemically inert
 - Have good tablet-forming and disintegration properties

مش بس filler، يستخدمهم كمان ك binder و disintegrant

- They are used also as dry binders and disintegrants in tablets.
- They are compatible with many drugs but, owing to their hygroscopicity, may be incompatible with drugs prone to hydrolysis in solid state.
- The most common type of cellulose powder used in tablet formulation is microcrystalline cellulose (Avicel®).

[MCC]

مطهّب

ال celluloses بمتصلو الرطوبة فلو جبت اي api حساسة للرطوبة
احسن خيار استخدم ال celluloses

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Tablet excipients

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Dicalcium phosphate dihydrate (Emcompress®)

- Insoluble in water and nonhygroscopic but is hydrophilic, i.e. easily wetted by water.

Phosphate و جو سیس

بما انه **alkalin** ما بقدر استخدم المواد الى بتتكسير

- It is slightly alkaline and thus may be incompatible with drugs sensitive to alkaline conditions.
- It can be obtained both in a fine particulate form, mainly used in granulation, and in an aggregated form, used in direct compression.

Dicalcium phosphate dihydrate anhydrous

raw material

fine particles → granulation

aggregates → direct compression

Tablet excipients

Piller $\xrightarrow{\text{نحوة}} \xrightarrow{\text{نفع}} \text{binder}$

3 civil service
lawyer

Sugarcane (serves also as binder)

SUCROSE - inert carrier – Sucrose-based tablet diluent-binders are available under a number of trade names which include: *to use &*

- Sugartab® (90 to 93% sucrose plus 7 to 10% invert sugar).
- Di-Pac® (97% sucrose plus 3% modified dextrins),
- NuTab® (95% sucrose, 4% invert sugar, and 0.1 to 0.2% each of cornstarch and magnesium stearate).

الحلويات سكر Confectioner's sugar is a mixture of sucrose (not less than 95.0%) and corn starch.

Tablet excipients

Other examples on diluents:

- Glucose
- Sorbitol, Mannitol
 - They are optical isomers.
 - Used in chewable tablets since they have negative heat of dissolution
- Calcium carbonate
- Calcium sulphate dihydrate

تعطيك شعور بارد زي لما تأكل حبه ملمس بتحس
ببرودة بالحق



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Tablet excipients

• Direct compression diluents:

– Examples on diluents:

- Spray dried lactose, Anhydrous lactose
- Sucrose based excipients (Di-Pac®)
- Sorbitol, mannitol
- microcrystalline cellulose (Avicel®)
- Dicalcium phosphate (anhydrous, dihydrate)
- Spray crystallized maltose dextrose
- hydrolyzed starches (like Emdex®)
- Pregelatinized starch (e.g. Starch 1500®)
- Ludipress® (93.4% α -lactose monohydrate, 3.2% polyvinylpyrrolidone and 3.4% crospovidone)

حيث انه في direct compression بالـ diluant يكون لها خصائص خاصة

حيث يعرضه انه الصاد
التجاريه حفظ

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Tablet excipients

- **Coprocessed Excipient Products:**

- Ludipress® (93.4% α -lactose monohydrate, 3.2% polyvinylpyrrolidone and 3.4% crospovidone)
- Cellactose 80_{TM} contains α -lactose monohydrate and cellulose powder
- Prosolv SMCC, silicified MCC, contains 98% MCC and 2% colloidal silicon dioxide, which provides a better granule flow and an opportunity for smaller and denser tablets upon direct compression.
- MCC microcrystalline Cellulose

هون بحكيلى عن ال excipient الي ببتكون من اكتر من مادة combination طيب ليش بستخدمهم؟
لانه ممكن ال excipient الوحدة ما تعطيني كل ⁶¹ الخصائص الي بدبي ايها

حكينا الي قبل عن اول نوع من ال excipient الي هو ال **filler** هسا بدنا ننتقل للنوع الثاني الي **bindr**

Tablet excipients

رح استخدمهم عشان تخلی ال tablet تضل متماسكة

Binders (Adhesives)

- A binder is added to ensure that granules and tablets can be formed with the required mechanical strength.
- Typical concentration 2 – 10 % by weight.
- Binders can be added to a powder in different ways
 - ① As a solution which is used in wet granulation (solution binder) محلى اهنيف الد binder
 - ② As dry powder which is mixed with the other ingredients before wet granulation wet mass
 - ③ As a dry powder which is mixed with other ingredients (powders or granules) before compaction (dry binder) dry Powder
بآخر حملته mixing قبل ما افخده dry powder
- Solution binders are generally considered the most effective

حكينا انه ال binder الي نوعين واحد dry والثاني wet solution binder
dry binder وهو بجكي انه ال solution binder احسن من ال
لأنه ال solution binder لما ينشف روح يعمل bridge وروح يمسك
ال particel بشكل ممتاز

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Tablet excipients

Binders (Adhesives)

- Examples:

organic ← Common traditional solution binders (starch, sucrose and gelatin)
 — Acacia, sodium alginate, tragacanth. → wet binder

inorganic ← Synthetic polymers used as solution binders (Polyvinylpyrrolidone (PVP), hydroxypropyl methylcellulose (HPMC) and methyl cellulose, polyethylene glycol)

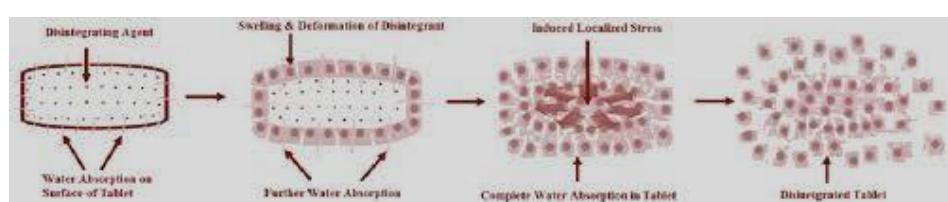
- Dry binders include: microcrystalline cellulose(MCC), methylcellulose, polyethylene glycol and crosslinked PVP).

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Tablet excipients

Disintegrants

- A disintegrant is added to most tablet formulations to facilitate the breakup (disintegration) of the tablet when it contacts water in the GIT, which promotes rapid drug dissolution.
- The disintegration process for tablets occurs in two steps: First, the liquid wets the solid and penetrates the pores of the tablet. Then, the tablet breaks into smaller fragments.



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الخطوة الاولى انه لما حبة الدوا تفوت على المهد
 water particel تجتمع على السطح وهيك رح
 تسهل عملية ال water penetration لل water penetration
 تسهل الخطوة الثانية وهي انه ال water يصير
 يدخل tablet وتكسرها ليصير الها
 على surface area

ال Disintegration
 يحصل بـ

Tablet excipients

Disintegrants

- Several mechanisms of action have been suggested.
- The most common and effective disintegrants act via a swelling mechanism. disintegration mechanism disintegrant swelling mechanism
- Disintegrant can be added to the granules just before compaction (extragranular) or to the powder before granulation (intragranular) or part of the amount is added intragranularly and the other part extragranularly.

محتوى انتيجرانت جزء
قبل ما اعمل (الآن)
جزء بعد ما اعمل

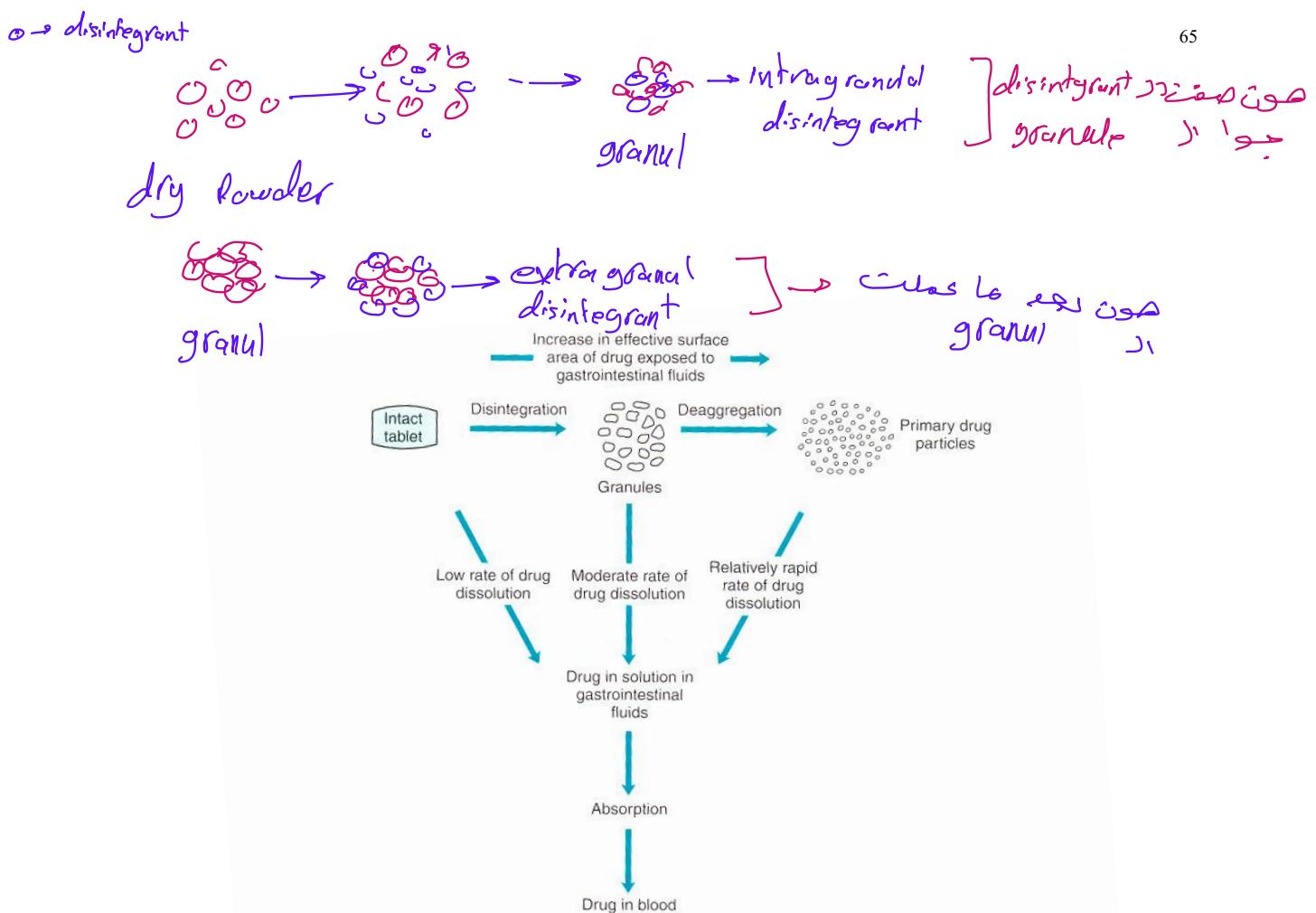


Fig. 31.7 Mechanistic representation of the drug release process from a tablet by disintegration and dissolution. (From Wells, J.I., Rubinstein, M.W. (1976) *Pharm. J.*, **217**, 629.)

