



لجان الدفوعات

DISPENSING



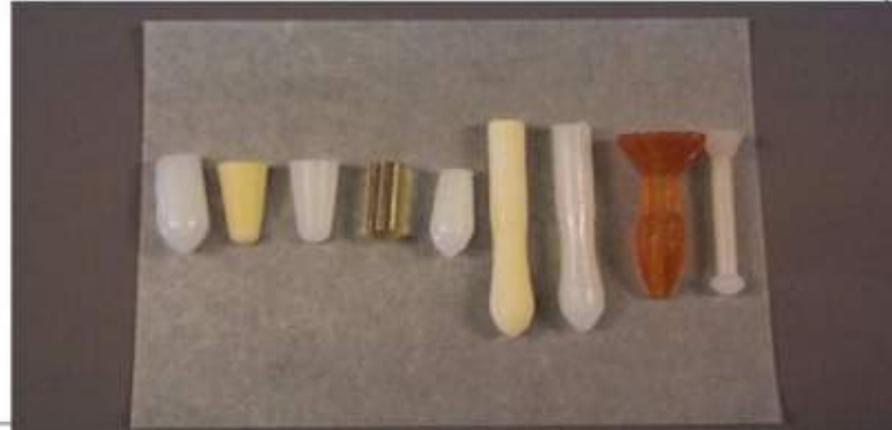
MORPHINE ACADEMY

MORPHINE
ACADEMY

Suppositories

Introduction

- Medicated semisolid formulation that are inserted into body cavities
تركيبة شبه صلبة طبية تُدخل في تجاويف الجسم
- Once inside cavity they melt, soften, or dissolve, releasing the drug
تهدئة أنسجة اليواسير الملتهبة
- For local effect (soothing inflammed hemorrhoidal tissues and promoting relaxation and evacuation)
تعزيز الاسترخاء والإفراغ
- and for systemic effects (to treat asthma, nausea, motion sickness, anxiety...etc)
الربو الغثيان دوار الحركة
- Route of administration:
طرق اخذ التحميلة
 - Rectal الشرج
 - Vaginal المهبل
 - Urethral الإحليل



Introduction

- **Suppositories** are solid dosage forms intended for insertion into body orifices where they melt, soften, or dissolve and exert local or systemic effects.
- **Rectal suppositories** are inserted with the fingers, but certain vaginal suppositories may be inserted high in the tract with the aid of an appliance. بالاصابع
- **Vaginal suppositories**, also called *pessaries*,
- **Urethral suppositories**, also called *bougies*

Rectal Route

- Advantages of rectal route:

- For patient with nausea and vomiting

الغثيان

القيء

- For unconscious patient

فاقد الوعي

- Infants and small children

- No taste limitations

عادةً لما تاخذ الدواء عن طريق الفم، بروح أول إشي للكبد (قبل ما يوصل الدم) وهذا اسمه ، ويخلي جزء من الدواء يتحطم. في بعض الطرق بيتجنب الدواء الكبد جزئياً، وبالتالي فعاليته بتزيد.

- Partial avoidance of hepatic first-pass metabolism

- Drugs avoid gastric fluid and enzymes. تجنب تعرض الدواء لعصارة المعدة والأنزيمات الهاضمة.

Rectal Route

- Disadvantage of this route:

- Absorption may be interrupted by defecation قد ينقطع الامتصاص بسبب التغوط
- Has small surface area for passive absorption (Drug absorption is less extensive and slower than after oral administration: SA of rectal mucosa is 1 / 10,000 the SA of small intestine)
- Small rectal fluid content السوائل الشرجية may cause problems with drug dissolution and absorption
- Inconvenient غير مريح
- Rectal absorption of most drugs frequently is erratic and unpredictable غير منتظم غير متوقع
- Some suppositories “leak” or are expelled after insertion تخرج بعد ادخالها تتسرب

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
- Thus, doses greater than 500 mg **cannot** be delivered with rectal suppositories but **can** be administered easily with vaginal suppositories

Rectal Route

العوامل التي تؤثر على الامتصاص!؟

- 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

- Colonic Content محتويات القولون
- Circulation Route مسار الدورة الدموية
- 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.

