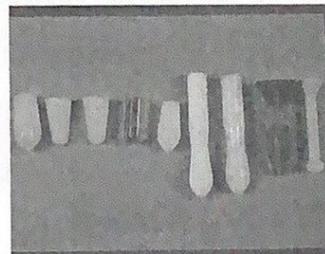


1

Introduction

verb of Suppository ←

- Medicated semisolid formulation that are **inserted** into body cavities
- Route of administration:
 - Rectal **شرجية**
 - Vaginal **مهبلية**
 - Urethral **في المثالب** ① ②
- Once inside cavity they **melt**, **soften**, or **dissolve**, releasing the drug



← نادرة ويحبب معوية عنها

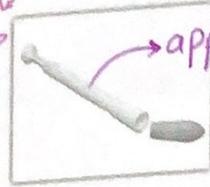
1. For **local effect** (soothing inflamed hemorrhoidal tissues and promoting relaxation and evacuation) + **Constipation** (الإمساك) + **itching** (حكة)
2. for **systemic effects** (to treat asthma, nausea, motion sickness, anxiety...etc) + **analgesic**

2

← للأطباء

Introduction

- Rectal suppositories are inserted with the fingers, but certain vaginal suppositories may be inserted high in the tract with the aid of an appliance. (applicator)
- Vaginal suppositories, also called pessaries, ^{لا تكون بطرية}
- Urethral suppositories, also called bougies ^{بتكون أطول}

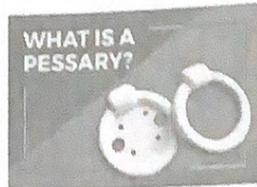
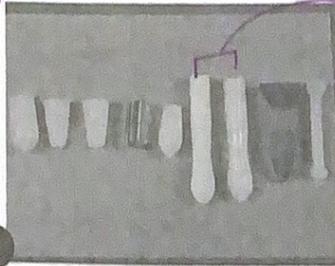


لا تكون بطرية

لا تكون
طرية

applicator

أعرض وأقصر



3

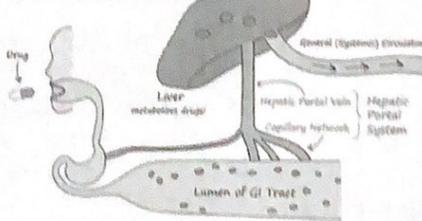
Rectal Route

مميزاتها

- Advantages of rectal route:

- For patient with nausea and vomiting
- For unconscious patient
- Infants and small children
- No taste limitations
- Partial avoidance of hepatic first-pass metabolism
- Drugs avoid gastric fluid and enzymes

First Pass Metabolism



عصوية
فقد الوعي/ Comma

إذا كان المريض من متحمل
طعم الدواء.

العدة فيها إنزيمات HCL +
وال PH قلبي جدا ويمكن
الدواء يخرج فيبدا للتسليم.

4

الطرق التي يكون (oral)
تذهب للكبد أولاً

ويعملها (first-pass metabolism)

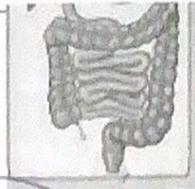
وتذهب من الكبد وتبقى فيها

30-40% يروح الدم ليعطى تأثير

يعني فيه حوا (oral) إنه تأخر 100%

فينصح بأخذ السطح قبل الإخراج.

Disadvantage of this route Rectal Route الإخراج



- a. Absorption may be interrupted by defecation
- b. Has **small surface area for (passive absorption)** Drug absorption is less extensive and slower than after oral administration: **surface area (SA)** of rectal mucosa is **1/10,000** the surface area of small intestine
- c. **Small rectal fluid content** may cause problems with drug dissolution and absorption
- d. Inconvenient (غير مريح)
- e. Rectal absorption of most drugs frequently is **erratic and unpredictable**
- f. Some suppositories **"leak"** or are **expelled** after insertion

لأن يكون حجم الدواء صغير حتى يمتصه الجسم

adult خصوصاً لا

لا يمكن التنبؤ به

أفضل وقت للإعطاء السطح عند النوم at bed time.

لا يمكن التحكم به بلع وبنزله

Rectal Route

- Most commercially prepared rectal are **torpedo-shaped**
- **20 mm in length and weigh about 2 gm**
- **Infant** rectal suppositories are **half the size of adult suppositories**
- The maximum amount of solid material that can be incorporated into a suppository is about 30% of the blank weight (**suppository base**)
- Thus, **doses greater than 500 mg cannot be delivered with rectal suppositories but can be administered easily with vaginal suppositories**



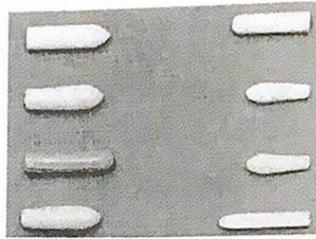
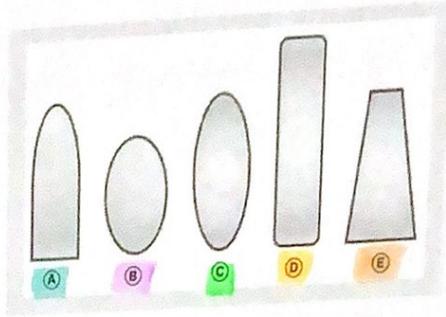
الرجوع
يتم تحضيرهم في المسائل

(والا Vagina ممكن تكون أكبر)

الشعافى عليه

Common in vaginal ←

- (A) Bullet or torpedo;
- (B) round oval;
- (C) elongated oval;
- (D) tampon;
- (E) teardrop or cone



adult

جدهم أكبر وأطول

Infant

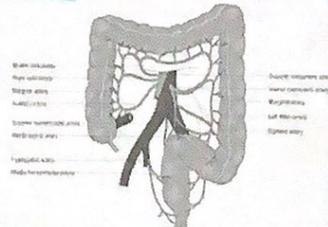
جدهم أصغر وأقصر

7

Rectal Route

- The factors that affect rectal absorption of a drug may be divided into two main groups:
- (a) *physiologic factors* and
- (b) *physicochemical factors* of the drug and the base.