Tablet excipients

Disintegrants

Examples:

• Starches (up to 10 %)

- Most commonly used
- Include corn starch, potato starch and rice starch, wheat starch.
- Advantages
 - Safe (used as food)
 - Low cost \rightarrow رخيصة
 - efficient \rightarrow فعالة
- Disadvantages
 - Poor flowability and compressibility \rightarrow صعب الالصاف \rightarrow منخفضة
 - hygroscopicity \rightarrow بمحاذة الماء
- Some new modified forms of starch have been developed like pregelatinized starches (about 5 % conc. Used).
 - \rightarrow بضمينة ملحقة أقل من لا starch
 - \rightarrow بضمينة ملحقة بتحفظ فعالة

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Tablet excipients

Disintegrants

Examples:

- Sodium starch glycolate (Primogel®, Explotab®)
- Alginates
- Crosslinked polyvinylpyrrolidone (CROSS PVP)
- Cellulose and Cellulose derivatives

- Include microcrystalline cellulose and carboxymethyl cellulose.

- Effervescence inducing disintegrants \rightarrow disintegration بصير من ال نفسها مش من formula مادة انا بضيفها عليها

 - Used in effervescent tablets
 - Composed of Citric or tartaric acid with a source of CO₂ (like bicarbonates or carbonates) \rightarrow acid مع ال base واطلاق ال CO₂ هو disintegration التي رح يعمل ال

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Tablet excipients

④ Glidants flow رح يحسنو ال

- These are materials intended to promote the flow of powders or granules.
- Examples:
 - Colloidal silica (0.2 %)
 - Talc (1 -2 %)
 - Mg stearate (< 1 %) محتوى الـ Mg من 1%
 - Maize starch

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Tablet excipients

⑤ Lubricants die تلزق بال formula تمنع ال

- These are materials intended to reduce friction during tablet ejection between tablet and the walls of the die.
الـ tablet لما تلزق بال die رح تنكسر لما اعمل الـ ejection ورح تطلع tablet متداشكة
- High friction during tableting may cause a series of problems (capping, fragmentation of tablet, vertical scratches on tablet edges) and may even stop production.



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Tablet excipients

ممكن يكون في مشاكل بالtablet التي عملتها
بسبب الـ lubricant الذي ضفتها

Lubricants

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

الـ lubricant يمكن تضييف
الـ particels الروابط الـ بين الـ particels وهيدر رح تطلغز الحبة غير
متناسكة فبحل المشكلة عن طريقة اضافة binder قوي او
زيادة كمية الـ binder

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.

- 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**

الـ lubricant عبارة عن مواد tablet عشان ما تخللي الـ die صبح؟
بس هذا الاشي يعني انه الـ particel حواليها طبقة hydrophobic ويعني انه

الـ disintegratin رح يصير اصعب وبالتالي الـ dissolution مكن ما يصير واكثر مادة

بتعمل هذا الاشي هي الـ mg sterate عشان هيكل بتجل المشكله حيث انه ما بنضيف كمية

كبيرة منه وبنضيفه باخر خطوة mixin يعني ما بنعمل الله mixing كثير

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Tablet excipients

- Lubrication is achieved by mainly two mechanisms:

كيف بخسيف الـ lubricant

a) *fluid lubrication*

زي بخاخ الزيت الي نستخدمه للقلاليه الهوائية

- 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.

نادرا ما نستخدمهم بالـ tablet بالـ capsule

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Tablet excipients

هذا يكون powder وحجمها لازم يكون صغير

b) boundary lubrication

- 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.
لubricant عن طريق أنها ما عندها احتكاك عشان هي رح
تزرق بسهولة بين الـ particel
- Examples: Stearic acid and its salts (e.g. Mg stearate is the most widely used lubricant), sodium lauryl sulphate, sodium stearyl fumarate, glycetyl behenate, sodium benzoate and PEG.

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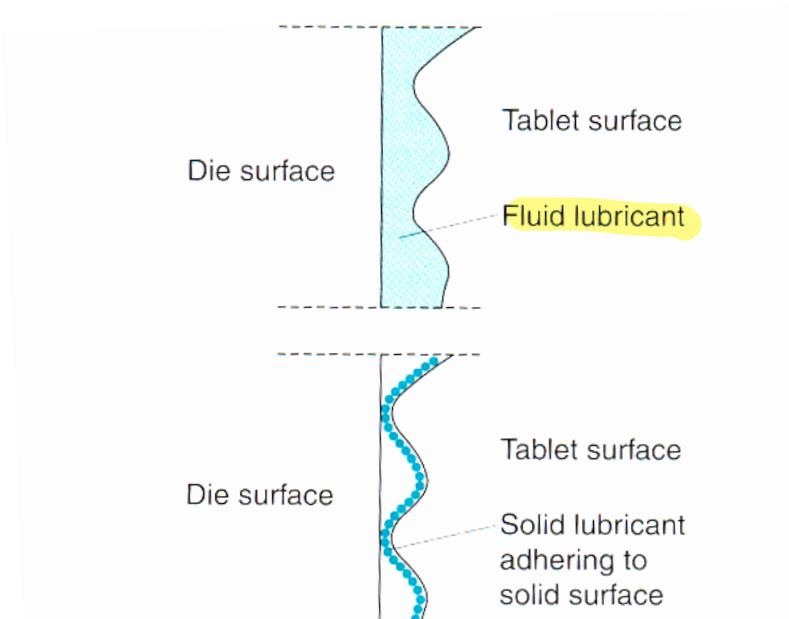


Fig. 31.8 Schematic illustration of lubrication mechanisms by fluid and boundary lubrication.

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Tablet excipients



⑥ 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. 
ر اشوف كثير من ال **lubricant** تشتغل **anti adherence**
- However, other substances with limited ability to reduce friction can also act as antiadherents such as talc and starch.

های رح تمنع الاحتكاك الي بين ال powder و بين
ال die and punches طیب شو فرقها عن
ال lubricant
ال lubricant بمنع الاحتكاك بين ال particels
نفسها و تمنع الاحتكاك بين ال pwder و بين ال
 بينما ال anti adherent بمنع الاحتكاك الي بين
ال powder وبين ال die فقط

Tablet excipients

7 Sorbents

وظيفتها الأساسية أنه رح يصير adsorption على سطحها من oil او سائل ثاني ويعدين يصير لها incorporation بال formula يال solvent يعني رح يحملو ال oil

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

Tablet excipients

Colors

- Colors are added to the tablets for the following reasons:
 - Elegancy الجاذبية
 - To help the patient to distinguish the product عسان يدرنوا انه صار تغيرات خلال عملية
 - To provide control during manufacturing الطببي
 - To help in hiding color differences between drug and additives بسن لون دا آف دا عدو
- Colorants are added to uncoated tablets either as an insoluble powder or dissolved in the granulation liquid in case of wet granulation.
بضيف ال color اما as insoluble powder يعني بضيفها على السطح وما بخلطها مع المكونات وهيك الحبة لونها من برا اشي ومن جوا اشي ثاني او بذوبتها مع granulation liquid وهيك الحبة كلها لها نفس اللون
- Care should be taken in wet granulation as migration of soluble color may occur during drying.

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Tablet excipients

Colors

الالوان الصناعية ممكن تكون سرطانية

- Many synthetic dyes were decertificated because of their carcinogenic effect.
الاون ال natural مشكلتها انها unstable
- 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

1. تصنيف الألوان (أمريكا vs أوروبا)

- في أمريكا (FD&C): رموز تُعطى غالباً للألوان الصناعية المعتمدة للأغذية والأدوية والتجميل.
- في أوروبا (E numbers): رموز تشمل كل الإضافات (سواء طبيعية أو صناعية) المسموح بها في الغذاء.

2. أصباغ الليلك (Lakes)

- هي أصباغ يتم تثبيتها على مادة صلبة (أكسيد مائ).
- تتميز بأنها تُستخدم كبودرة جافة وغير قابلة للذوبان (تُستخدم لتلوين الأسطح والمنتجات الجافة).

Tablet excipients

Flavors and sweeteners

- 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.
- Flavors are usually used in effervescent, chewable tablets and other tablets intended to dissolve in the mouth.

• الغرض منها: تضاف المكملات لإعطاء القرص طعمًا أفضل أو لإخفاء الطعم غير المستساغ للدواء.
• الحساسية للحرارة: المكملات غالباً ما تكون حساسة للحرارة (Thermolabile)، لذا لا يمكن إضافتها قبل العمليات الصناعية التي تتطلب تسخينها
• الاستخدامات الشائعة: تُستخدم عادةً في الأقراص الفوارة (Effervescent)، والأقراص القابلة للمضغ (Chewable)، وأي أقراص أخرى مُصممة لتذوب في الفم.

