تفريغ حساب وتركيب الأشكال الصيدلانية

اسم الموضوع: Suppositories

إعداد الصيدلاني/ة: ياسمين خليل

Soul Academy

لجان الدفعات

السلام عليكم ورحمة الله وبركاته

ربّي اشرح لي صدري
ويسر لي أمري
واحلل عقدة من لساني

Suppositories and Pessaries

Definitions

- **Suppositories:** Solid medicated preparations designed for insertion into rectum where they melt, dissolve or disperse and exert a local , or a systemic effect.

- **Pessaries:** Solid medicated preparations designed for insertion into vagina where they melt or dissolve and exert a local or a systemic effect.

- **Urethral suppositories:** Are slender, pencil-shaped suppositories intended for insertion into the male or female urethra

	Suppositries	pessaries	urethral supp
	Solid	Solid	Solid
into	rectum	vagina	male/female urethra
	melt, dissolve, disperse	melt, dissolve	melt, dissolve, disperse
	local	local, systemic	local
			slender, pencil-shaped

تحاميل شرجية

Rectal Suppositories

Reasons for using rectal root

➢ The patient is unable to use the oral route:

- Nausea and vomiting
- Unconscious فقدان وعي
- Some categories of patients (very young, very old, mentally disturbed)

➢ The drug is less suitable for oral administration as in case of:

مثل الادوية إلي بتعمل انزعاج بالمعدة

- Drugs causing gastrointestinal side effects
- Drugs unstable at the pH of GIT
- Drugs susceptible to first pass metabolism
- Drugs with unacceptable taste

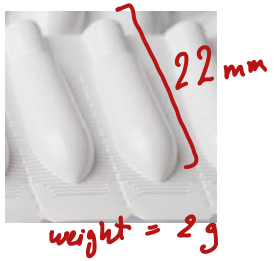
الحمد لله رب العالمين

Rectal Route

➢ **Disadvantage of this route:**

- Absorption may be interrupted by defecation
- 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 may cause problems with drug dissolution and absorption
- Inconvenient
- Rectal absorption of most drugs frequently is erratic and unpredictable
- Some suppositories "leak" or are expelled after insertion
- Problems with large scale production and the achievement of a suitable shelf -life.
- Rectal administration should not be the route of first choice.

Rectal Route



- Most commercially prepared rectal are torpedo-shaped
- 20 mm in length and weigh about 2 gm

تحا ميل الاطفال أصغر بحجم نصف تحا ميل الشباب والكبار

- 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 dose is smaller than vaginal dose

Rectal Route

➢ <u>The factors that affect rectal absorption of a drug may be divided into two main groups:</u>

خصائص تخص
rectal conditions

مثلاً لما نحكي للمريض استعمل التحاميل بعد عملية الاخراج لأنه بكون في مساحة أوسع للتحاميل.

1. *Physiologic factors and*

2. *Physicochemical* factors of the drug and the base.

خصائص تخص الدواء

اهدِني لما اختُلِفَ فيهِ منَ الحقِّ بإذنِك

Physiologic factors affecting drug absorption from rectal suppositories

Colonic Content

•Greater absorption may be expected from a void rectum than from one that is distended with fecal matter.

Circulation Route

•The lower hemorrhoidal veins surrounding the colon receive the absorbed drug and initiate its circulation throughout the body, bypassing the liver (avoid first pass metabolism).

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 affecting drug absorption from rectal suppositories

➢ Drug related factors:

all body tissues are phospholipids
mucos is aqueous medium

1. **Lipid–Water Solubility**
2. **Particle Size** → small particle size, better absorption

➢ Base related factors:

Nature of the Base:

-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.

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

- highly water-soluble drug partition
- highly lipophilic drug diffusion

Formulation of suppositories

Suppositories are composed of:

1. A suppository base
2. Active ingredient
3. Additives

أهم أشي

Suppository bases

- In suppositories and pessaries, the drug is incorporated into an inert vehicle. The vehicle is known as the base. Such bases should have some desirable criteria as:
- Melt at, or just below body temperature or dissolve in body fluids.
- Solidify quickly after melting.
- Be easily moulded and removed from the mould.
- Be chemically stable even when molten.
- Release the active ingredient readily.
- Be easy to handle.
- Be bland, i.e. non-toxic and non-irritant.

Suppository bases

1- The fatty bases: لونها قريبًا أصفر

i. Theobroma oil (cocoa butter).

ii. Synthetic fats

2- Water-soluble and water-miscible bases:

iii. Glycerol-gelatin bases

iv. Macrogols

ويكتب الله خيرًا
أنت تجهله !!

