Calculations for Suppositories Density (Dose Replacement)

- The density factors of various bases and drugs need to be known to determine the proper weights of the ingredients to be used. Density factors relative to cocoa butter have been determined. **If the density factor of a base is not known,** it is simply calculated as **the ratio of the blank weight of the base and cocoa butter**

- Three methods of calculating the quantity of base that the active medication will occupy and the quantities of ingredients required are illustrated here:

- (a) dosage replacement factor,

- (b) density factor, and

- (c) occupied volume methods

Determination of the dosage replacement factor method

$$f = \frac{[100\,(E - G)]}{[(G)(X)]} + 1$$

- **Where**

- **f is the dosage replacement factor of the drug**

- **E is the weight of the pure base suppositories, and**

- **G is the weight of suppositories with X% of the active ingredient.**

- **Cocoa butter is arbitrarily assigned a value of 1 as the standard base**

Dosage Replacement Factors For Selected Drugs

Balsam of peru	0.83	Phenol	0.9
Bismuth subgallate	0.37	Procaine HCl	0.8
Bismuth subnitrate	0.33	Quinine HCl	0.83
Boric acid	0.67	Resorcin	0.71
Camphor	1.49	Silver protein, mild	0.61
Castor oil	1.00	Spermaceti	1.0
Chloral hydrate	0.67	White or yellow wax	1.0
Ichthammol	0.91	Zinc oxide	0.15-0.25
Phenobarbital	0.81		

Example 1

- Prepare a suppository containing 100 mg of phenobarbital (f = 0.81) using cocoa butter as the base. The weight of the pure cocoa butter suppository is 2.0 g. What will be the total weight of each suppository?

- Because 100 mg of phenobarbital is to be contained in an approximately 2.0-g suppository, it will be about 5% phenobarbital.

- $f = \dfrac{[100(E-G)]}{[(G)(X)]} + 1$

- $0.81 = \dfrac{[100(2-G)]}{[(G)(5)]} + 1$

- G= 2.015g weight of the medicated suppository

Determination of density factor method

1. Determine the average blank weight, A, per mold using the suppository base of interest.
2. Weigh the quantity of suppository base necessary for 10 suppositories.
3. Weigh 1 g of medication. The weight of medication per suppository, B, is equal to 1g/10 supp = 0.1 g/supp.
4. Melt the suppository base and incorporate the medication, mix, pour into molds, cool, trim, and remove from the molds.
5. Weigh the 10 suppositories and determine the average weight (C).
6. Determine the density factor as follows:

$$density\ factor = \frac{B}{A - C + B}$$

- A is the average weight of blank,
- B is the weight of medication per suppository, and
- C is the average weight of medicated suppository

Determination of density factor method
Example 2

- Prepare 10 acetaminophen 300 mg suppositories using cocoa butter. The average weight of the cocoa butter blank is 2 g and the average weight of the medicated suppository is 1.8 g.

- Take the weight of the medication required for each suppository and divide by the density factor of the medication to find the replacement value of the suppository base

- $density\ factor\ D.F\ = \dfrac{B}{A-C+B} = \dfrac{0.3}{2-1.8+0.3} = 0.6$

Replacement value =B/D.F=0.3/0.6=0.5

- Subtract this quantity from the blank suppository weight

- 2-0.5=1.5g base for one supp.

- Multiply by the number of suppositories required to obtain the quantity of base and the drug required for the prescription

- 12X1.5= 18 g of cocoa butter required

- 12X0.3= 3.6g of the drug required

Determination of occupied volume method

1. Determine the average weight per mold (blank) using the designated base.
2. Weigh out enough base for 10 suppositories.
3. Divide the density of the active drug by the density of the base to obtain a ratio.
4. Divide the total weight of active drug required for the total number of suppositories by the ratio obtained in step 3. This will give the amount of base displaced by the active drug.
5. Subtract the amount obtained in step 4 from the total weight of the prescription (number of suppositories multiplied by the weight of the blanks) to obtain the weight of base required.
6. Multiply the weight of active drug per suppository times the number of suppositories to be prepared to obtain the quantity of active drug required

Example 3

- **Prepare 8 suppositories, each containing 200 mg of a drug with a density of 3.0. The base has a density of 0.9, and a prepared blank weighs 2.0 g. Using the determination of occupied volume method, prepare the requested suppositories.**

- **From step 1: The average weight per mold is 2.0 g.**

- **From step 2: The quantity required for 10 suppositories is 2 g× 10 = 20 g.**

- **From step 3: The density ratio is 3.0/0.9 = 3.3.**

- **From step 4: The amount of suppository base displaced by the active drug is 2.0 g (total wt. of drug)/3.3 = 0.6 g.**

- **From step 5: The weight of the base required is 20 - 0.6 g = 19.4 g.**

- **From step 6: The quantity of active drug required is 0.2 × 10 = 2.0g.**

- **The required weight of the base is 19.4 g, and the weight of the active drug is 2 g**

Displacement value DV

- **Displacement value is defined as the**
- **The quantity of drug that displaces one part of the base**
- **eg. hydrocortisone has a displacement value of 1.5**
- **Means 1.5g hydrocortisone displaces 1g the suppository base**
- **If the density of the drug equals the density of the base. The drug will displace the same amount of base**
- **If the density of the drug is more than the density of the base the drug will displace low amount of base**
- **if the density of the drug is less than the density of the base the drug will displaces high amount of base**
- **DV. for liquids equals 1**

Calculations using displacement values

- Prepare 8 codeine phosphate suppositories (D.V=1.1)using mold of 1g size each supp. Containing 60mg /supp.