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Tablet testing

اذا بدأ اعمل دوا جديداً واسجله لازم ينجح بعدي
الاختبارات
وبرضه هاي الاختبارات بتعملها للـ **control**
للادوية الموجودة من زمان عشان اثبت انه لسا
يشتغل مني

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.
- Uniformity of dose is tested in two separate tests: **uniformity of weight** and **uniformity of content of active ingredient**.

بحكيك هون انه الفروقات البسيطة بين الـ tablets زي الوزن والـ weight deviation
مثلاً لو عندي حبة فيها API يساوي 100mg والـ deviation يساوي 10% شو يعني؟ يعني
الحد المقبول لاختلاف الـ API من حبة لحبة يكون من 90-100 ونسبة الـ 10% بالمية تختلف
حسب قوة الدوا، يعني الأدوية الي لها low therapeutic index اكيد الـ deviation يكون
أقل طيب مين رح يحدد نسبة الـ pharmacopie deviation

عند تجربة tablets لا تستوف المعايير
بالتالي لا يتحقق
ـ "Uniformity of dose"

ـ "Uniformity of weight"
ـ "Uniformity of content of active ingredient"
ـ "Uniformity of active ingredient"

كيف اعمل هذا الـ **uniformity of weight test**؟
 بحسب 20 حبة يشكل عشوائي من الدوا، بعدها يوزنهم ويقسم الوزنـهـ اليـ طـلـعـتـ مـعـيـ عـلـىـ عـدـدـهـمـ (20)ـ عـشـانـ اـطـلـعـ
 الـافـرـيجـ طـيـبـ طـيـبـ لـيـشـ طـلـعـتـهـ؟ـ عـشـانـ اـطـلـعـ الـ SDـ لـانـهـ لـوـ
 حـبـهـ وـحـدـهـ طـلـعـتـ بـرـاـ الـ SDـ يـعـنـيـ اـنـهـ مـخـالـفـةـ
 طـيـبـ شـوـ اـعـمـلـ بـعـدـهـ؟ـ بـرـجـعـ اوـزـنـ كـلـ حـبـهـ لـحالـ وـبـقـارـنـهاـ
 بـالـ SDـ اـذـاـ كـانـتـ بـالـ rangـ المـسـمـوـحـ اـذـاـ بـعـتـرـهـ نـاحـجـهـ
 بـالـ testـ كـانـتـ بـرـاـ الـ SDـ rangـ ماـ بـتـكـونـ نـاجـجـةـ

Tablet testing

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

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طـيـبـ **Uniformity of active ingredient**ـ كـيـفـ اـعـمـلـهـ؟ـ
 بـجـيـبـ 10 tabletـ بـطـحـنـ كـلـ حـبـهـ وـبـذـوبـهـ بـ solutionـ وـبـعـدـهـ بـاـخـذـ
 عـيـنـهـ مـنـهـ وـبـقـيـسـهـاـ بـالـ Uvـ وـبـشـوـفـ كـمـ الـ Concـ الـيـ طـلـعـ لـكـلـ حـبـهـ
 بـعـدـهـ بـقـارـنـ النـتـيـجـةـ الـيـ طـلـعـتـ مـعـيـ بـالـ meanـ اـذـاـ كـانـتـ خـارـجـ
 الـ rangeـ بـتـكـونـ فـشـلـتـ بـالـاـخـتـيـارـ
 لـوـ كـانـ عـنـدـيـ الـقـيـمـهـ اـقـلـ مـنـ الـ rangeـ يـعـنـيـ فـيـ مـشـكـلـهـ
 بـالـ rangـ لـوـ كـانـ اـكـبـرـ مـنـ الـ rangـ بـكـونـ عـنـدـيـ مـشـكـلـهـ
 بـالـ safetyـ

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.

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طیب حکیتا کیف رح نعمل مل **test** منهم هسا بدن
نعرف ای واحد بدن نستعمل

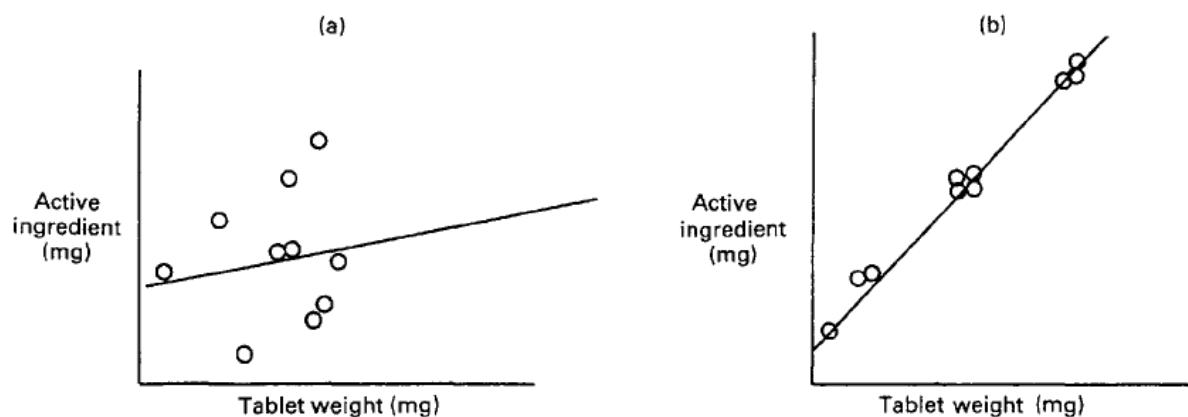


Fig. 27.18 Correlation between amount of active ingredient and tablet weight for (a) a low dose (drug content 23% of tablet weight) and (b) a high dose (drug content 90% of tablet weight) tablet. (From Airth, J.M., Bray, D.F., and Radecka, C. (1967). *J. Pharm. Sci.*, 56, 233–235.)

235. خلونا نشوف هذا الـ **curve**. رحلاحظ انه مافي اي علاقه بين الـ **weight** وبين الـ **Api** يعني ممكن الاقي حبه وزنها اكتر من المطلوب بس الـ **Api** فيها اقل من المطلوب وهومن ما رح اقدر استخدم الـ **weight** لانه **Api** مارح يعبر عن كميته **uniformity of contact** عشان هيك بروح مباشره لهون كميته الـ **Api** بالحبه الواحده اصلا لازم تكون قليله يعني اقل من **25%** عشلن هيك مارح يربط الـ **uniformity of weight**

اذا جبت دوا. فيه api عاليه مثلا اكتر من 25% من وزن الحبه عباره عن Api لما اجي اوزن مجموعه من ال tablet منهرمنه واشوف كم فيهوا اجي امثل النتائج على curve Api وعندى العلاقة r^2 طريده يعني في correlation كل ما زاد حجم الحبه زاد كمية api وهذا ندول الادوة الي زي هيلك بحسب الهم r^2 لانه بهاي الحاله رح uniformity of weight uniformity of contact weight بحسب وجود ال correlation بحسب weight r^2 وكميه api

Tablet testing

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%	<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

عاجلاً **uncoated** **اذا عندي دوا في Api نسبتها 40% مبس بالجهاز الواحد في 20mg اي test راح اعمل**

Solid oral drug products:

d) Uniformity of dosage units:

<905> UNIFORMITY OF
DOSAGE UNITS (USP
monograph)

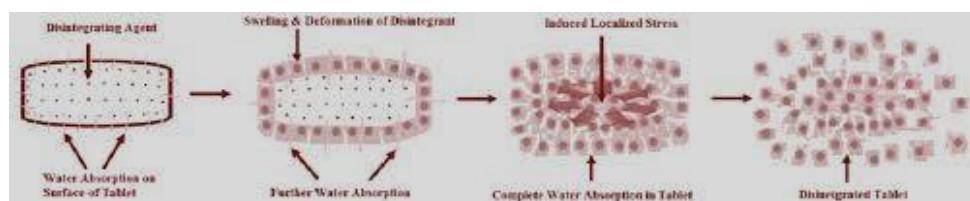
رح اختبر هل الحبة رح تتكسر ب solvent
 معين ووقت معين او لا
 اذا ما تتكسر رح اعرف انه في مشكله با
 ممكن disintegration او اشي
 ثاني عشان هيك بضل اعدل على
 formula واعيد ال test حتى ينجح وتتكسر
 الحبة

Tablet testing

Disintegration

• **خطواتها** [من قبل] 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.



صح هذا ال test رح يعطيك تصور عن ال drug solubility بس مش دائم رح يعبر عن ال dissolution test⁸⁵ لانه الي يعبر عنه هو ال dissolurion test في حالة وحده بقد استخدم disintegration test ويكون يعبر عن عن highly hydrophlic وهي لما الدوا يكون dissolution لل

→ (سنه الالمنيوم)

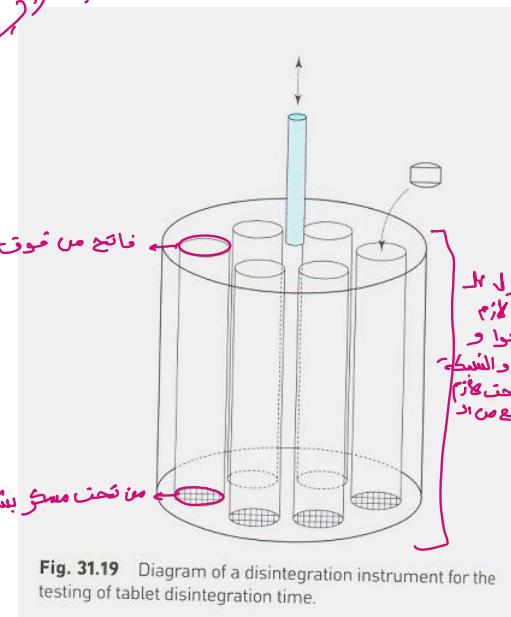
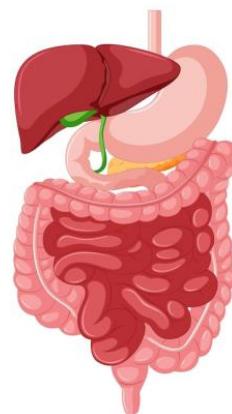


Fig. 31.19 Diagram of a disintegration instrument for the testing of tablet disintegration time.