Physiologic factors



ال Colon آخر جزء فيه هو ال Rectum

- **Colonic Content**
- **Circulation Route (Blood Supply)**

pH in rectum about 7,8

pH and Lack of Buffering Capacity of the Rectal Fluids:
Because rectal fluids are essentially neutral in pH and have no effective buffer capacity, the form in which the drug is administered will not generally be chemically changed by the environment.

8

* Buffering Capacity

بعض الأدوية عندما توضع في العين مثلاً للدوا سوائها العين يتعدل ال (PH) ليصبح طبيعى ولا يسبب ألم

وفي أجزاء بالجسم ما نعرفها صاى الحامضية (أعطيت دواء ال PH ال 3 ال 3 و 3) ← مثل ال Rectum

1/18/2020

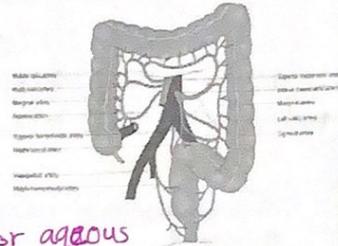
* الاختيار باختيار
excipient هو
ال drug ويجعل على
أساسه .

12/18/20

Drug

Physicochemical factors of the drug and the (suppository base) → Vehicle

- relative **solubility** of the drug in lipid and in water
- the **particle size** of a dispersed drug.
- Physicochemical factors of the **base** include its ability to **melt, soften, or dissolve** at body temperature,
- **Drug** ability to release the drug substance, and its **hydrophilic** or **hydrophobic** character
- The rate limiting step is the **drug partitioning** and **diffusing out** of the base material in rectal lumen



قاعدة عامة :
كلما قلت حجم الجسيمات تزيد الامتصاص Solubility وال absorption.

lipid membrane
حول الغشاء

Balance يوزن
hydrophilic ما يكون محس

Hydrophobic
و لا محس Phobic

for aqueous media

توزيع الدواء

(مقاسة)

PH = 6.8 (rectum)

Vaginal Route of Administration:

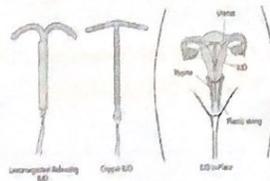
Advantages:

1. Generally there is **less drug degradation** via this route of administration compared to oral administration
2. The dose **can be retrieved** if necessary
3. Potential of long term drug administration with various **intrauterine device (IUDs)** → مواقع الحمل لفترة طويلة (Prolong use)

Disadvantages:

- A. Absorption can be **erratic** because vagina is a **physiologically and anatomically dynamic organ**
- B. Retention of some delivery systems during menstruation could dispose the patient to **toxic shock syndrome**
- C. Can **interface with sexual activity**
- D. **Can be expelled**

Toxic shock syndrome is a rare, life-threatening complication of certain types of bacterial infections



mostly hormones or antibiotic or antifungal

الدواء يمكن ان يتسحب من الجسم عن طريق contraction

بسبب قلة النظافة أثناء الدورة الشهرية عند النساء .

يمكن ان يكون للدواء علاج

10

Vaginal Route of administration

- Vaginal suppositories are employed as: contraceptives/feminine hygiene antiseptics/antibiotics
- **Vaginal suppositories = pessaries** (rectal) أكبر من
- Globular or oviform or cone-shaped and **weigh 3-5 gm**
- **Inserted high in the tract with the aid of a special applicator** → to allow easy Insertion
- Patient should be instructed to **dip the suppository quickly in water before insertion**
- **Women should wear a sanitary napkin to protect nightwear and bed linens**

وضع السجول عليها
تلك التي في بطون
السجول بالي لتسهيل
insertion



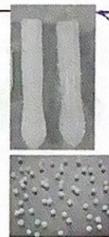
11

Urethral Route of Administration

- **Bougies** اسم آخر غير شائع
- **Antibacterial, local preparative anesthetics**
- Urethral suppositories are **not specifically described in the USP 24/NF19** either by weight or dimension.
- Traditionally, they are cylindrical in shape (3 - 6 mm in diameter) and vary in length according to gender.
- Female urethral suppositories can be 25 - 70 mm in length while male urethral suppositories can be about 50 - 125 mm in length.
- The one commercially available urethral suppository is actually marketed as a "pellet," and is (1.4 mm) in diameter and 3 or 6 mm in length depending on strength.
- Urethral suppositories are **unusual** and may **not be encountered in a compounding practice**.

(Urinary System) UHI

في الرجال
يكون أعرض
وأطول



Uses ←
مسحوق مشروط بال USP

الإبراق لها
عريه كروي

Spherical
in shape
وصف بزقطة
أو ينكسو (strong)
تتبرم كروي

12

Suppository Bases:

Classified by composition and physical properties:

- 1 - Oleaginous (fatty) bases
- 2 - Water soluble or miscible bases



Ideal properties:

1. Nontoxic
2. Nonirritating
3. Inert (doesn't react)
4. Compatible with the drug (لا يتفاعل الدواء معهم)
5. Easily pliable into the desired shape
6. it should remain solid at room temperature but soften, melt, or dissolve readily at body temperature so that the drug is fully available soon after insertion
7. Should dissolve or melt in the presence of mucous secretions at body temperature and allow release of the drug

المرونة في الشكل
للشكل المطلوب

not completely liquid
Convert completely to liquid
باليد الرطبة
ويكونها سائلة
في جسمه

13

Oleaginous bases



- Mild and nonirritating action on the rectal mucosa
- Have a tendency to melt in 3 to 7 minutes so the drug can be released quickly from the formulation
- Have a lower melting points than the water miscible bases → must be kept in controlled room temperature environments or refrigerated in warmer climates
- e.g. Cocoa butter (Theobroma oil) and synthetic triglyceride mixtures.