physicochemical factors of the drug and the base

- relative solubility of the drug in lipid and in water
- and the particle size of a dispersed drug.
- Physicochemical factors of the base include its ability to melt, soften, or dissolve at body temperature, its ability to release the drug substance, and its hydrophilic or hydrophobic character

الخطوة المحددة لسرعة الامتصاص هي انقسام الدواء وانتشاره خارج مادة القاعدة إلى تجويف المستقيم

- (The rate limiting step) is the drug partitioning and diffusing out of the base material in rectal lumen

في التحاميل الدواء يكون ممزوج مع قاعدة (base material) بعد إدخال التحميلة في المستقيم، القاعدة بتذوب أو تلين حتى يتم امتصاص الدواء، لازم يمر بمرحلتين أساسيتين:

اما Drug partitioning: يعني انقسام/انتقال جزيئات الدواء من القاعدة إلى السوائل المحيطة في المستقيم.

او Diffusing: انتشار الدواء من القاعدة المذابة إلى تجويف المستقيم (Rectal lumen).

هاي العملية (الخروج من القاعدة إلى التجويف) هي اللي بتحدد سرعة الامتصاص وتسمى الخطوة (Rate limiting step).

Vaginal Route of Administration:

Advantages:

- Generally there is less drug degradation via this route of administration compared to oral administration تدهور أقل للدواء
- The dose can be retrieved if necessary يمكن استرجاع الجرعة
- Potential of long term drug administration with various intrauterine device (IUDs) امكانية اعطاء الدواء على المدى الطويل

Disadvantages:

- Absorption can be variable because vagina is a physiologically and anatomically dynamic organ
- Retention of some delivery systems during menstruation could dispose the patient to **toxic shock syndrome** الدورة الشهرية احتباس بعض أنظمة توصيل الدواء أثناء فترة الحيض قد يعرض المريضة للإصابة بهذه المتلازمة
- Can interface with sexual activity يتفاعل
- Can be expelled طرده خارج الجسم

Vaginal Route of administration

- Vaginal suppositories are employed as: contraceptives, feminine hygiene antiseptics, antibiotics وسائل منع حمل مطهرات مضادات حيوية
- Vaginal suppositories = pessaries او مخروطي او بيضوي شكل كروي
- Globular or oviform or cone-shaped and weigh 3-5 gm تُدخل عميقاً في القناة المهبلية بمساعدة أداة خاصة
- Inserted high in the tract with the aid of a special applicator
- Patient should be instructed to dip the suppository quickly in water before insertion يُنصح المريضة أن تغمس التحميلة بسرعة في الماء قبل إدخالها ، هذا يساعد على سهولة الإدخال
- Women should wear a sanitary napkin to protect nightwear and bed linens فوط صحية يُفضل أن ترتدي المرأة فوطاً صحية لحماية الملابس الليلية وأغطية السرير

Urethral Route of Administration

- Bougies التحاميل الاحليلية مخدرات موضعية
مضادات بكتيرية
- 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.
الشكل التقليدي الشكل اسطواني حسب الجنس
- 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. التحميلة الوحيدة المتوفرة تجارياً تُسوق باسم (pellet)
- Urethral suppositories are unusual and may not be encountered in a compounding practice.

Suppository Bases:

- Classified by composition and physical properties:
 - Oleaginous (fatty) bases
 - Water soluble or miscible bases
- Ideal properties:
 - Nontoxic
 - Nonirritating
 - Inert
 - Compatible with the drug
 - Easily pliable into the desired shape
 - 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
 - Should dissolve or melt in the presence of mucous secretions at body temperature and allow release of the drug



Oleaginous bases

تأثير خفيف وغير مهيج

- 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.

Cocoa Butter (Theobroma Oil)

- Cocoa Butter, NF, is defined as the fat obtained from the roasted seed of بذور شجرة الكاكاو Theobroma cacao.
- At room temperature, it is a yellowish-white solid having a faint, agreeable تشبه رائحة الكاكاو 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. لانه يلبي متطلبات القاعدة المثالية



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. في المناخات الدافئة لازم
انحطها في التلاجة
- Thus it melts just below body temperature and yet maintaining its solidity at usual room temperatures

Cocoa Butter (Theobroma Oil)

- Particular attention must be given to two factors when preparing suppositories with cocoa butter base: بحكيك انه لازم ننتبه على شوية شغلات واحنا بنحضر زبدة الكاكاو
- 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.