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.

87 باللحظة التي يختفي فيها الحبة بسجل

drug release يعبر عن ال

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. **نعمل هذا الـ in vitro test بالـ vitro (يعني باللاب)**

- During the dissolution study the cumulative amount of drug that passes into solution is studied as a function of time.

ندرس الـ drug release بالـ vitro يعني قدره الـ drug release بالـ vitro تغير خلال وقت معين **function of time** يعني باخذ عينه من الـ solution الى ذوبان الحبة فيه وشوف كم تركيز الدوا فيها فيعرف كمرصار في release من الحبة

مثلاً بعد خمس دقائق ذاب 10% من الحبة

وبعد بنين باخذ عينه ثانية بعد عشر دقائق وبلاحظ انه ذاب 15% وهذا

بدى اشوف تأثيرات
التحغير بالـ formula
على الـ dissolution

Aims of dissolution studies:

ـ To indicate the performance of a formulation under in vivo conditions.

ـ To evaluate the effect of formulation and process variables on the bioavailability.

ـ To ensure that preparations comply with product specifications.

ـ بدى اشوف النتائج الي طلعت هل تتوافق مع الـ pharmacopie

كيف اعمل هذا الـ **test**؟

بجipp الحبّه بحطّها بـ **vessel** وبعبيه
بـ **solvent**
هذا الـ **solvent** الي بدي استخدمه لازم
يكون مواصفات معينه محدديته
بالـ **pharmacopia**
زي ١,٢

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.

1
2



شو هي الـ **solvent**؟
بمكنته اعلى من **sink condition** فمثلاً لما حط الحبّه بالدوا
ويذوب منها اشي لازم مباشره اخذ الـ **solution** الي في كمية الدوا المذاب وابدله بالـ **solvent** الي مافيه
عشان احافظ على فرق التركيز ويصل الـ **dissolution** ماشي تمام
لازم احافظ على نسبة الـ **solubility** فيها حيث ما تتعدي الـ 10% متراً
عشان اضل محافظ الـ **sink condition**
ليش بدي احافظ على الـ **sink condition** لانه المعدّه فيها **sink condition** وانا بهذا الـ **test** بدي
احاكي الوضع بالـ **vivo**

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. **حسب الدوا او ظروف الفحص رج تختلف** **PH**
- A number of official and nonofficial methods exist for dissolution testing, which can be applied for both drug substances and formulated preparations.

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

المعنى: يتم تحليل كمية الدوا التي ذابت في السائل بطرفيتين حسب الهدف من الاختبار:

1. التحليل **مرة واحدة** (Analyzed once):
 - يتم أخذ عينة في وقت محدد (مثلاً بعد 30 أو 45 دقيقة).
- الهدف: التحقق من الجودة الروتينية للتأكد من أن الدوا يذوب ضمن المعايير المطلوبة (مثل ادوية **Immediate release** التحرر السريع).
2. التحليل في سلسلة اوقات متتابلة (Series of consecutive times):
 - يتم أخذ عدة عينات في اوقات مختلفة (مثلاً بعد 15، 30، 60، 120 دقيقة).
 - الهدف: رسم ما يسمى بـ "منحني الدوا" (Dissolution Profile) او عند مقارنة دوا جديداً بدوا اصلي للتأكد من تطابقهما.

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توضّح هذه الجملة أن هناك طرقاً متنوعة لاختبار الدوا (Dissolution Testing)، وتتقسّم إلى نوعين:

- طرق رسمية (Official): وهي الطرق المعتمدة عالمياً في دسّتور الأدوية (مثل الـ **USP**).
- طرق غير رسمية (Non-official): وهي طرق قد تُستخدم في الابحاث أو التطوير الداخلي للشركات.

الهدف من هذه الاختبارات:

- تُستخدم للتأكد من مدى وسرعة ذوبان الدوا، وتُطبق على حالتين:
 1. المواد الدوائية الخام (Drug Substances): المادة الفعالة وحدها.
 2. المستحضرات الصيدلانية (Formulated Preparations): الدوا في شكله النهائي (مثل الحبوب أو الكبسولات) بعد خلطه مع المواد المضافة.

تُتّصّر الاختبار بهدف للتأكد من أن الدوا يذوب بشكل صحيح ليتمكن الجسم من امتصاصه، سواء كان مادة خام أو منتجًا ثانوياً.

Tablet testing

Dissolution test official

Stirred vessel methods

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

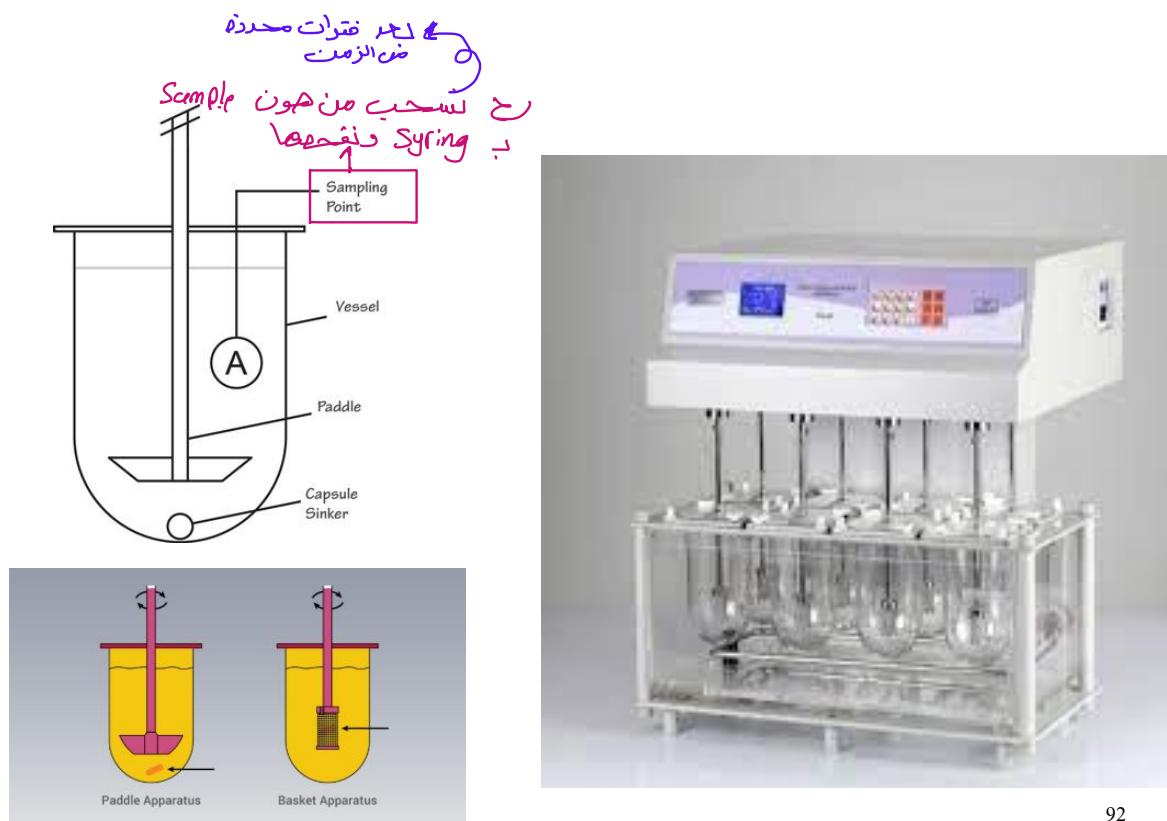
- Both use the same type of vessel, which is filled with certain volume of a dissolution medium of certain temperature.

بكون في vessel معينه temp and PH معينه slovent بكون معينه

- In the paddle method, the tablet is placed in the vessel and the dissolution medium is agitated by rotating the paddle. هاي ال vessel بكون فيها paddle ولا تلف حبه الدوة رح تلف agitation وتعمل

- 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.

ال vessel ممكن يكون فيها basket شكلها استطوانى وفيها screen واحدنا بنحط حبه الدوا جوا ال basket وبعدها ال basket بتصير تلف



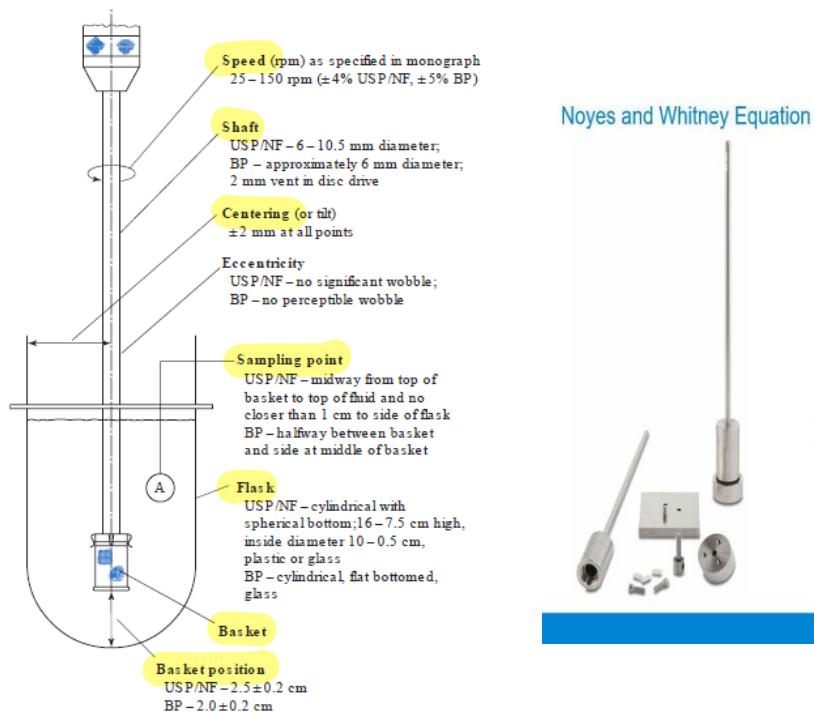
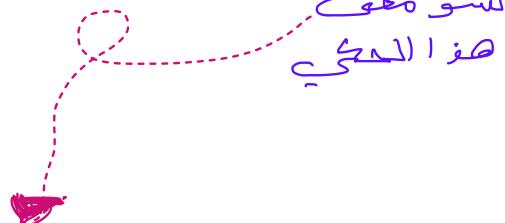


Fig. 30.20 • Diagram of a dissolution instrument based on the rotating-basket method for the testing of tablet dissolution rate. (Courtesy of Banakar, 1992, with permission.)