If release the drug by melting:

*Rectal: aqueous
*Base: Oleaginous
فما زال يهرس عنده
dissolve/dissolution
الBase في rectum
يهرس
by (melting)

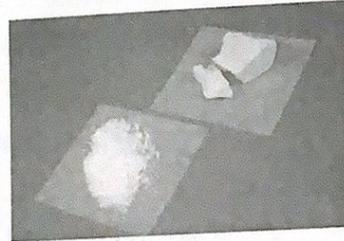
زيادة الكافيو
natural (النوع الطبيعي)

النوع الصناعي

14

Cocoa Butter (Theobroma Oil)

- Cocoa Butter, NF, is defined as the fat obtained from the roasted seed of *Theobroma cacao*.
- At room temperature, it is a yellowish-white solid having a faint, agreeable chocolate-like odor.
- **Theobroma Oil** or **cocoa butter** is used as a suppository base because, in large measure, it fulfills the requirements of an ideal base.



→ Solid at room temperature & melted at body temperature

15

Cocoa Butter (Theobroma Oil)

- At ordinary room temperatures of 15° to 25°C (59° to 77°F), it is a hard, amorphous solid, but at 30° to 36°C it melts to a bland, nonirritating oil. Thus in warm climates, theobroma oil suppositories should be refrigerated.
- Thus it melts just below body temperature and yet maintaining its solidity at usual room temperatures



16

Crystalline (m.p) ←

note: Polymorph
Crystals

Cocoa Butter (Theobroma Oil)

- Particular attention must be given to **two factors** when preparing suppositories with cocoa butter base:
 - **First, this base must not be heated above 35°C (95°F) because cocoa butter is a polymorphic compound with four structural forms and if overheated will convert to a metastable structure (alpha crystals) → that melts in the 25° to 30°C (77° to 86°F) range.** Thus, the finished suppositories would melt at room temperature and not be usable.
 - **The second factor is the change in melting point caused by adding certain drugs to cocoa butter suppositories.** ↓ m.p
 - For example, **chloral hydrate and phenol** tend to **lower the melting point.**
 - It may be necessary to add **spermaceti or beeswax** as a **hardening or solidifying agents** to raise the melting point of finished suppositories **back to the desired range.** m.p ↑

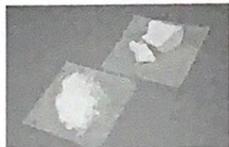
صعب يمسكه المريض
بنوب على درجة حرارة
الغرفة.

لا تأخذ انه drug
ما تأخذ على m.p
لذا الدواء low m.p
يستعمل معه شيء يرفع
m.p ولذا m.p
للهو كثير على يستعمل
اشي يقاتل m.p

Cocoa Butter (Theobroma Oil)

- The **proper method** of melting cocoa butter is to **use a hotplate or water bath (just warm water)** at about **55°C** and **melt the base carefully**
- Correctly melted cocoa butter should have an **opalescent, creamy appearance** *opaque (non-transparent)*
- Cocoa butter that has been overheated **will change to clear golden liquid and should not be used**

القوام المناسب والمثلالي
لو تغير لونها للذهبي
تكون تفتت
وتغيرت خصائصها



18

التقاليد من أسهل

Synthetic triglycerides

• Synthetic triglycerides consist of hydrogenated vegetable oils.

لا تدهون مثل ضروري
(heat) تسخن

• Their advantage over cocoa butter is that they do not exhibit polymorphism.

• They are, however, more expensive.

• Some of the bases are single entity formulations. Some of the names may denote a series of bases. In a series, the bases are varied to give a range of melting points.

• For example, Fattibase® is a single entity base that consists of triglycerides from palm, palm kernel, and coconut oils. Wecobee® is a series of bases. Wecobee FS, M, R, and S are all made from triglycerides of coconut oil. But FS has a melting point range of 39.4 to 40.5°C, M has a range of 33.3 to 36.0°C, R has a range of 33.9 to 35.0°C, and S has a range of 38.0 to 40.5°C.

هذا يعني فرق في أن
ال range يكون
(narrow ضيق)
مثل زي ال (Cocoa)
ال أو مع
30-36°

• Other triglyceride type bases include Dehydag®, Hydrokote®, Suppocire®, and Witepsol®.

هذا الأسماء التي
Wecobee®

النوع الثاني من ال Bases :

Water Soluble/Water Miscible Bases

don't melt &
don't soften
يعتقدوا على ال
dissolution.

• Water soluble/water miscible bases are those containing glycerinated gelatin or the polyethylene glycol (PEG) polymers.

Synthetic
يمكن التسمية
بها

• These bases dissolve in rectal mucosal fluids in contrast to (Cocoa + triglycerides) which melt at body temperature.

• Therefore the problems of handling, storage, and shipping are simplified.

• The glycerinated gelatin base is slower to soften and mix with the physiologic fluids than is cocoa butter and therefore provides a slower release.

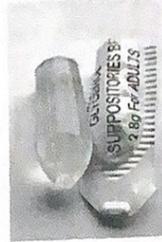


20

"melt" لا يذوب
at room Temperature.
فيمكن الرطب بضعف يكون
ما يتبوا بايه فما رة يكون
عند مسك بال storage
ال

Glycerinated Gelatin

- Because glycerinated gelatin-based suppositories have a tendency to absorb moisture as a result of the **hygroscopic** nature of glycerin, they must be protected from **atmospheric moisture** and must be kept in **(well-closed containers)** in a cool place since they will absorb and dissolve in atmospheric moisture.