ما نزيد الحرارة فوق 35C عشان ممكن يتحول الى مركب اخر اسمه alpha crystals وهذا المركب بيذوب على 25C تقريبًا درجة حرارة الغرفة و هيك بتخرب التخميلة وبتنوب

- The second factor is the change in melting point caused by adding certain drugs to cocoa butter suppositories. 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.

او نضيف مواد بتخلي درجة حرارة ذوبان التخميلة اقل فضروري انضيف spermaceti او beeswax عشان اتزيد من درجة حرارة ذوبان التخميلة وما تخرب

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
- Cocoa butter that has been overheated will change to clear golden liquid and should not be used

لازم يعطينا مظهر كريمي لامع

Synthetic triglycerides

- **Synthetic triglycerides** consist of **hydrogenated vegetable oils**.
- Their advantage over cocoa butter is that they do not exhibit polymorphism. They are, however, **more expensive**. تعتبر أغلى ثمناً
- 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.
- Other triglyceride type bases include **Dehydag®**, **Hydrokote®**, **Suppocire®**, and **Witepsol®**.

Water Soluble/Water Miscible Bases

- Water soluble/water miscible bases are those containing glycerinated gelatin or the polyethylene glycol (PEG) polymers.
- These bases dissolve in rectal mucosal fluids in contrast to 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.

Glycerinated Gelatin

- Because glycerinated gelatin–based suppositories have a tendency to absorb moisture as a result of the ^{طبيعتها الماصة للرطوبة} **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.
- As a result of the hygroscopicity of the glycerin, the suppository may also have a **dehydrating effect** and **irritate the tissues** upon insertion.

Glycerinated Gelatin

- 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

يساهم الغليسرين في التأثير الملين زي لما يسحب الماء من الامعاء وكمان لما يحدث تهيج بسيط في الغشاء المخاطي للامعاء ليحفز التبرز

وجود الماء ضمن تركيبة التحميلة يساعد على تقليل سحب السوائل من الأغشية المخاطية و التقليل من التأثير المهيج للغليسرين

- 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.

إذا لزم الأمر، يمكن ترطيب التحميلة بالماء قبل إدخالها وهذا يقلل من ميل القاعدة في البداية إلى سحب الماء من الأغشية المخاطية ويخفف من تهيج الأنسجة.

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.
- 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 ^{شفاف} translucent, ^{مرنة} resilient, gelatinous solids that tend to dissolve or disperse slowly in mucous secretions to provide prolonged release of active ingredients.

لتوفير إطلاق مطول للمكونات الفعالة.

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%)
- 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



Polyethylene Glycol Polymers

- They are chemically stable, nonirritating, miscible with water and mucous secretions, and can be formulated, either by molding or compression, in a wide range of hardness and melting point.
- Certain polyethylene glycol polymers may be used singly as suppository bases but, more commonly, formulas call for compounds of two or more molecular weights mixed in various proportions as needed to yield a finished product of satisfactory hardness and dissolution time.
- Since the water miscible suppositories dissolve in body fluids and need not be formulated to melt at body temperature, they can be formulated with much higher melting points and thus may be safely stored at room temperature.

Polyethylene Glycol Polymers



- Polyethylene glycols are polymers of ethylene oxide and water prepared to various chain lengths, molecular weights, and physical states.
- They are available in a number of molecular weight ranges, the most commonly used being polyethylene glycol 300, 400, 600, 1,000, 1,500, 1,540, 3,350, 4,000, 6,000, and 8,000.
- The numeric designations refer to the average molecular weight of each of the polymers.
- Polyethylene glycols having average molecular weights of 300, 400, and 600 are clear, colorless liquids.
- Those having average molecular weights of greater than 1,000 are waxlike white solids whose hardness increases with an increase in the molecular weight.