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basket method \rightarrow No floating problem
paddle method \rightarrow floating problem

نفس ال basket بس الفرق
انه بالـ basket الحبه رح
تكرن بالاستوانه الي
عليها شبكة يعني الحبه ما
رح تتطلع وتنزل لفوق
ومافي احتمال انها تطلع
من ال vessel بس
ممكن تطلع بكل
سهوله طيب اكيد في حل
للمشكله هاي صح؟ انه في
حل بجيبيو زي حديده
بربطوها بحبه الدوا وهيك
مارح تتطلع لفوق

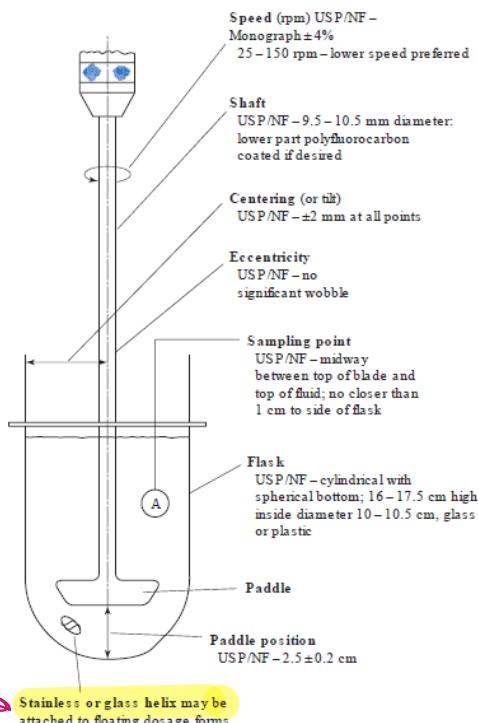


Fig. 30.21 • Diagram of a dissolution instrument based on the rotating paddle method for the testing of tablet dissolution rate. (Courtesy of Banakar, 1992, with permission.)

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Tablet testing

Dissolution test بجیب ال tablet وبخخ علیها ال solvent ببدل ما احاط
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 مخزن (ال solvent) يد رح نفخ \rightarrow منهار solvent

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

ال solvent الي رح يطلع بعد ما عملت ال pump (ضخ) على حبه الدوا \rightarrow

بجمعه عشان احل العینه

- Advantages

— Maintain sink conditions throughout the experiment

— Avoid floating of the preparation.



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هساحر نروح test الثاني وهو
ال mechanical strength حيث بده يقيس انه
ال tablet رح تتكسر خلال عمليات النقل او لا او
خلال التخزين (بده يقيس قدیه الحبہ بتتحمل
الضغط)

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: **mechanical strength** على **formulation** يعني ازيد **binder** او لا
 - To assess the effect of formulation and production variables on their resistance towards fracturing and attrition.
 - To characterize the fundamental mechanical properties of materials used in tablet formulation.
 - To control the quality of tablets during production (in-process control).

هذا **control** رح اعمل **processing** خلال عملية التصنيع (processing) مش بروح
in process control **tablet** وبعدين اروح افحصها بسمیه **control**

Tablet testing

Mechanical strength

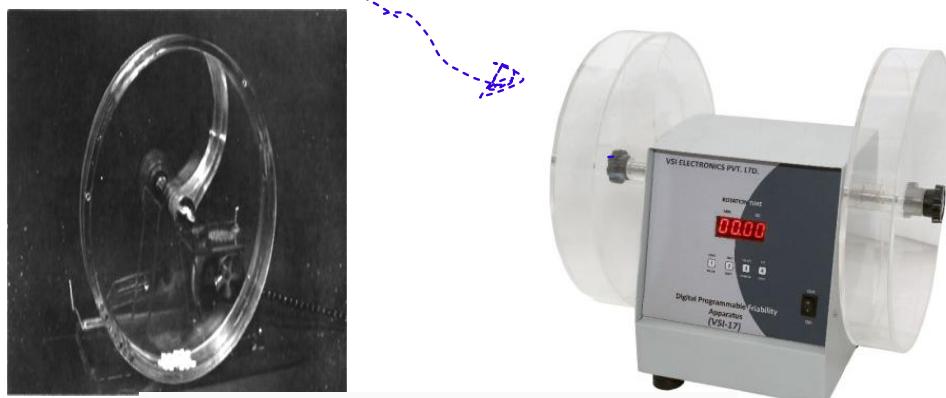
- The most commonly used methods for strength testing are the resistance to abrasion test (friability test) and the crushing strength (fracture resistance).

↓
Attrition tablet ارجاعی tablet مکانیکی tablet [Hardness]

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

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Fracture test نسخی ←

↓
non-optical test

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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. لما اجي اقارن كم بدي pressure (force) عشان اكسر tablet بال pressure على tablet 2 لانه tablet 2 يكون الهم نفس الحجم وال dimentions يتوزع على tablet 2 لانه tablet 2 dimentions

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Tablet testing

Mechanical strength الافتراضي ideal test يقيس hardness ويقارن

Crushing (Fracture) resistance methods

- An ideal test, however, should allow comparison of tablets of different sizes or even shapes. كيف هذا الحكي رح يصبر رح احسب force التي احتاجتها عشان اكسر وحدة مساحة معينة وهيك بقدر الغي الاختلافات بين tablet
- 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:

$$\sigma_t = \frac{2F}{\pi D t}$$

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

$$\sigma_t = \frac{2F}{\pi D t}$$

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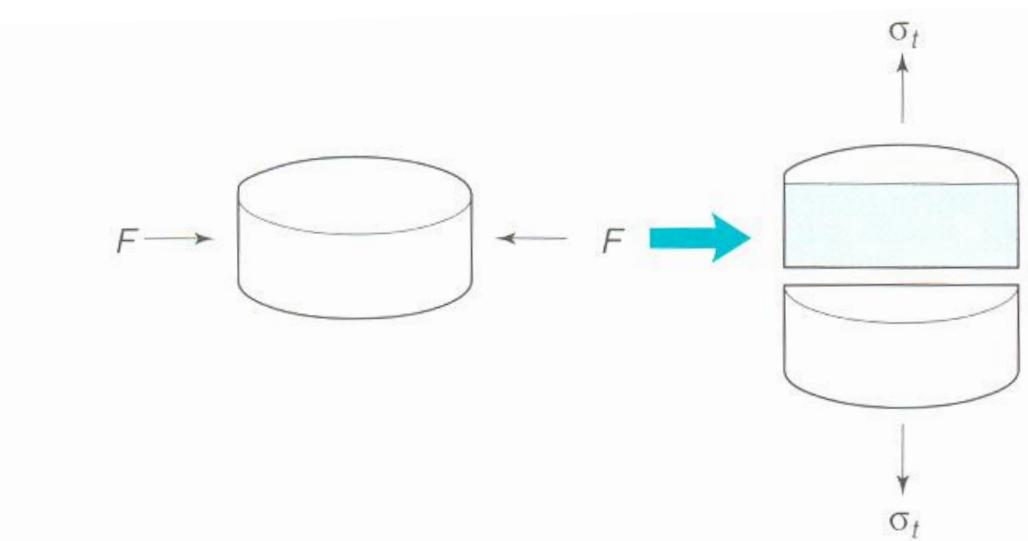


Fig. 31.22 Illustration of the tensile failure of a tablet during diametral compression.

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قدرة المادة على انه يقل حجمها وتنكبس لما اسلط عليها ضغط معين مثلا لو كانت قابلية انه يقل حجم المادة هي لحجم اكبر يعني عندها **compressibility** عالية

Fundamental aspects of compression of powders

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

- ① • The compression of a powder bed is started by rearrangement of particles in the die, resulting in reduced porosity (closer packing).
- ② • 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).
 - Elastic deformation: reversible on removal of the load
 - Plastic deformation: Irreversible
 - Fragmentation: particles are fractured to smaller size
- Sometimes the degree of deformation is time-dependent and is referred to as **viscous deformation** and **viscoelastic deformation**.