بسبب الرطوبة ←

aluminium foil ←

بسبب الرطوبة من
مس rectum
dehydration
Irritation
(تقرح)

- As a result of the hygroscopicity of the glycerin, the suppository may also have a **dehydrating effect** and **irritate the tissues** upon insertion.

21

Glycerinated Gelatin



مادة سائلة

- Thus glycerin contributes to the **laxative effect** of the suppository by drawing water from the intestine and from its **irritant action** on the mucous lining

Glycerin ← بسبب

وجود المكون الرطوبتي
يختف من التهييج
لكن الأفضل لانه
ناعم (wetting)
للحتمة قبل الاستعمال
(تطرية بالماء)

- The **water** in the formula for the suppositories **minimizes this action**; however, if necessary, the suppositories may be **moistened** with water prior to insertion to reduce the initial tendency of the base to draw water from the mucous membranes and irritate the tissues.

22

Glycerinated Gelatin

- is a useful suppository base, particularly for vaginal suppositories.
- It is suitable for use with a wide range of medicaments including **alkaloids, boric acid, and zinc oxide.** → astringent
- In addition, those intended for extended shelf-life should have a preservative added, such as methylparaben or propylparaben, or a suitable combination of the two.
- Glycerinated gelatin suppositories are translucent, **resilient,** gelatinous solids that **tend to dissolve or disperse slowly in mucous secretions** to provide prolonged release of active ingredients.

antiseptic
Systemic effect

(مرونة)
تعود للشكل
الطبيعي بعد الاستخدام



23

* تأشيرهم بغير فلوسه أكلهم
الأطباء كمنافس حارة بولهم
(تأشيرهم) Synthetic of Cocoa

glycerin/ PEG base! Long release نازلي*
النازلي

Glycerinated Gelatin

- Glycerinated gelatin suppositories may be prepared by dissolving granular **gelatin (20%)** in **glycerin (70%)** and adding water or a solution or suspension of the medication **(10%)** → q.s water

• The glycerin and water are mixed and heated (**steam bath or a boiling water bath**). Then the gelatin is added **slowly** with gentle mixing so air is not entrapped in the mixture)

أحرار
(heat)

السبب



جودة جيدة
good hydration.

24

Polyethylene Glycol Polymers

Disadvantages of PEG bases:

1. Produce **stinging or a burning sensation** التي :
2. and may cause a **defecating reflex** when used rectally (**minimized by adding water to PEG base and moistening with water before insertion**)
3. Polyethylene glycol suppositories that **do not contain at least 20% water** should be **dipped in water just before use to avoid irritation of the mucous membranes after insertion**. This procedure prevents moisture being drawn from the tissues after insertion and the stinging sensation.
4. **Incompatible with large number of drugs** (i.e. aspirin...)
5. Should not be stored in **polystyrene vials** because PEG reacts with the polystyrene ببغية

لسعة/حرقه

إذا غوطها ماء أقل من 20% لا زلنا أظلمها أرطبها بالماء وإذا فيها 20% فما فوق فنسحب أرطبها.

ممكن يجرى reaction وما يشغل الدواء مع ال-PEG

بمحتاجوا عبوة مناسبة من مادة ال-PEG

Similarities between glycerinated gelatin and PEG bases

التشابه بين PEG و gelatin

release 11

1. They both **dissolve in about 30 to 50 minutes**, providing a more **prolonged release** of drug than cocoa butter
2. Both should be **moistened with water before insertion**
3. They **do not melt in the fingers while being inserted**
4. They do not leak from **body orifices**

الشين بعصوا الرطوبة

فمن داعي يضل مستحق المريض فترة طويلة (تسرب)

طريقة قديمة حالياً غير شائعة

Methods of Preparation of Suppositories:

1. Hand Rolling

لما تكون برين أحضرتك ليس مثل

• is the **oldest and simplest method** of suppository preparation and may be used when **only a few suppositories** are to be prepared in a cocoa butter base.

heat فيها
يعني ما فيها مشكلة ال
(Polymorphism)

• It has the advantage of avoiding the necessity of heating the cocoa butter.

• A plastic-like **mass** is prepared by tritulating (grated) cocoa butter and active ingredients in a mortar. The mass is formed into a ball in the palm of the hands, then rolled into a uniform cylinder with a large spatula or small flat board on a pill tile.

• The cylinder is then cut into the appropriate number of pieces which are rolled on one end to produce a conical shape.

تقطع وتجن

ماتر

بجمل شكل اسطوانة

تخروم شكل

29

بجملها على شكل
معيون اسطوانة
بعدين بتقطعها
لتقطع صغيرة



30

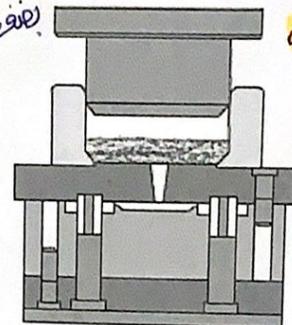
Methods of Preparation of Suppositories:

2. Compression

- is a method of preparing suppositories from a mixed mass of **grated suppository base** and medicaments which is **forced into a special compression mold**.
- Compression is especially suited for making suppositories that contain **heat-labile medicinal substances** or a great deal of substances that are **insoluble in the base**. (drug insoluble in base)

مطبوقة ومطبوقة

تفتتها



disadvantage: تحتاج different molds for infant, adult لأن الحجم يتنوع حسب العمر

ما فيها heat يعني يستعملها للمواد (thermolabile)

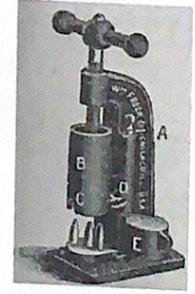
صناعتها

يكون عندي خلة في مخزن وخذني قالب (mold) ورضف الخلة في mold وسطيس العمل

31 + بعمل أعداد كبيرة بنفس الوقت (automatic)

لأنها يتكيس كبس فمن حال ترسب (صيرة)

