Pharmaceutical Calculations

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- One of the greatest potentials for error in prescription compounding is in the area of pharmacy math or pharmacy calculations
- A misplaced decimal or “estimated” value for a medication can have serious consequences including death
- There is no excuse for ignorance in this area and an individual unprepared to do the necessary calculations should not be involved in pharmaceutical compounding

Numbers and Numerals

- Number: a total quantity or amount
- Numeral: a word, sign, or group of words and signs representing a number:
- Roman Numerals:

  A numeral system of ancient Rome based on letters of the Alphabet

  I: one, V: five, X: ten, L:50, C:100, D: 500, M:1000

  The first ten Roman numerals are: I, II, III, IV, V, VI, VII, VIII, IX, X

  XXX:?

  LX:?

I 1 V 5 IX 9
II 2 VI 6 X 10
III 3 VII 7
IV 4 VIII 8

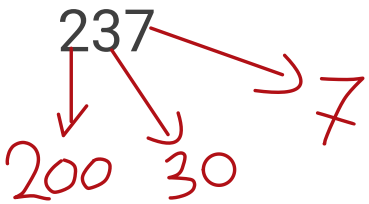
Numbers and Numerals

- Arabic Numerals:

  Most common symbols used to represent numbers

  The basic symbols called digits (أرقام) are: 0,1,2,3,4,5,6,7,8,9

  The position of a digit determines its value

Decimals

الفواصل العشرية

- A decimal is a fraction whose denominator is 10 or a multiple of 10

كسر مقامه مضاعفات الـ ١٠

- e.g.:
- 0.7= 7/10
- 0.06= 6/100
- 0.006= 6/1000
- 0.3 = 0.30 = 0.300
- 0.3= 3/10
- 0.03=3/100
- 0.003=3/1000

Using ratios, proportions, and percentages in dosage calculations:

- Example: a vial of Rociphen contains 100 milligrams per milliliter. How many milliliters should be given to a patient to obtain 650 milligrams?
- 100 mg 1 ml

  650mg X ml
- X= 6.5 ml

100 mgm → 1 mL

650 mgm → X

$$\frac{650 \times 1}{100} = 6.5 \text{ mL}$$

Using ratios, proportions, and percentages in dosage calculations:

- Always look for what is being asked:
- Number of doses
- Total amount of drug
- Size of dose
- Given any two of the above, you can solve for the third
- General Formula:

Number of doses= Total amount/Size of dose

Total amount= number of doses X size of dose

Size of dose= Total amount/number of doses

Using ratios, proportions, and percentages in dosage calculations:

- Example: how many milligrams of theophylline does a patient receive per day, if the prescription وصفة طبية indicates 300mg tid? ter in die (three per day)
- X total amount= 3 X 300mg

X= 900 mg total

- How much propranolol will a patient receive every 6 hours if he is to receive 160 mg per day?

X dose=160 mg/4 doses

X= 40 mg

24 Hours per day

$\frac{24}{6} = 4$

160 mg in 4 times

$\frac{160}{4} = 40$ mg every 6 Hours

Using ratios, proportions, and percentages in dosage calculations:

$\frac{120}{5} = 24$

Solve by your self:

- How many doses are in 120ml of Benadryl Elixir, if one dose is 5ml? (Answer 24 doses)
- When erythromycin lactobionate is reconstituted, it yields a concentration of 50 mg/ml. How many milliliters are required to give a 0.9 gm dose? (Answer: 18 ml)… be careful for the unit

$50\ mg \longrightarrow 50 * 10^{-3}\ gm$

$\frac{50}{1000} = 0.05\ gm$

$0.05\ gm \longrightarrow 1\ mL$

$0.9\ gm \longrightarrow X$

$X = \frac{0.9}{0.05} = 18\ ml$

Percentage

- 45% = 45/100= 0.45
- It is not correct to divide by 100 and use the percent sign at the same time:

e.g. 25%= 25/100 and not 25%/100

- To calculate a percentage of a percentage:

50% of 40% is:

(50/100) X (40/100) = 0.5 X 0.4= 0.2 = 20/100 = 20%

25% of a

1% Solution

$= \frac{25}{100} \times \frac{1}{100}$

Mass percentage (fraction)

- Wt%: Percent weight-in-weight (w/w) expresses the number of grams of a drug or active ingredient in 100 grams of a mixture (g/g)

- If a bottle contains 40 gm of ethanol and 60 gm of water then it contains 40% ethanol by mass or 0.4 mass fraction ethanol

total mass = 40+60 = 100 gm

$$\text{mass percent} = \frac{\text{mass of solute}}{\text{total mass}} \times 100$$

40 gm ethanol per 100 gm

Mass percentage (fraction)

- Examples: Prepare 500 ml of Phenol glycerin

  Phenol: 150 gm

  Glycerin 850 gm

  Weight per ml of glycerin: 1.25g

Mass = density X volume
= 1.25 x 500

So for preparing 500 ml of phenol glycerin the quantity of glycerin required = 500ml X 1.25= 625 gm

- Quantity of phenol required= 150*625/850= 110 gm
- So for preparing 500 ml of phenol glycerin the formula becomes:
- Phenol 110 g
- Glycerin 625 g

150 gm → 850 gm
X → 625 gm
X = 625 x 150 / 850

Phenol Glycerin IP

Indian pharmacopia

- Method: Phenol and glycerin are mixed in a beaker. The beaker is warmed gently until is becomes a solution.
- Use: Local anesthetic and local antiseptic. Phenol glycerin is used to prepare Phenol Gargle and Phenol Glycerin Ear Drop.
- Cautions: Phenol Glycerin when diluted with water becomes caustic so it is diluted with glycerin.
- Label: FOR EXTERNAL USE ONLY should be displayed in the label.

Water mass required = 1 × 500 = 500 gm

- Examples:

Prepare 500 ml of sugar solution

Sugar 100 gm

Water 900 gm

100 gm → 900 gm

x → 500 gm

Weight per ml of water= 1 gm

The quantity of water required ? (500g)

The quantity of sugar required ? (55 g)

$$X = \frac{500 \times 100}{900} = 55.5 \text{ gm}$$

Mass of sugar required

Mass-volume percentage:

- Weight-in-volume (w/v) percentage: expresses the number of grams of a drug or active ingredient in 100 milliliters of a mixture
- Often used for solutions made from a solid solute dissolved in a liquid
- For example a 40% w/v sugar solution contains 40 gm of sugar per 100 ml of resulting solution

$$w/v\,\% = \frac{\text{gm of solute}}{\text{100 ml of solution}}$$

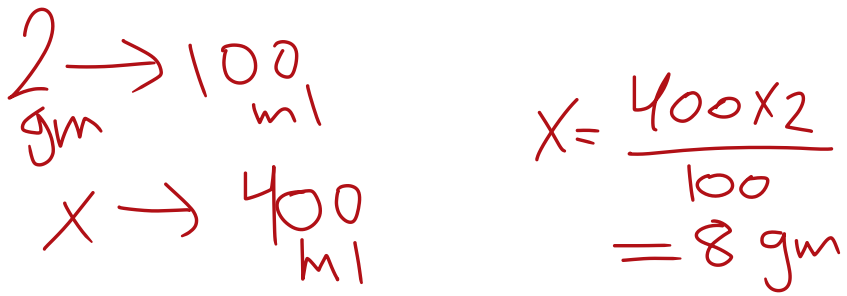
Mass-volume percentage:

- Example:

Calculate the quantity of sodium chloride required to prepare 400 ml of 2 (w/v)% solution

2g NaCl 100 ml solution

X 400 ml



X= 8 g of sodium chloride is dissolved in water to produce 400 ml makes 2% w/v solution

Mass-volume percentage:

- Example:

Prepare 500 ml of a 1 in 10000 solution from 1 in 5000 solution?