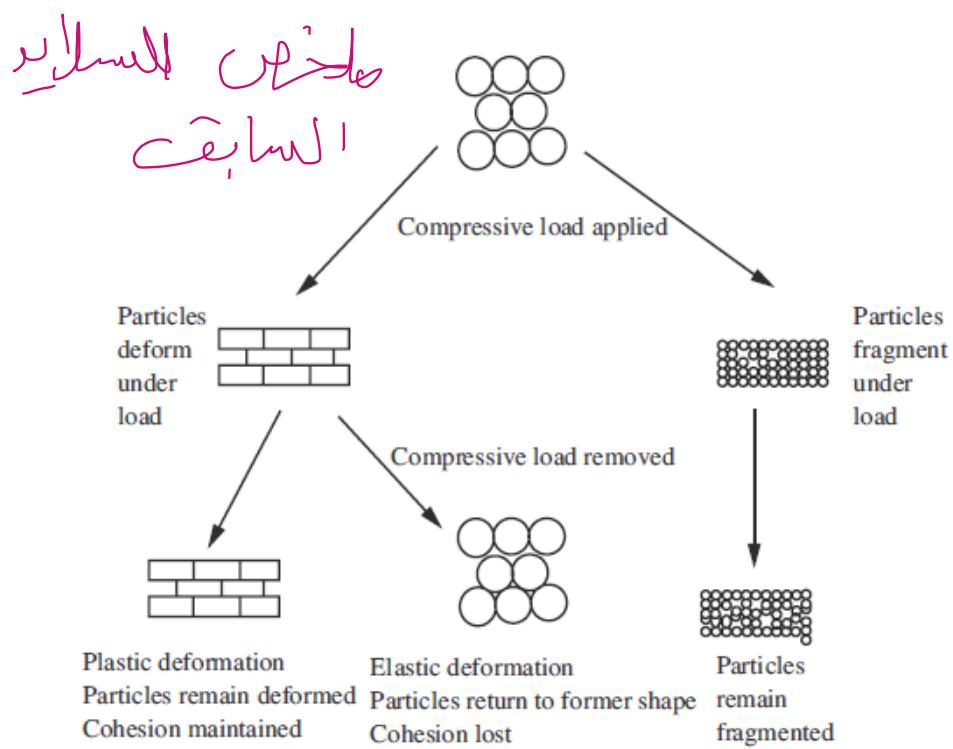
زباده الفضفط
زباده بسبب
ال اتساع
ال اتساع
ال اتساع
ال اتساع

زباده الفضفط
زباده بسبب
ال اتساع
ال اتساع
ال اتساع
ال اتساع

ال مرحله من مراحل تغير حجم ال powder هي ال rearrangement of particel و هي رح يصير particels هي ما في عشان ما في particels movment لل particels

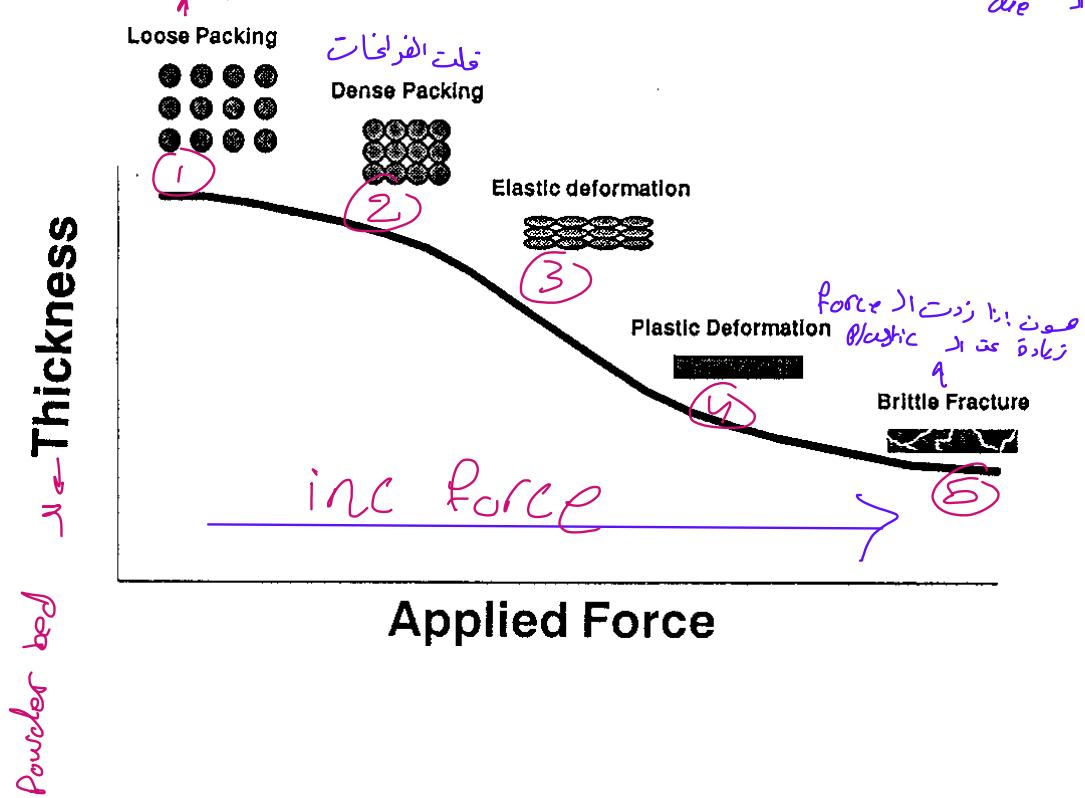
ال الحاله هاي احنا ما خلينا فراغات بين ال particels بتعتمد على الوقت يعني بتلاقي لما اسلط عليها ضغط لفترة معينة وبعدين شلت الضغط ال particel بس لو زدت الوقت الي رح تتعرض له ال particel بنفس قيمه الضغط ما رح يرجع لشكله الطبيعي

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هذه المراحل الخمسة تكونوا
لـ 1) أكبسات Powder بلـ 2)
3) لا UPPer Punch بلـ 4)
5) لا Lower Punch



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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.

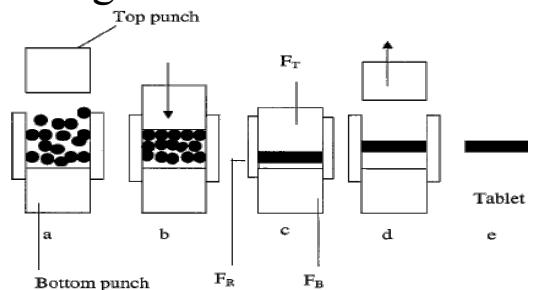
ببدايه الـ **compression** رح يصير تغير
بالـ **volum** للـ **particel** فبالاول بصير
وهيك **rearrangement** وهيك بتقل الفراغات
بالـ **physical chang** وبصير في **die** وبعدها بصير التغير
بالـ **primary paarticel**

الـ **الـ granules** يصير في الـ **Compresion**
خلال الـ **الـ granule arrangement**

تغير الـ **الـ granule arrangement**

عندما نقوم بعكس "الحببات" (Granules) لصنع قرص دواء، فإن هذه الحبيبات ليست أجساماً صلبة غير قابلة للتحبيب، بل هي مكونة في الأصل من جزيئات صغيرة جداً تسمى الجزيئات الأولية (Primary Particles).

الجملة تشير إلى أن الضغط المطبق يؤدي إلى تغييرات في هذه الجزيئات الصغيرة، وتشمل هذه التغييرات:



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Fundamental aspects of compression of granules

- With increased loading the granules can:
 - Deform elastically
 - Deform plastically
 - Densify (i.e. reduce their **intragranular porosity**)
 - Broken into smaller units by different mechanisms

كيف رح تغير **granule** **granule** ارجع الـ **الـ granule** على **الـ granule**
1 Primary particles might be removed from the surface of granules when they slide against each other or against the die wall (granule attrition). **primary particel** من سطح الـ **granule**
2 Granules can fracture into a number of smaller ones (granule fragmentation)

الـ **granule** تتكسر اصغر (تقريباً الـ **size** الـ **الـ granule** منشأها)

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قدرة الـ powder على تكوين tablet صلب ومتصل بالشكل المضغوط (يعني زي شكل الحبة التي كبستها بالـ die)

Fundamental aspects of compaction of powders

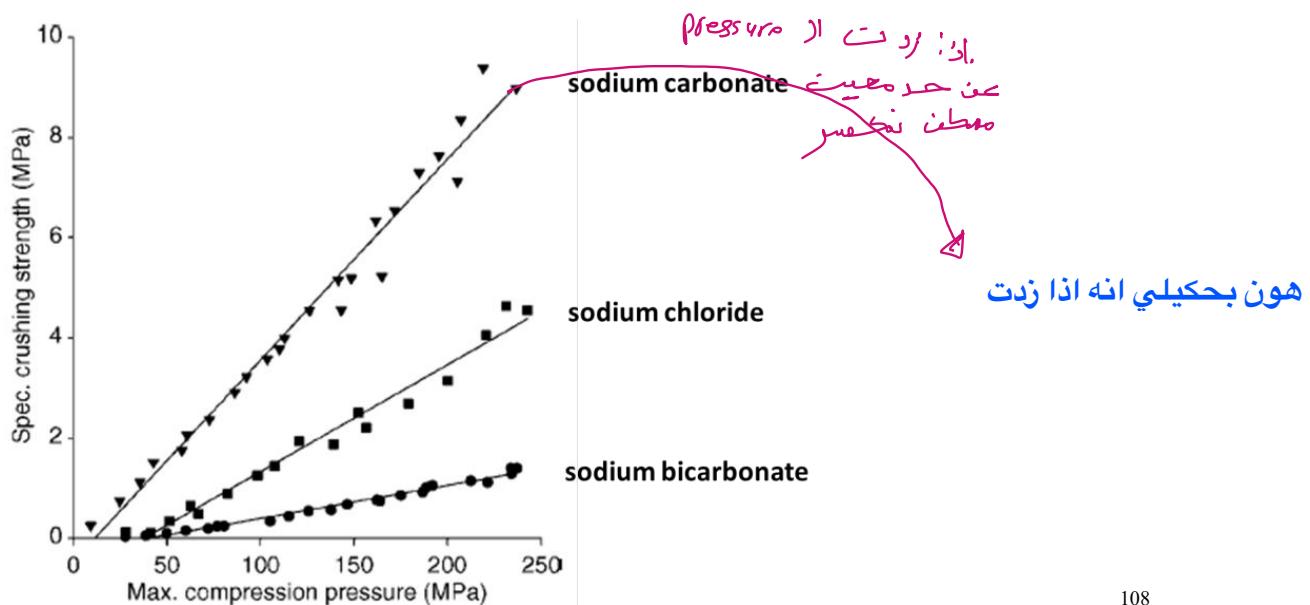
Compactability: The propensity of powder to form a coherent tablet.

المواد المساعدة

- 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.