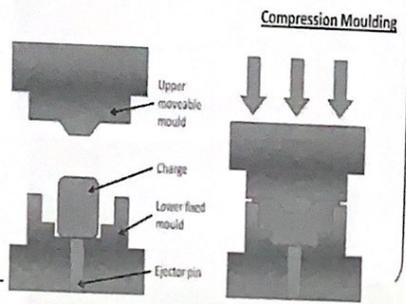
In contrast to the molding method, **compression permits no likelihood of insoluble matter settling during manufacture.**



كما قلنا سابقاً مسبقاً يحتاج أكثر من ماكينة لتتلف الأشكال والأحجام

The disadvantage to compression is that the **special suppository machine is required** and there is some limitation as to the **shapes of suppositories that can be made.**

32



أدوية حساسة للحرارة
thermolabile drugs
لا يتربط
لا يتربط للحرارة

Methods of Preparation of Suppositories:

3. Fusion or molding ^{الأكثر شيوعاً}

- Cocoa butter, glycerinated gelatin, polyethylene glycol, and most other bases are suitable for preparation by molding.
- The steps in molding include
 - (a) melting the base,
 - (b) incorporating any required medicaments,
 - (c) ^{صب} pouring the melt into molds,
 - (d) allowing the melt to cool and ^{تفاسك} congeal into suppositories, and
 - (e) removing the formed suppositories from the mold..

33

في تسخين (heat)

Methods of Preparation of Suppositories:

3. Fusion or molding

- ^{نادراً} **Lubrication** is seldom necessary when the base is cocoa butter or polyethylene glycol, as these materials contract sufficiently on cooling to separate from the inner surfaces and allow easy removal.
- Lubrication is ^{بمحتاجون أكثر} usually necessary with glycerinated gelatin. A thin coating of (mineral oil) applied with the finger to the molding surfaces usually suffices.



34

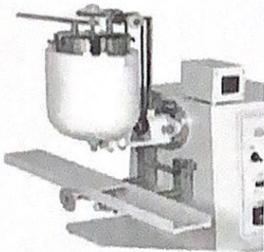
إذا المادة aqueous
بمحتاجون بـ oil
فإذا Olegenous
بمحتاجون water
الهدف أن لا تتصلق
ونشيلها بسهولة.
ولازم أن نحسن كمية
قليلة عشائر ما
تاخذ مكان الدواء

Lubrication
محتاجون في
Cocoa & PEG
شدهم يفتقوا ويصغر
بمحتاجون فيسحبهم
سهولة بعد ما
يبروا.

Methods of Preparation of Suppositories: 3.Fusion

Suppository molds:

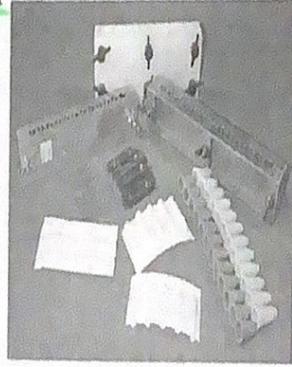
1- **Industrial molds:**
produces hundreds of suppository in a single batch



2- Small hand-held molds:

Are made of:

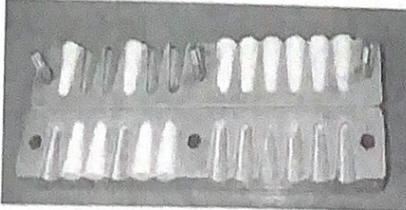
1. Stainless steel
2. Aluminum
3. Brass
4. Plastic
5. Rubber



تصنيع (roll) وتسم

Methods of Preparation of Suppositories: 3.Fusion or molding

- Suppositories are generally made from solid ingredients and drugs which are measured by weight.
- When they are mixed, melted, and poured into suppository mold cavities, they occupy a volume – the volume of the mold cavity.
- Since the components are measured by weight but compounded by volume, density calculations and mold calibrations are required to provide accurate doses.



الكثافة بتربط بين الحجم والوزن

Note: 2g mold (Blank / Unmedicated) Suppositories or pure Base

5/17/2022

حفظ هذه الصيغة
 Total كلهم بلوغ على الـ
 Base التي رز أمزج منه (Base) (ويكون في السؤال)
 ← متحيلة بدون أي دواء

• For example: Aspirin has a density factor in cocoa butter of 1.3.

Done ← • If a suppository is to contain 0.3 g of aspirin, it will replace 0.3 g ÷ 1.3 or 0.23 g of cocoa butter.

Base ← عشان أعرف كم
 مع أوزن الصيغ
 Total - Base
 displaced
 2g - 0.23 = 1.77

• If the blank suppository (suppository without the drug) weighed 2 g, then 2 g - 0.23 g or 1.77 g of cocoa butter will be needed for each suppository, and the suppository will weigh 1.77 g + 0.3 g = 2.07 g.

لو جعنا الـ Bases
 بطنى < 2 وذلك
 لا تلافى الـ density

• So if a pharmacist was making 12 aspirin suppositories using cocoa butter as the base, he would weigh 1.77 g × 12 or 21.24 g of cocoa butter and 0.3 g × 12 or 3.6 g of aspirin.

Base ← كفاى كمية الـ
 التي رز أوزنها.

Aspirin 0.3 X 12	3.6g
Base 1.77 X 12	21.24g

Note: سبب في المسائل يطلب منك
 متحسب حساب بتحصين زيادة
 (2 excess) لتوضيح النقص
 أثناء التحضير.

والآن نضرب عدد
 السطيل المطلوب
 من الـ Base & drug

3

• When a drug is placed in a suppository base it will displace an amount of base as a function of its density.