Polyethylene Glycol Polymers

- Disadvantages of PEG bases:

- Produce stinging or a burning sensation
أحساس وخز أو حرق
- and may cause a defecating reflex when used rectally (minimized by adding water to PEG base and moistening with water before insertion)
رد فعل التبرز
- 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.
- Incompatible with large number of drugs (i.e. aspirin...)
غير متوافق
- Should not be stored in polystyrene vials because PEG reacts with the polystyrene

Similarities between glycerinated gelatin and PEG bases

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

Methods of Preparation of Suppositories:

1. Hand Rolling

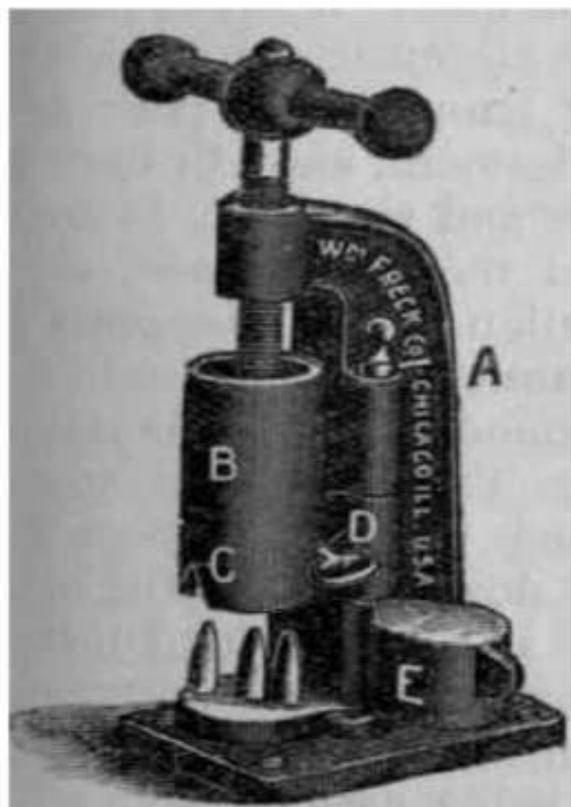
- is the oldest and simplest method of suppository preparation and may be used when only a few suppositories are to be prepared in a cocoa butter base.
- It has the advantage of avoiding the necessity of heating the cocoa butter.
- A plastic-like mass is prepared by triturating grated cocoa butter and 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.



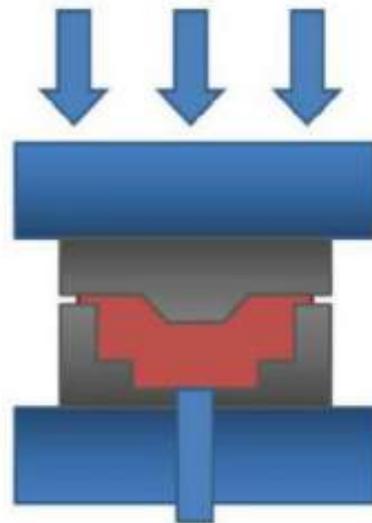
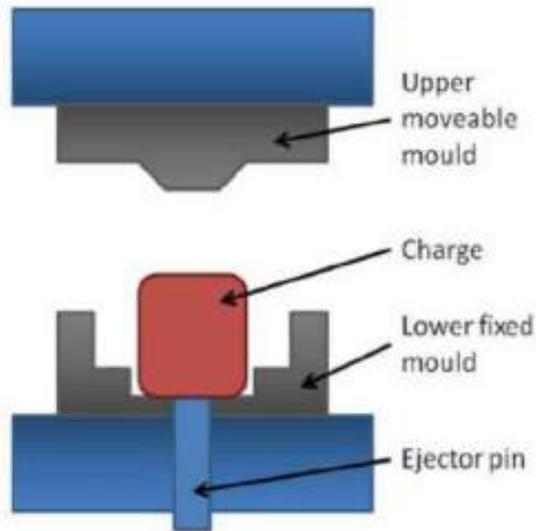
Methods of Preparation of Suppositories:

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



Compression Moulding



Methods of Preparation of Suppositories:

3. Fusion or molding

- 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) *pouring the melt into molds*, (d) *allowing the melt to cool and congeal into suppositories*, and (e) *removing the formed suppositories from the mold*..