احسن طريقة لقياس الـ compactability هي ابني اشوف تأثير الـ compaction pressure على الـ resulting tablet pressure، يعني لما اطبق هذا الـ tablet رح يعطيوني pressure صلب او لا وهكذا مافي قاعدة انه اذا زدت الـ pressure رح تكون الـ tablet احسن يعني في optimum pressure اذا زدت عنه او نقصت منه الوضع مارح يكون الشغل صحيح

Fundamental aspects of compaction of powders



Fundamental aspects of compaction of powders

- Mechanisms of bonding in tablets include: 

- Solid bridges **solid** صار **drying** **liqiuid bridge** **كان** **syrpe** **بعد الـ** **بكون الـ** **particel** **حواليها سائل وبصیر**
- Bonding by liquid (surface tension forces) **بينهم** **ورح تضل** **surface tension** **تماسكة**
- Binder bridges
- Intermolecular and electrostatic bonding
- Mechanical interlocking

Van-der force

Intermolecular and electrostatic bonding

- Mechanical interlocking

A diagram showing the sternal border of the pectoral muscle. The muscle is represented by a pink shaded area. A blue line outlines the border, and a red arrow points upwards along this border, indicating its course.

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هو * بدنانشوف خصائص المادة رح
تأثير على ال strength

Relationships between material properties and tablet strength

لِيَنَانْسُوفْ سُو سُور
Strength لِيَرْطُوبْ كِلار

① Role of moisture ↑

- Small percentage of moisture in tablet formulas can dramatically affect the behavior of these feed materials and that of finished products.
strength (dramatically change) او قلت رح تعمل تغيير كبير بـ (excipient)
لـ tablet بعد ما تطبيـ اذا قلت الرطوبـة عن الحـد الـ optimum
- 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.

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Relationships between material properties and tablet strength

The compaction of granules

- The compactability of granules is affected by:
Primary properties of granule لـ Compaction
Primary component طبيعة المكون – the mechanical properties of the primary components (i.e. particles before granulation)
arrangement تصميم – the design of the granulation process
Primary component
- Granules may deform or fragment into smaller components during compression.

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Relationships between material properties and tablet strength

Post compaction tablet strength changes

ممكن انه بعد ما تصنع ال tablet ما تظهر مشاكل
بس مثلا خلال عملية التخزين ممكن يتآثر
ال strength يعني مع الوقت ممكن يتغير

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

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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:

- the properties of the powder intended to be formed into tablets, and
- the design and conditions of the press.

السلسلة بالحجاز نفسه

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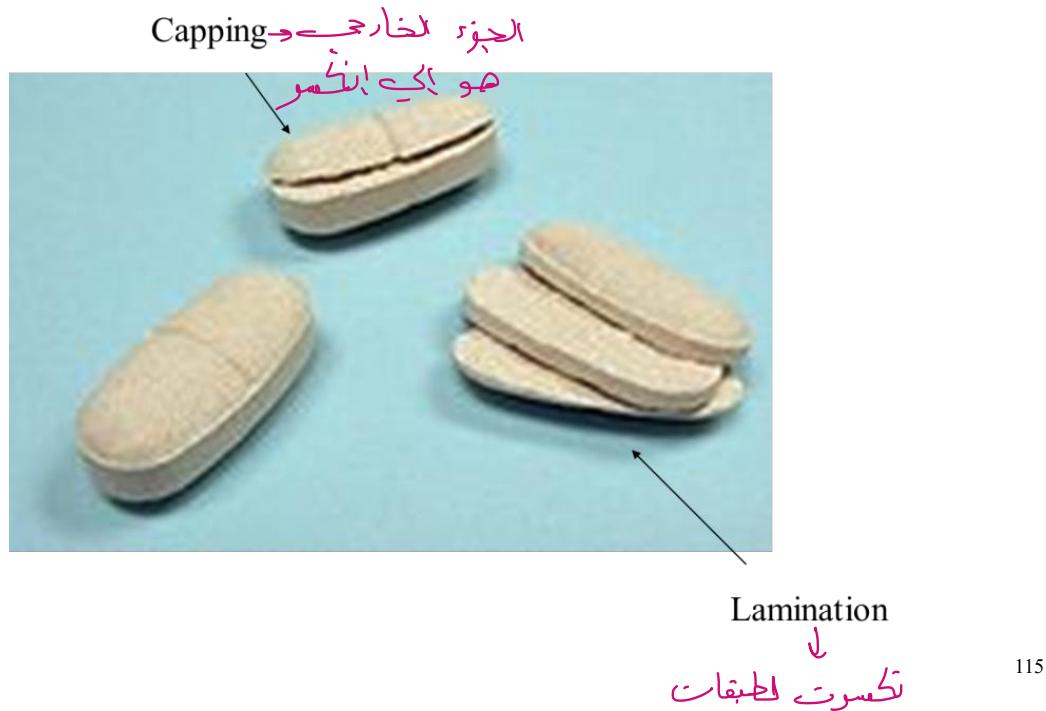
Problems and difficulties in tableting

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.
های المشاکل غالباً تظهر اول ما اطلع ال tablet من ال die بس احياناً ممکن تظهر بعد ساعات او ایام
- **Causes of capping and lamination:** 

- Causes of capping and laminating.
 - tablet مکبستہ بسرعہ وہیں الهوا لطلع ملکرات بیت اد Particles اد تعل Rapid speed of compression: air is not given enough time to escape.
 - Presence of excessive fines → کمیں اد اکٹیل Particles
 - Over drying of granules → Powder بخارہ تشفیر اد اکٹیل
 - Incorrect setup at the press → بالجھاڑ اکٹیل

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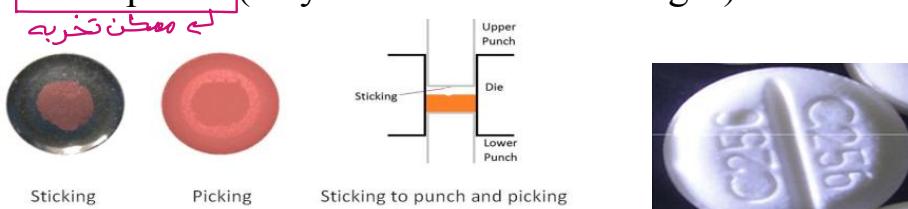


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Problems and difficulties in tabletting اخذ نام باللاب

Picking and sticking في جزء من الـ tablet يخل ملزق بالـ die

- **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).



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وجه المقارنة	Picking (الالتقاط)	Sticking (الالتصاق)
مكان الالتصاق	على وجه الخاز (Punches)	على جدران القالب (Die walls)
التأثير البصري	تشوه في حواف القرص	تشوه في حواف الحروف أو سطح القرص
السبب الشائع	نقش الحروف المعقدة	بطء الماكينة، مما قد يؤدي لتنفتها.

:(Picking) 1. هو التصاق المسحوق بوجه المكبس (Punch). يظهر غالباً في الحروف المنقوشة (مثل A و B) حيث تعلق البودرة داخل فتحات الحرف وتخرج من سطح القرص.

:(Sticking) 2. هو التصاق المسحوق بجدران القالب (Die walls).

- يسبب تكسير حواف القرص ويعيق حركة الماكينة، مما قد يؤدي لتنفتها.
- الفرق باختصار: (Picking) تشوه في السطح والحواف، (Sticking) خشونة وتكسير في الجوانب.

Problems and difficulties in tabletting



Picking and sticking

- Solving of picking and sticking:

- Engraved letters should be designed as large as possible اداریه نقش حروف لها بمساحة اكبر ما يمكن
- Addition of lubricants and ant-adherents يمكن اضافة مانيلز ايشنجل Anchors
- Additional binder or change of binder may make the granules more cohesive and therefore less adhesive to the punches and die ازير او اغيره ل اقوى binder binder

compression الضغط
 يجعل حرارة ممكن بعض الحرارة التي لها
المواد التي لها الحرارة التي لها
تدوب وتعمل تدوب وتعمل
عشان هيكي ببدلها بمواد عشان هيكي ببدلها بمواد

higher M.P الحرارة التي لها High moisture content may cause sticking and this is solved by further drying

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الالوان غير متناسقة
بالtablet حيث رح
الاقي اماكن غامقة
واماكن فاتحة بنفس
tablet

Problems and difficulties in tabletting

Mottling

- It is unequal distribution of color on tablets



- Reasons:

- Difference in color between drug and excipients
- Colored degradation products الاصlorون مختلف عن tablet
- 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). الحل ① ② ③ ④
- In direct compression formulations, uneven distribution of dye or large particle size may cause mottling



يكون المسار بطلع
الدمرات ويدفعه لونها
افت وعدها الاسمية
ذئب وذئبها
جوا

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Problems and difficulties in tableting

Weight variation

- Reasons

- bad flowability of powder *بأنز علی او flow*
- Variation in size and size distribution of granules *بأنز علی از size*
- Poor mixing with glidants and lubricants
- Punch variation (lower punches are unequal in lengths) *بكون مابنزل تحت كلر*