DF ← نفس الـ DDF

A Density Displacement Factor (DDF) is used to determine how much base a drug will displace. □

• DDF Definition: "the weight of drug, in grams, that will displace 1 gram of base"

• Example: If 0.5 g boric acid (BA) is added to cocoa butter (DDF = 1.5), how many grams of CB is displaced by 0.5 g of BA

1.5 g BA → will displace → 1 g CB → Cocoa butter
 0.5 g BA → will displace??? → X g CB □

1.5 g boric acid
 will displaced
 1 g Cocoa butter

(0.5 × 1) / 1.5 = 0.3 gm. Then 0.3 g CB is displaced by 0.5 g of BA

1.5 = 0.5 × 1

Displaced base = (Weight of blank (pure) suppositories - Weight of the base in the medicated suppositories)

• Displacement value = $\frac{\text{the weight of the drug}}{(\text{the weight of pure base suppositories} - \text{weight of the base in the medicated suppositories})}$ = Displaced base

قانون آخر...

DV: $d / (a - c)$

← يكون المطلوب
 حساب (DV)
 أو (C) فقط

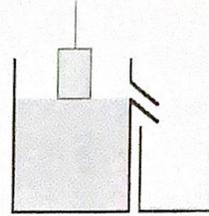
4
 توضيح القانون → $DV = \frac{\text{weight of the drug (d)}}{\text{weight of Pure base (a) - displaced Base (c)}}$ → $DV = \frac{d}{a - c}$
 (unmedicated) (medicated)

Density Factors:

من حفظ تفضل في السؤال

- Some example density factors of drugs in cocoa butter are shown in the table below
- (see Remington's) also see Table 17.4 pg 138

Aspirin	1.3
Barbital	1.2
Bismuth salicylate	4.5
Chloral hydrate	1.3
Cocaine hydrochloride	1.3
Codeine phosphate	1.1
Diphenhydramine hydrochloride	1.3
Morphine hydrochloride	1.6
Phenobarbital	1.2
Zinc Oxide	4.0



5

- **Formula (1):**
- *
- DV of Bismuth subgallate = 2.7
- **Rx 6 Bismuth Subgallate suppositories by molding.**

Rx 4 Bismuth Subgallate suppositories by molding:

Rx
Bismuth subgallate 300 mg → (3g)
Cocoa butter (Theobroma oil) q.s

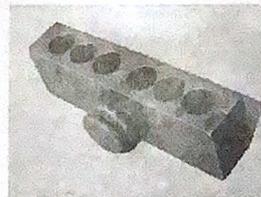
(8 زوايا لها لفرام)

- Rx
- Bismuth subgallate 300 mg
- Cocoa butter (Theobroma oil) q.s
- Quantities are calculated for an excess of TWO to account for incomplete recovery from the evaporating basin.
- *Mould calibration = 1g.
- *DV of Bismuth subgallate = 2.7

• Displacement value = $\frac{\text{the weight of the drug}}{\text{(the weight of pure base suppositories - weight of the base in the medicated suppositories)}}$

← في حصة 2 زيادة

- Calculate for extra 2 → 6 suppositories
- a = Pure base for 6 suppositories = 6gm
- d = 300 mg * 6 = 1800mg = 1.8gm



DV: $d / (a - c)$

• $2.7 = 1.8 / (6 - c)$

• $6 - c = 0.666 = 6 - c \rightarrow c = 6 - 0.666 = 5.3 \text{ gm}$

Bismuth sub gal 0.3x 6	1.8g
Base	5.3g

6

في هذا القانون
نرى صيغة a
وقد ا
بعد التحليل
دات
ليجاء صيغة c

Base كمية ال
التي نضيفها

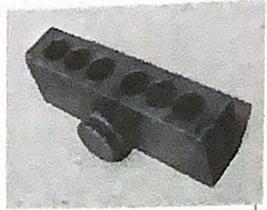
بعض PEG blank ووزنهم
ويأخذ الأفرنج ويصير
Cocoa butter وزن لا
ويأخذ الأفرنج ويصير
على وجهه

هذا بي أحضر Suppository من
Non-Cocoa butter
لازم أعدل نسبة مع ال
Cocoa butter لأن ال
molds أصلاً
لا Cocoa butter
من ال PEG

When the Density Factor is Not Known

When bases other than cocoa butter are used, or when the density factor for a drug in cocoa butter is not known, then the density factor can be estimated by calculation or experimentally determined by the double (casting) technique.

- A. The weight of the blank suppository is easily determined.
- B. A portion of the suppository base is melted, poured into the suppository mold and allowed to congeal.
- C. The suppositories are removed from the mold, and the total weight of the suppositories is determined.
- D. The average weight of the blank suppository is determined by dividing the total weight by the number of suppositories.



average weight of blank Cocoa + average weight of blank Non Cocoa (PEG)

factor هو ال
الـ

كوب ويأخذ شكل

When the Density Factor is Not Known: A. Estimation by Calculation



- One method to determine the density factor of a drug in a base other than cocoa butter requires the use of the ratio of a blank suppository of the non-cocoa butter base to a blank suppository of the cocoa butter base.
- This information is generally obtained by calibrating the mold first with one base and then the other base.
- As an example of the method, a mold was calibrated with the PEG base and the average blank suppository weighed 2.24 grams. The same mold was calibrated with cocoa butter and those blank suppositories weighed 1.87 grams on average. Therefore, the ratio of the two weights was:

$$\frac{\text{weight of PEG suppositories}}{\text{weight of cocoa butter suppositories}} = \frac{2.24 \text{ g}}{1.87 \text{ g}} = 1.20$$

$$\frac{\text{دosis الدواء}}{\text{طريقة العمل}} \Rightarrow \frac{\text{dose of drug}}{\text{DU of drug in Cocoa butter}} * \frac{\text{النسبة التي بدلتها}}{\text{PEG}} \text{ Cocoa}$$

والرقم الذي يطرح به من (PEG Blank)