Theobroma oil

- Theobroma oil has a melting point range of 30-36°C and so readily melts in the body.

- **Advantages:** ⇒
- It liquefies easily on heating but also sets rapidly when cooled.
- It is also bland, therefore no irritation occurs.

- **Disadvantages:**
- Polymorphism: Stable β form vs. unstable α and γ forms
- Shrinks only slightly on cooling and therefore tends to stick to the mould thus needs a lubricant.
- Storage in hot climates. →
- Reduction of melting point by the addition of soluble drugs.

➢ *Note: for the previous two points, melting point can be raised by the addition of beeswax (up to 10%).*

- Prone to oxidation.
- Batch to batch variation.

Synthetic fats

- These are prepared by hydrogenating suitable vegetable oils. They have many of the advantages of theobroma oil but fewer disadvantages.
- Their solidifying points are unaffected by overheating.
- They have good resistance to oxidation because their unsaturated fatty acids have been reduced.
- No mould lubricant is necessary because they contract significantly on cooling.

Disadvantages:

- The viscosity of the melted fats is lower than that of theobroma oil. As a result there is a greater risk of drug particles sedimentation during preparation leading to a lack of uniform drug distribution which can give localized irritancy. This problem is partly compensated for in that these bases set very quickly.
- These bases become brittle if cooled too rapidly, so should not be refrigerated during preparation.
- There is a series of grades of synthetic fatty bases, each with different hardness and melting point ranges resulting in a variety of drug absorption and release profiles. This can be used to compensate for melting point reduction by soluble drugs. However, release and absorption of the drug in the body may vary depending on the base being used.

Glycerol-gelatin bases

water + glycerol + gelatine

- These bases are a mixture of glycerol and water stiffened with gelatin. The commonest is Glycerol Suppositories Base BP, which has 14% w/w gelatin, and 70% w/w glycerol. In hot climates the gelatin content can be increased to 18% w/w.

gelatin 14%
glycerol 70%
اشهر مثال هو glycerol supp الذي يحتوي

- Gelatin is a purified protein produced by the hydrolysis of the collagenous tissue, such as skins and bones, of animals.

- Two types of gelatin are used for pharmaceutical purposes, Type A, which is prepared by acid hydrolysis and is cationic, and Type B, which is prepared by alkaline hydrolysis and is anionic.

acid hydrolysis , cationic
alkaline hydrolysis , anionic
base

- Type A is compatible with substances such as boric acid and lactic acid while Type B is compatible with substances like zinc oxide.

control of pH
مادة قابضة
astringent

gelatine types

Type A	Type B
acidic hydrolysis	alkalin hydrolysis
cation	anion
lactic acid	zinc oxide
boric acid	

Glycerol-gelatin bases

Disadvantages:

- They are also hygroscopic and therefore require careful storage.
- Glycerol-gelatin bases cause rectal irritation.
- As they dissolve in the mucous secretions of the rectum, osmosis occurs producing a laxative effect.
- Because of the water content, microbial contamination is more likely than with the fatty bases. Preservatives may be added to the product, but can lead to problems of incompatibilities.
- They are much more difficult to prepare and handle than other bases. Lubrication of the mould is essential. Cause there is no shrinking
- The solution time depends on the content and quality of the gelatin and also the age of the suppository.
  - is the time in which the preparation converted from low viscosity to high ones

This type of base is commonly used for pessaries rather than suppositories.
- Vagina

Macrogols highly water soluble cause it has alot of OH

- These polyethylene glycols can be blended together to produce suppository bases with varying melting points, dissolution rates and physical characteristics. اختلاف
- Drug release depends on the base dissolving rather than melting (the melting point is often around 50°C).
- Higher proportions of high molecular weight polymers produce preparations which release drug slowly and are also brittle. هش

هي semisolid بس متماسكة
ولكن بنفس الوقت صايرة تنشق كتير وتتكسر

Advantages:

1. They have no physiological effect.
2. Are not prone to microbial contamination. Cause it's natural
3. Have a high water-absorbing capacity.
4. As they dissolve, a viscous solution is produced which means there is less likelihood of leakage from the body. يعني طارح تطلع من الجسم بعدما يأخذها الجديد
5. The base contracts on cooling and no lubricant is necessary.

shrinking
So, there is no need to lubrication تزييت

M.wt ↓ dissolution ↑ سريع

Macrogols

تغير طبيعة الدواء بسبب تغير base الـ M.wt

Disadvantages:

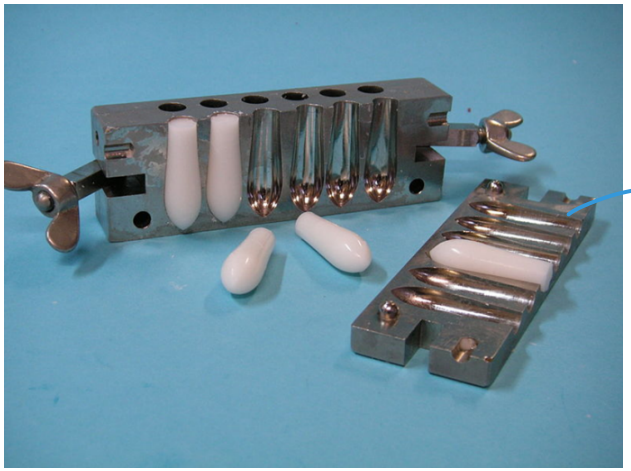
- They are hygroscopic which means they must be carefully stored and this could lead to irritation of the rectal mucosa.
- In addition crystal growth occurs with some drugs causing irritation to the rectal mucosa and, if the crystals are large, prolonged dissolution times.
- They become brittle if cooled too quickly and also may become brittle on storage.
- Incompatibility with several drugs and packaging materials, e.g. benzocaine, penicillin and plastic, may limit their use.

قال تعالى :
(لئن شكرتم لأزيدنكم)

Preparation of suppositories

- Suppository mould (metal or plastic)
- Moulds are made in four sizes: 1, 2, 4 and 8 g.
- Some bases need lubrication as follows:
- Theobroma oil: soap spirit
- Glycerol-gelatin base: almond oil, mineral oil
- Synthetic fats and macrogols: no need

التزييت بكون بصابون صادتنا ما بتنكسش



هاي mould

Mould calibration

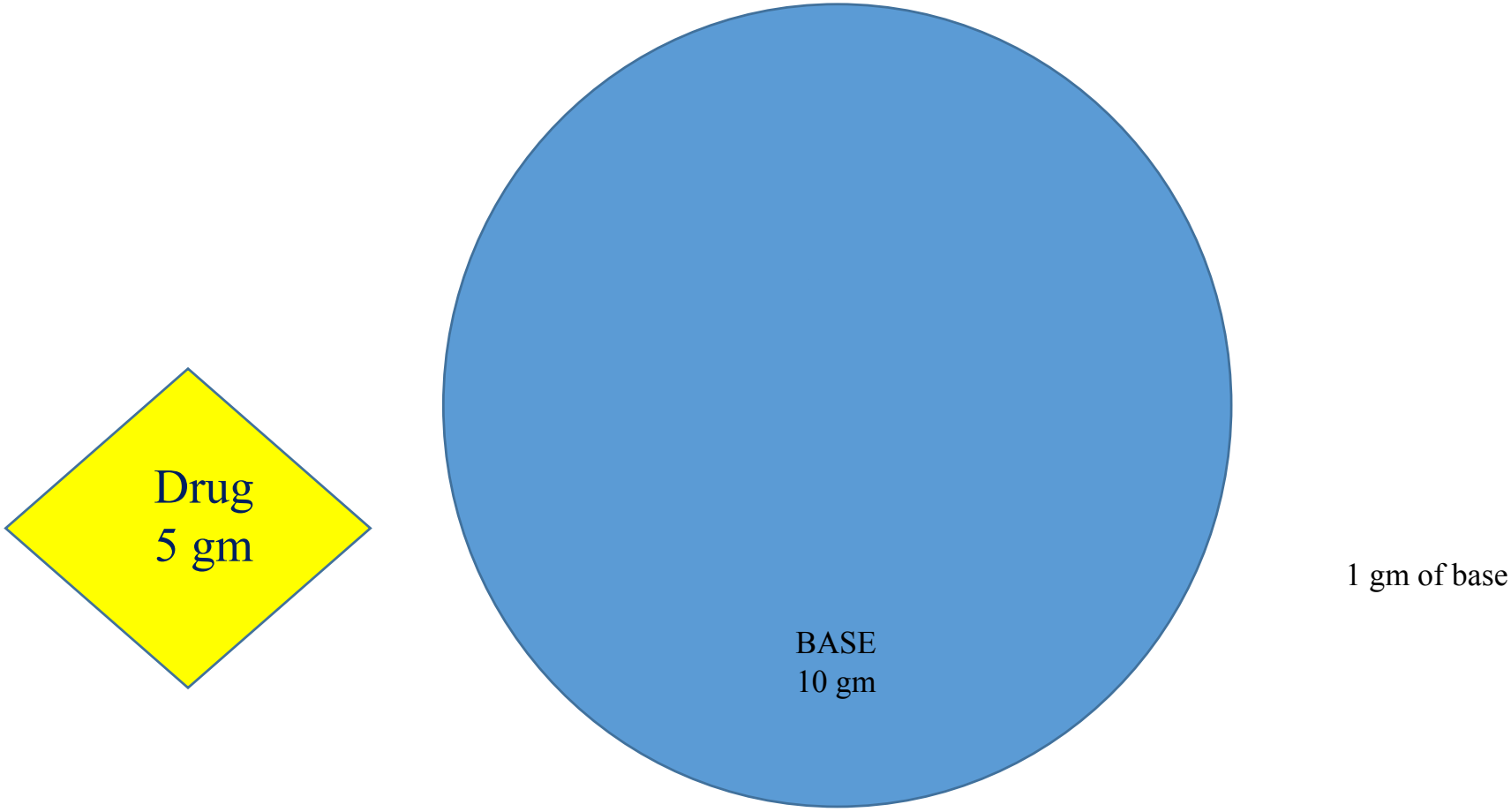
- The capacity of a suppository mould is nominal and each mould will have minor variations. Therefore the weight of material contained in different moulds may be different and will also depend on the base being used.
- It is therefore essential that each mould be calibrated for each different base.
- The capacity of the mould is confirmed by filling the mould with the chosen base.
- The total weight of the perfect suppositories is taken and a mean weight calculated. This value is the calibration value of the mould for that particular base.