Strength of concentrate 1 in 5000= 100/5000=0.02%

Strength of dilute solution= 1 in 10000= 100/10000= 0.01%

Degree of dilution= strength of concentrate/strength of dilute solution = 0.02/0.01= 2 times

Volume of solution to be prepared = 500 ml

Therefore, dilute solution is obtained by diluting 500/2=250 ml of 1 in 5000 solution to 500 ml

Mass-volume percentage:

- Solve by yourself:

How much of a 5% will be required to prepare 1000 ml of a 1 in 500 solution?

$1_{gm} \rightarrow 500\ ml \Rightarrow w/v\% = \frac{1}{500} \times \% = 0.2\%$

Strength of concentrate= 5%

Strength of dilute solution= 0.2%

محلول مطلوب

Degree of dilution= 25 times

Volume to be prepared = 1000 ml

$\text{Degree of dilution} = \frac{\text{Strength of Concentrate}}{\text{Strength of dilute}} = \frac{5\%}{0.2\%} = 25$

Therefore dilute solution is obtained by diluting ~~40 ml of 5%~~ solution to 1000 ml

$\text{Volume of Concentrate} = \frac{\text{Final Volume}}{\text{dilution factor}} = \frac{1000}{25} = 40m$

$C_1V_1 = C_2V_2$

$5 \times V_1 = 0.2 \times 1000$

$V_1 = 40\ ml$

Volume-volume percentage:

- (v/v) percentage expresses the number of milliliters of a drug or active ingredient in 100 milliliters of a mixture
- Most useful when a liquid-liquid solution is being prepared
- For example, a 40% v/v ethanol solution contains 40ml ethanol per 100ml total volume
- Example:

5 ml → 100 ml
x → 500 ml

Prepare 500 ml of 5% solution of chloroform in 50% alcohol

5 ml chloroform 100 ml of 50% alcohol

X ml 500 ml of 50% alcohol

$$X = \frac{500 \times 5}{100} = 25 \text{ ml}$$

X= 25 ml of chloroform dissolved in sufficient quantity of 50% alcohol to make 500 ml of solution

5 % solution of chloroform means 5mL in 100 ml

5 ml $\xrightarrow{in}$ 100 ml

X ?? $\longleftarrow$ 500 ml

$$X = \frac{5 \times 500}{100} = 25 \text{ ml}$$

∴ add 25 ml chloroform to a sufficient quantity of 50 % alcoholic solution to make 500 ml solution

Ratio strength

- Ratio strength (1:N) is one part by weight or volume in N parts by weight or volume
- 1:200 ratio strength can be
- 1gm solid to 200 gm solid
- 1 ml liquid to 200 ml liquid
- 1 gm solid to 200 ml liquid

- Example:

If 2000 gm of ointment contain 75 gm of hydrocortisone, what is the percentage strength (w/w) of the ointment?

2000 gm ointment 75 gm hydrocortisone

100 gm ointment X

X=3.75%

$2000 \rightarrow 75$

$100 \rightarrow X$

$$X = \frac{75 \times 100}{2000} = \frac{75}{2000} = 0.0375$$

$$\text{Percent } \% = \frac{375}{10000} \times 100 = 3.75$$

Ratio strength

- If 8 ml of phenol were added to 480 ml of lotion what is the percentage of phenol in the lotion?
- X=1.6% of phenol
- 100 ml of lotion contain 1.6 ml of phenol

$8 \longrightarrow 480$

$\frac{8}{480} = 0.016$

$\text{Percent} = \frac{16}{1000} \times 100 = 1.6$

%

Ratio strength

- Solve:

1. If 1.2gm of menthol is added to 480 ml of lotion, what is the percentage of menthol in the lotion? $\frac{1.2}{480} \times 100 = 0.25$