When the Density Factor is Not Known: A. Estimation by Calculation

- If 200 mg of aspirin is to be incorporated into each PEG suppository, it is necessary to determine how much PEG base will be displaced by the aspirin. That displacement amount can be calculated as follows:
 - density factor of aspirin in cocoa butter = 1.3 (from reference sources)
 - density of PEG base relative to cocoa butter = 1.20 (the ratio obtained from the calibrations)
 - 0.2 g of aspirin will displace $\frac{0.2 \text{ g}}{1.3} \times 1.20 = 0.18 \text{ g PEG base}$
- For each PEG suppository to be formulated, 0.2 g of aspirin and 2.06 g (2.24 g - 0.18 g = 2.06 g) of the PEG base will be needed

طريقة 1 (direct)

التي حسناها بالاول

من السابق

average of PEG (Blank)
 كمتال Base التي (2.06g)

Aspirin	0.2g
Base	2.06g

- As an example of the method, a mold was calibrated with the PEG base and the average blank suppository weighed 2.24 grams.
- density factor of aspirin in cocoa butter = 1.3 (from reference sources)
- density of PEG base relative to cocoa butter = 1.20 (the ratio obtained from the calibrations)

طريقة 2 (Indirect) (نسبة وبتا ب)

1.2g PEG will displace 1g Cocoa butter

- 1.3 gm aspirin 1g coco butter
- 0.2gm???? (0.2 / 1.3 = 0.153gm cocoB)
- 1.2 gm PEG 1gm of coco Butter
- ??? 0.153gm
- (1.2 X 0.153 = 0.184 PEG)

- 0.2 g of aspirin will displace 0.184gm of PEG base

- 2.24gm suppository - 0.18 = 2.06 g PEG base

Aspirin	0.2g
Base	2.06g

شرح مكرر لكن بخط اليد.

جدول مكرر لقيم DF

Aspirin	1.3
Barbital	1.2
Bismuth salicylate	4.5
Chloral hydrate	1.3
Cocaine hydrochloride	1.3
Codeine phosphate	1.1
Diphenhydramine hydrochloride	1.3
Morphine hydrochloride	1.6
Phenobarbital	1.2
Zinc Oxide	4.0

Density factor = $\frac{\text{wt. of drug}}{\text{wt. of base displaced}}$

على طريقة 1 (Direct)

For 200mg (0.2g) Aspirin:

① In Cocoa Butter:

$1.3 = \frac{0.2}{\text{wt CB}} \rightarrow \text{wt. CB} = \frac{0.2}{1.3}$

* But remember from the estimated DF calculation

$\frac{\text{wt PEG supp}}{\text{wt CB supp}} = 1.2$

so:
 ② $\text{wt PEG supp} = \text{wt CB supp} \times 1.2$
 $= \frac{0.2}{1.3} \times 1.2 = 0.18\text{g}$

* 0.18g of PEG base will be displaced by 0.2g of Aspirin.

* For each PEG supp \rightarrow 0.2g Aspirin

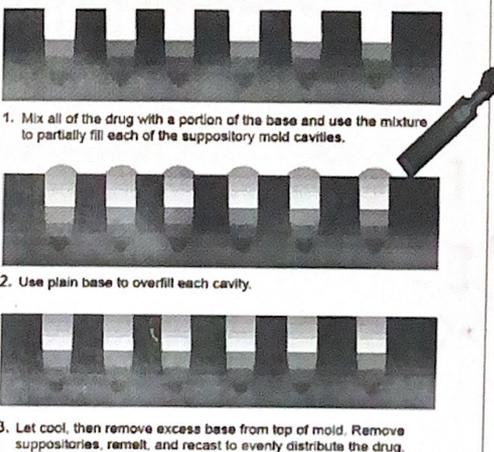
$2.24 - 0.18 = 2.06\text{g}$ of PEG will be needed

الهدف من هذي الطريقة:
 أنا ما أعني DF وما يعرف
 كم أصيف Base لكن
 أنا صايف لأنه الدواء كله
 انصاف والوزن صحيح
 (موني ما استعملت)
 DF محاسبا

When the Density Factor is Not Known: B. Double Casting Technique

- By determining the weights of suppositories at the various steps the density factor can be calculated.
- The double casting techniques can be used to determine the density factor of any drug in any base

Double Casting Method of Suppository Preparation



في هذه الطريقة: نقوم بصب كل الدواء (drug) مع جزء من

ال (Base) و نصبهم في mold ← partially fill
 بصب فقط

و بعد من بجد إضافة ال Base ← over fill (excess) زيادة

ويعد ما سرد وتفاصيل بعد (Scrapping) حتى للزيادة لكن هذه

الطريقة تجعل اللط غير متجانس فباخذ التحصيلة و يرجع بنوبها (remelt) ويحركها لتجانس.

When the Density Factor is Not Known: B. Double Casting Technique

- Using a particular mold, the average weight of a plain cocoa butter suppository was found to be 2.0 g. Using the same mold, cocoa butter suppositories, each containing 300 mg of drug A, were found to weigh 2.1 g each. So,

Base ← weight of blank suppository of cocoa butter = 2.0 g
 Drug ← weight of drug in each medicated suppository = 0.3 g
 Base + drug ← weight of suppository with drug and cocoa butter = 2.1 g
 weight of base in medicated suppository = $2.1 \text{ g} - 0.3 \text{ g} = 1.8 \text{ g}$
 weight of displaced base = $2.0 \text{ g} - 1.8 \text{ g} = 0.2 \text{ g}$ → displaced base
 Therefore, density factor of drug A = $0.3 \text{ g} \div 0.2 \text{ g} = 1.5$

القانون المستخدم

$$\text{Density Factor} = \frac{\text{Weight of drug}}{\text{Weight of base displaced}}$$

$$0.3 / 0.2 = 1.5$$

Displacement value = $\frac{\text{the weight of the drug}}{\text{(the weight of pure base suppositories - weight of the base in the medicated suppositories)}}$

13

- Mold calibration
- Q1: Prepare six suppositories each containing 250 mg bismuth subgallate.