Methods of Preparation of Suppositories:

3. Fusion or molding

• هذه معناتها (تزييت) القالب يعني زي لما نحط زيت في القلاية عشان ما يلزق الاكل

مش ضروري

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.

هذه المواد تنكمش عند التبريد وبالتالي تنفصل بسهولة عن جدران القالب، مما يجعل إخراج التحميلة سهلاً.

ضروري

- Lubrication is usually necessary with glycerinated gelatin. A thin coating of mineral oil applied with the finger to the molding surfaces usually suffices.

يتم ذلك عن طريق وضع طبقة رقيقة من زيت معدني (Mineral oil) على سطح القالب باستخدام الإصبع.

Methods of Preparation of Suppositories:

3.Fusion

Suppository molds:

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



- **Small hand-held molds:**

Are made of:

Stainless steel

Aluminum

Brass

Plastic

Rubber



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.

Density Factors

- When a drug is placed in a suppository base, it will displace an amount of base as a function of its density.
- If the drug has the same density as the base, it will displace an equivalent weight of the base.
- If the density of the drug is greater than that of the base, it will displace a proportionally smaller weight of the base.
- Density factors for common drugs in cocoa butter are available in standard reference texts.

Density Factors:

- The density factor is used to determine how much of a base will be displaced by a drug. The relationship is:

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

- For example: Aspirin has a density factor in cocoa butter of 1.3. If a suppository is to contain 0.3 g of aspirin, it will replace $0.3 \text{ g} \div 1.3$ or 0.23 g of cocoa butter. If the blank suppository (suppository without the drug) weighed 2 g, then $2 \text{ g} - 0.23 \text{ g}$ or 1.77 g of cocoa butter will be needed for each suppository, and the suppository will weigh $1.77 \text{ g} + 0.3 \text{ g} = 2.07 \text{ g}$. So if a pharmacist was making 12 aspirin suppositories using cocoa butter as the base, he would weigh $1.77 \text{ g} \times 12$ or 21.24 g of cocoa butter and $0.3 \text{ g} \times 12$ or 3.6 g of aspirin.

$$DF = \frac{\text{وزن الدواء}}{\text{وزن القاعدة المُزاحة}}$$

ال DF للاسبرين في زبدة الكاكاو = 1.3

الاسبرين = 0.3g

$$0.23g = \frac{0.3}{1.3} = \text{وزن القاعدة المُزاحة}$$

وزن زبدة الكاكاو المُزاحة

وزن التحميلة الفارغة = 2g

وزن زبدة الكاكاو = 2 - 0.23 = 1.77g

الوزن الكلي للتحميلة = 1.77 + 0.3 = 2.07g

إذا بدنا نعمل 12 تحميلة

زبدة الكاكاو = 1.77 * 12 = 21.24g

اسبرين = 0.3 * 12 = 3.6g

- When a drug is placed in a suppository base it will displace an amount of base as a function of its density.
- 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 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 $\xrightarrow{\text{will displace}}$ 1 g CB
 0.5 g BA $\xrightarrow{\text{will displace???$ } X g CB □

Then, 0.3 g CB is displaced by 0.5 g of BA

Density Factors:

- 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

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

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:

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

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 $\frac{0.2 \text{ g}}{1.3} \times 1.20 = 0.18 \text{ g}$ of PEG base
- For each PEG suppository to be formulated, 0.2 g of aspirin and 2.06 g ($2.24 \text{ g} - 0.18 \text{ g} = 2.06 \text{ g}$) of the PEG base will be needed

بس في كم تقريـب منهم
انا ما قريت بس

$$1.19 = \frac{2.24}{1.87} = \text{في البداية جبنا النسبة بين كثافة PEG و زبدة الكاكو}$$