- prepare 10 supp. to compensate for any loss

- 60X10=600mg=0.6g codeine phosphate

- Supp. Base 1gX10=10g total wt. of pure base

- <u>Drug</u>   <u>base</u>

- 1.1 <u>displace</u>   1g   base displaced=(1gX0.6)/1.1=0.55

- 0.6   ?

- Amount of base needed is 10g-0.55= 9.45g

- **Example:** Calculate the quantities required to make 8 theobroma oil supp. (2g mold) each containing 400 mg of zinc oxide (DV= 4.7).

1. Calculate the total weight of zinc oxide required. 0.4X10=4g

2. Calculate what weight of base would be required to prepare10 un medicated supp. 2gX10=20g

3. Determine what weight of base would be displaced by the medicament. **Replaced base =wt. of drug/DV = 4/4.7=0.85**

4. Calculate, therefore, the weight of base required to prepare the medicated supps.   20-0.85= 19.15g wt of base required

- Glycero-gelatin base has a density 1.2 times greater than theobroma oil. Therefore, a 1 g supp. mold will produce a 1 g theobroma oil supp., but a 1.2 g glycero-gelatin supp. This factor must be taken into account in displacement value calculations.

Example

- **Calculate the quantities required to make six glycero gelatin supp. (4 g mold), each containing100 mg aminophylline (Displacement value = 1.3)**

- **Drug   6X100=0.6g**

- **glycerin gelatin Base   6X4gX1.2 =28.8g**

- **glycerin gelatin Base replaced = 0.6/1.3=0.46 (by theobroma oil base)**

- **0.46 X1.2=0.55g base displaced by the base (gly.gelatin)**

- **Base required   28.8-0.55g=28.25g of the base required**

Displacement values D.V. of some common drugs incorporated into suppositories

Drug	D.V.	Drug	D.V.
Aminophylline	1.3	Morphine sulphate	1.6
Aspirin	1.1	Paracetamol	1.5
Bismuth subgallate	2.7	Phenobarbital	1.1
Castor oil	1	Phenobarbital Sod.	1.2
Chloral hydrate	1.4	Resorcinal	1.5
Codeine phosphate	1.1	Sulfur	1.6
Diphenhydramine HCl	1.3	Theophylline sodium acetate	1.7
Hydrocortisone	1.5	Zinc oxide	4.7
Metronidazole	1.7	Zinc sulphate	2.4
Morphine HCl	1.6		

Examples of Rectal Suppositories

SUPPOSITORY	COMMERCIAL PRODUCT	ACTIVE CONSTITUENT	TYPE OF EFFECT	CATEGORY AND COMMENTS
Bisacodyl	Dulcolax (Boehringer-Ingelheim)	10 mg	Local	Cathartic. Base: hydrogenated vegetable oil
Hydrocortisone	Anusol-HC (Salix)	25 mg	Local	Pruritus ani, inflamed hemorrhoids, other inflammatory conditions of the anorectum. Base: hydrogenated glycerides
Indomethacin	Indocin	50 mg	Systemic	Anti-inflammatory: Base: polyethylene glycols

Vaginal inserts

Vaginal tablets are more widely used nowadays than are commercial vaginal supps; but compounded vaginal supps are very widely used. The tablets are easier to manufacture, more stable, and less messy. Vaginal tablets, frequently referred 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. Vaginal tablets contain the same types of anti-infective and hormonal substances as vaginal supps.

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.

Packaging and storage

Most commercial supps are individually wrapped in either foil or plastic. Some are packaged in a continuous strip, separated by tearing along perforations or otherwise separated in compartmented boxes to prevent contact and adhesion.

Supps containing light-sensitive drugs are individually wrapped in an opaque material such as a metallic foil.

Because supps are adversely affected by heat, it is necessary to maintain them in a cool place.

Cocoa butter supps must be stored below 30°C and preferably in a refrigerator (2°C to 8°C).

Glycerinated gelatin supps can be stored at controlled room temperature (20°C to 25°C). Supps made from a base of **PEG** may be stored at usual room temperatures.

Supps stored in high humidity may absorb moisture and tend to become spongy, whereas supps stored in places of extreme dryness may lose moisture and become brittle.

THANK YOU