Displacement value

- In the prescription of medicated suppositories to be prepared extemporaneously by the pharmacist, only the amount of the medicinal substance is indicated. >>>> The required amount of base is left for the pharmacist to figure out.

- A suppository mould is filled by volume, but the suppository is formulated by weight.

- The volume of a suppository from a particular mould is uniform but its weight can vary when a drug is present due to difference in densities between the drug and base.



Therefore DV is (5)

As the displacement equal in volume not the mass !

Containers for suppositories

glass, plastic are the best

- Each suppository should be wrapped in greaseproof paper.
- Glass or plastic screw-topped jars are possibly the best choice of container for extemporaneously prepared suppositories and pessaries.
- Cardboard cartons may be used but these offer little protection from moisture or heat. They are therefore not suitable for hygroscopic materials.

كرتون صقوى

رطوبة

اللهم إني أسألك أحسن الأخلاق

Shelf life

- Provided they are well packaged and the storage temperature is low, suppositories and pessaries are relatively stable preparations. Unless other information is available, an expiry date of 1 month is appropriate.

Labelling for suppositories

- How to use the product.
- 'Store in a cool place'
- 'For rectal use only' or 'For vaginal use only', whichever is appropriate.
- 'Do not swallow' can be put on the label but do not use 'For external use only'. The preparation is being inserted into a body cavity and this instruction is therefore incorrect.

ربنا آتنا في الدنيا حسنة
وفي الآخرة حسنة
وقنا عذاب النار

Key points

- Both rectal and vaginal administration can be used for local or systemic drug action,
- Bases may be fatty or water miscible.
- Synthetic fatty bases, made from hydrogenated vegetable oils, are easier to use than theobroma oil.
- Glycerol-gelatin base produces a laxative effect.
- Type A (cationic) or Type B (anionic) gelatin can be used to avoid incompatibilities.
- Macrogol bases are blends of high and low molecular weight polymers which dissolve in rectal contents.
- Suppositories have nominal capacities of 1,2,4 and 8 g and must be calibrated with the base to be used.
- When using theobroma oil and glycerol-gelatin base, the mould has to be lubricated.

Key points

- To allow for contraction on cooling, overfilling with oily bases is required.
- Each mould should be calibrated for each base.
- Because glycerol-gelatin base has a higher density than fatty bases, moulds hold approximately 1.2 times the nominal weight.
- The displacement value is the number of parts by weight of drug which displaces one part by weight of base.
- Unless the density of the drug and base are the same, a displacement value is required to calculate the amount of base displaced by the drug.
- Labels should include either "For rectal use only" or " For vaginal use only", and "Store in a cool place".

اللهم إني أسألك الجنة وما قرب إليها من قول أو عمل
وأعوذ بك من النار وما قرب إليها من قول أو عمل