ال DF للاسبرين في زبدة الكاكو = 1.3

وزن الاسبرين = 200mg = 0.2g

$$0.15 = \frac{0.2}{1.3} = \text{حسا بدنا نطلع كم ازاحة لزبدة الكاكو}$$

بما انه PEG أثقل من زبدة الكاكو بـ 1.19

بنحكي كم بدنا نعمل ازاحة لل PEG بنضرب ازاحة زبدة الكاكو بالنسبة = $0.17 = 1.19 * 0.15$

وزن التحميلة الفارغة في PEG تساوي = 2.24

مقدار الازاحة = 0.17

وزن ال PEG المطلوب = $2.07 = 2.24 - 0.17$

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

For 200mg (0.2g) Aspirin:

① In Cocoa Butter:

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

* But remember from the estimated DF calculation

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

so ::

$$\begin{aligned} \textcircled{2} \quad \text{wt PEG supp} &= \text{wt CB supp} \times 1.2 \\ &= \frac{0.2g}{1.3} \times 1.2 = 0.18g \end{aligned}$$

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

* For each PEG supp \rightarrow 0.2g Aspirin

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

From capsule

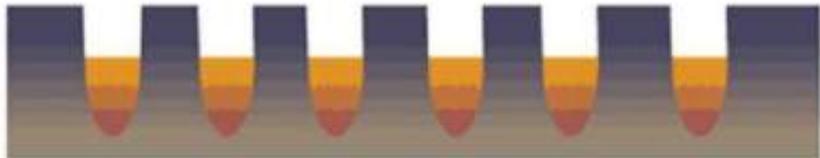
When the Density Factor is Not Known:

B. Double Casting Technique

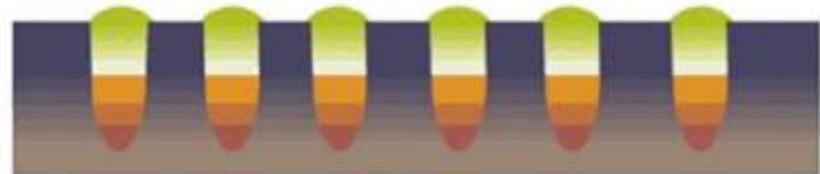
- By determining the weights of suppositories at the various steps the density factor can be calculated.

- The double casting techniques can be used to determine the density factor of any drug in any base

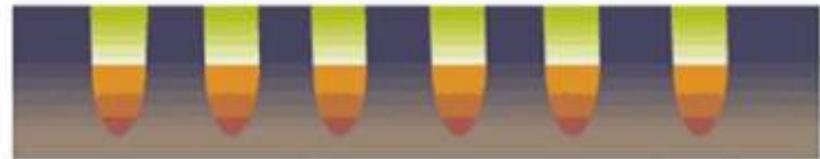
Double Casting Method of Suppository Preparation



1. Mix all of the drug with a portion of the base and use the mixture to partially fill each of the suppository mold cavities.



2. Use plain base to overfill each cavity.



3. Let cool, then remove excess base from top of mold. Remove suppositories, remelt, and recast to evenly distribute the drug.

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,

- weight of suppository of cocoa butter = 2.0 g
weight of drug in each medicated suppository = 0.3 g
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 base displaced = $2.0 \text{ g} - 1.8 \text{ g} = 0.2 \text{ g}$

Therefore, density factor of drug A = $0.3 \text{ g} \div 0.2 \text{ g} = 1.5$

- 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?

هسا لازم يكون معطيني كم وزن التحميلة الفارغة في زبدة الكاكاو = 2g
عشان احكي وزن المزاج من زبدة الكاكاو هو = $0.2g = \frac{0.3}{1.5}$

وزن زبدة الكاكاو = $2 - 0.2 = 1.8g$

وزن الدواء = 0.3g

ال DF يساوي = 1.5

* بدنا 10 تحميلات

الدواء = $10 * 0.3 = 3g$

زبدة كاكاو = $10 * 1.8 = 18g$

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.

Packaging and storage

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

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.

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
- Suppositories should be observed for:
 - excessive softening
 - Drying out
 - Harden or shrivel
 - Oil staining on the packaging

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.
- 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

Vaginal inserts

- Some vaginal inserts are capsules of gelatin containing medication to be released intravaginally.