Quantities are calculated for an excess of two suppositories.

Therefore calculate

8 جر

for eight suppositories.

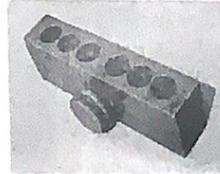
DV of bismuth subgallate = 2.7

A 1 g mould will be used with mould calibration $y = 0.94$.

(calculate amount of both drug and base need)

the amount of base required:

A 1 g mould will be used with mould calibration = 0.94.



$$\text{Amount of base} = (N \times y) - (N \times D / DV)$$

N = number of suppositories = 8, $y = \text{mould calibration} = 0.94$

D = amount of drug = 250 mg = 0.25 g

Amount of Drug for 8 suppositories = $8 \times 0.25 \text{ g} = 2 \text{ g}$

DV = 2.7

Amount of base required

$$= (8 \times 0.94) - ((8 \times 0.25) / 2.7) = 7.52 - 0.741 = 6.779 \text{ g} = 6.78 \text{ g}$$

القانون الثالث يطبق
كم توزن Base مباشرة

dose of drug
(بالغرام)

طبق مباشرة

طابعات المولد
للأول من 1

Base ←
الوزن أوزنها

14

على نفس القانون السابق
بس موشين
1 صنف 2 drugs

• Example on 2 drugs within the suppository

- Q2: Calculate the quantities required to make 15 suppositories each containing
- 150 mg hamamelis dry extract and 560 mg of zinc oxide. A 2g mould, with mould calibration of 2.04, will be used. Calculate for 17 suppositories (2 excess).

بس موشين
2,04

17 بجسب

$$\bullet \text{ Amount of base} = (N \times y) - (N \times D / DV)$$

[موشين

$$DV \text{ of hamamelis dry extract} = 1.5$$

$$DV \text{ of zinc oxide} = 4.7$$

- Weight of hamamelis dry extract = $17 \times 0.15 = 2.55 \text{ g}$.
- Weight of zinc oxide = $17 \times 0.56 = 9.52 \text{ g}$.
- Weight of base =

$$\bullet 17 \times 2.04 - \left(\frac{2.55}{1.5} + \frac{9.52}{4.7} \right) = 34.68 - (1.7 + 2.03) = 30.95 \text{g}$$

hamamelis

zinc oxide

حکمة ما إله داعي .

- Homework?

Using the density factor determined above, how much cocoa butter and drug A are needed to make 10 cocoa butter suppositories each containing 0.3 gm of drug?

47

Packaging and Storage

- Because suppositories are adversely affected by heat, it is necessary to maintain them in a cool place.
- Cocoa butter suppositories must be stored below 30°C (86°F), and preferably in a refrigerator (2°C to 8°C, or 36°F to 46°F).
- Glycerinated gelatin suppositories can be stored at controlled room temperature (20°C to 25°C, or 68°F to 77°F).
- Suppositories made from a base of polyethylene glycol may be stored at usual room temperatures.

يمكن تخزينها على حرارة
الغرفة بس ما تتجاوز
الـ 30 والأفضل تخزين
في البراد (2-8°)
وينطبق هذا على أي
Base (melted)



48

Packaging and storage

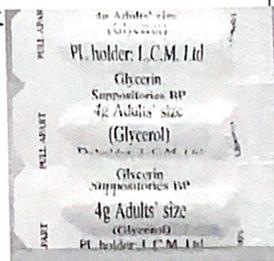
- If they must be stored in the refrigerator, suppositories should be **allowed to warm** to room temperature before **insertion**. *تدفئ قليلاً ←*
- The patient should be advised to **rub cocoa butter** suppositories **gently** with the fingers to melt the surface to provide lubrication for insertion. *نحك ←*
- **Glycerinated gelatin** or polyethylene glycol suppositories should be **moistened** with water to enhance lubrication. *بلع بلع ←*

بلع بلع ← Irritation



Packaging and Storage

- Glycerin suppositories and glycerinated gelatin suppositories are packaged in tightly **closed glass containers** to prevent a change in moisture content.
- Suppositories stored in high humidity may absorb moisture and tend to become **spongy**, whereas suppositories stored in places of extreme dryness may lose moisture and become **brittle**.



*تدلى على أناسه
التي فيها نسف ←*

*تدلى في الهواء
الطوي ← Soft*

*(Spongy + brittle) → يمكن استعمال كواء
و زير طهارة*

Observing formulations for evidence of instability

- Should be stored protected from heat, and may be stored under refrigeration but not frozen
- Glycerin and PEG base suppositories should be kept in airtight containers because they are hygroscopic

علامات تلف التامبل • Suppositories should be observed for:

1. excessive softening ← تكون امتصت الرطوبة
2. Drying out ← تكسرت
3. Harden or shrink ← تكسرت نتيجة تبخر الماء منها
4. Oil staining on the packaging ← يتسرب تسرب

51

VAGINAL INSERTS

- Vaginal tablets are more widely used nowadays than are commercial vaginal suppositories
- Vaginal tablets, frequently referred to synonymously as vaginal inserts, are usually ovoid and are accompanied in their packaging with a plastic inserter, a device for easy placement of the tablet within the vagina. (applicator)
- They are prepared by tablet compression and are commonly formulated to contain lactose as the base or filler, a disintegrating agent such as starch, a dispersing agent such as polyvinylpyrrolidone, and a tablet lubricant such as magnesium stearate.
- The tablets are intended to disintegrate within the vagina, releasing their medication
- Some vaginal inserts are capsules of gelatin containing medication to be released intravaginally.



زيت الجيوب بس
جميعها أخضر
ويتصنع بنفس
مكونات كبس
الجيوب
وإنها Base

52

سجل تصفيتها بالعلم

تم بحمد الله



**Trust me, I'm a
Pharmacist.**