Hardness variation

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

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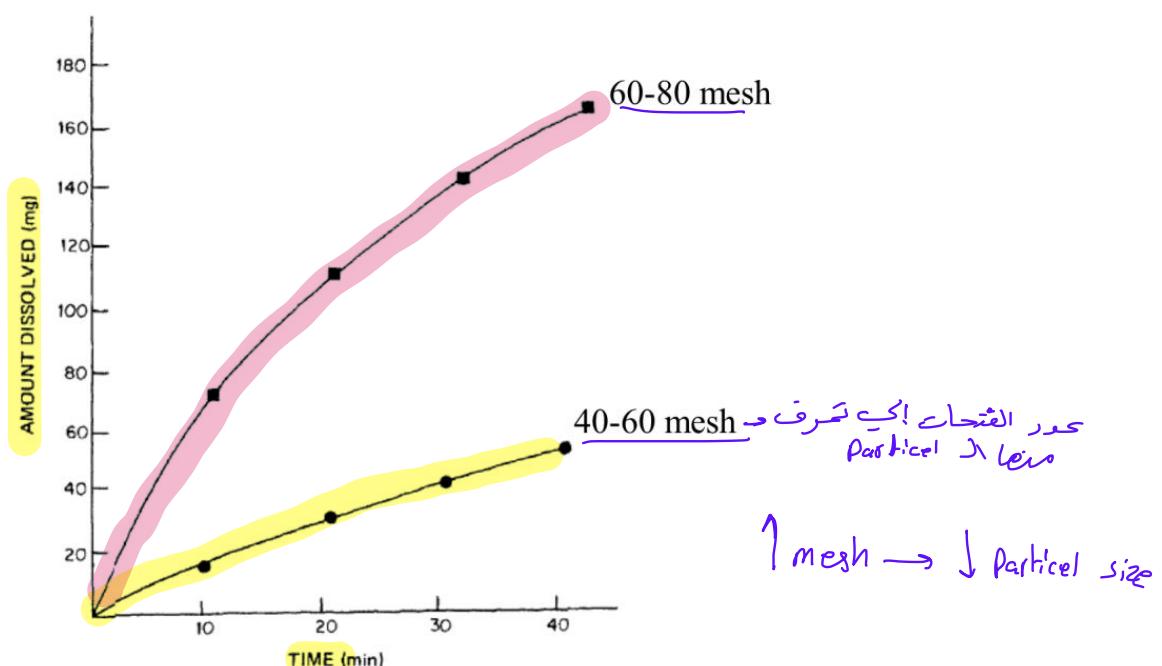
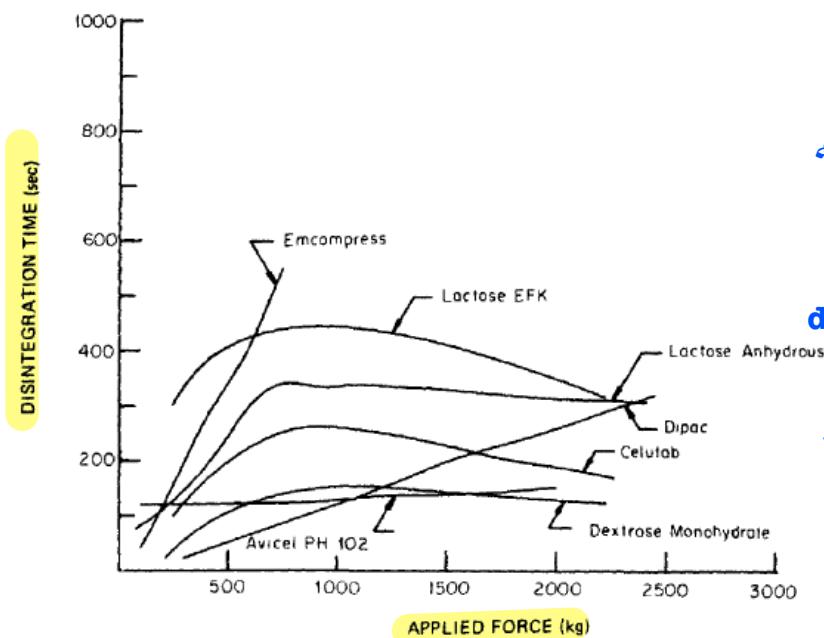


Figure 2 Effect of granule size on the dissolution rate of salicylic acid contained in compressed tablets. Key: • 40- to 60-mesh granules; ■ 60- to 80-mesh granules.

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أقل mesh *أقل size*
dissolution *يغطي رج ميون العال*
أقل *أقل size*



الـ particel الي لها
hardness عاليه رح
تحاج وقت اطول عشان
تتكسر (بكون خلال عملية
التصنيع عملت عليها
ضغط high) ورح احتاج
disintigration time لـ
اعلى (بس العلاقة مع
disintegration time الـ-رح
حاله بدون الـ-رح تكون عكسيه)

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

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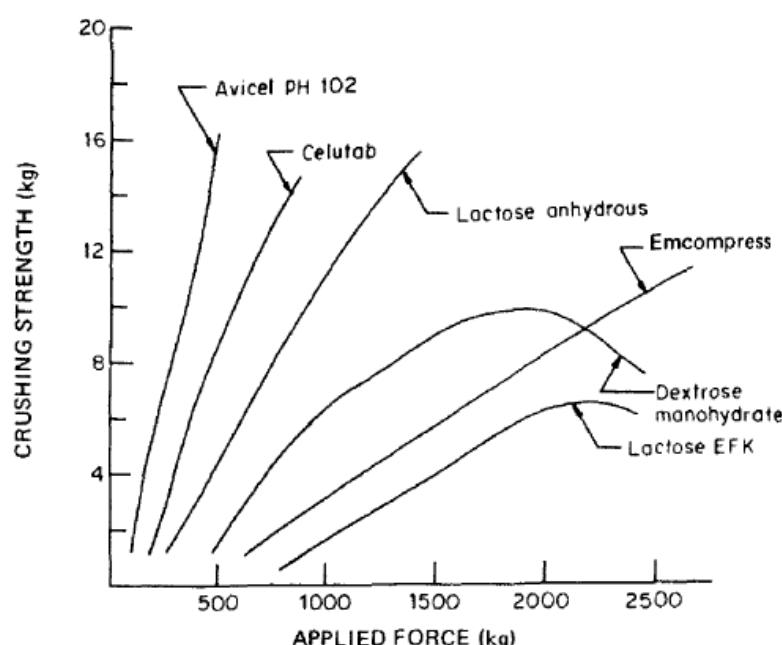


Figure 5 Crushing strength versus applied force for compacts of various materials.

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هذه الـ Curve ما فهمته مني من المحن
لله في المفتاح انزل التفريغ بعده شردة
وبس (فهمني بتزيل المحتوى الشرع على المحن)

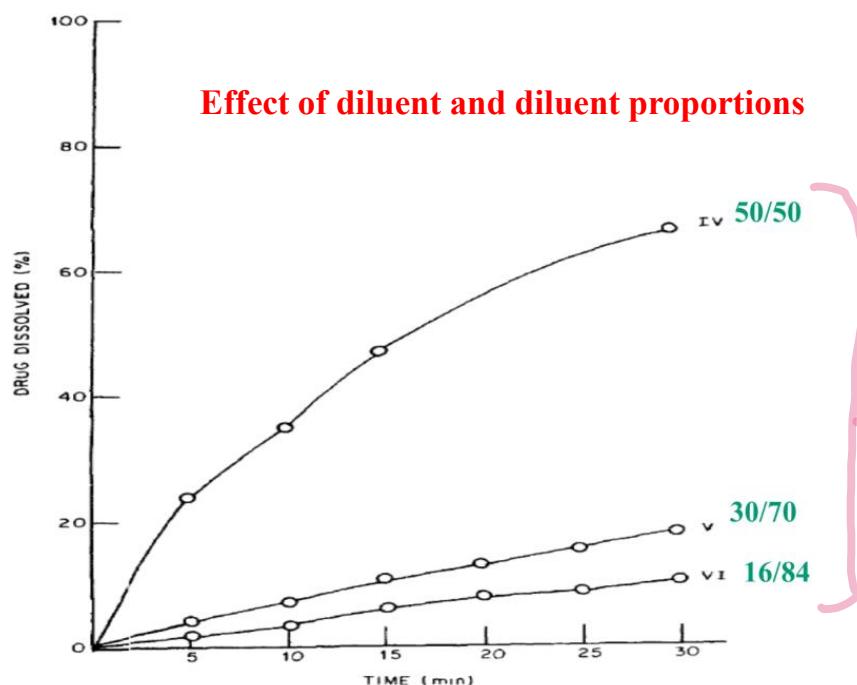
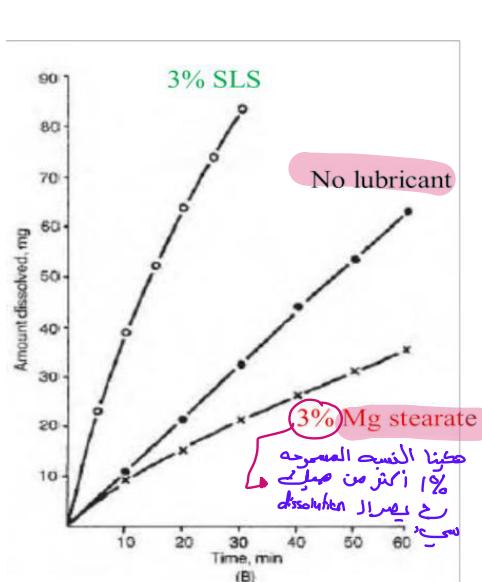


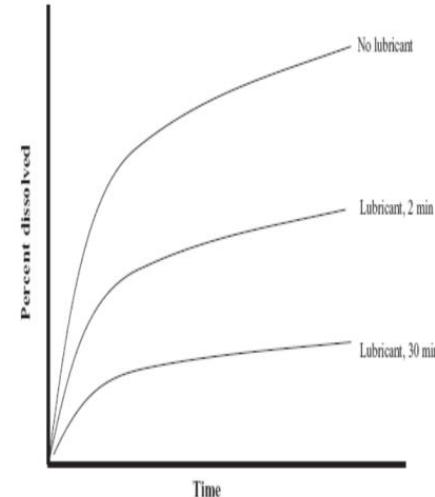
Figure 7 Drug release of an insoluble drug from direct-compression diluents (see text). IV = microcrystalline cellulose N.F. / dibasic calcium phosphate N.F., 50:50. V = microcrystalline cellulose N.F. / dibasic calcium phosphate N.F., 30:70. VI = microcrystalline cellulose N.F. / dibasic calcium phosphate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

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

Lubricant اور لبیرن اس



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

Lubricant اور mixing time اس کی وجہ سے dissolution rate کا اثر

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