Answer= 0.25% of menthol

0.1 gm in 100 ml

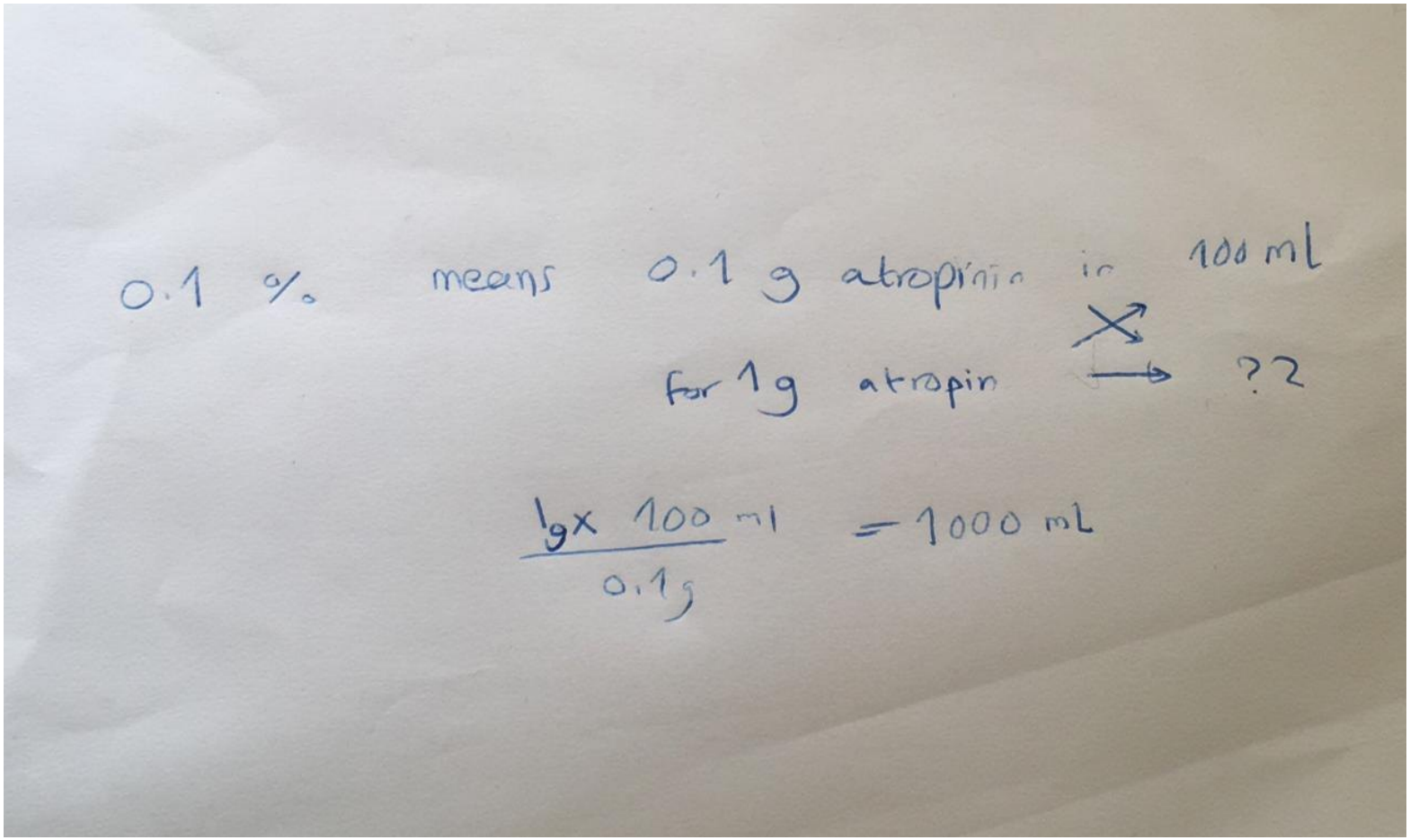
2. How many milliliters of a 0.1% solution can be made from one gram of atropine sulfate?

Answer: 1000ml

$0.1 \rightarrow 100$

$1 \rightarrow X$

$X = \frac{100}{0.1} = 1000$ ml


0.1 % means 0.1 g atropin in 100 ml
for 1 g atropin → ?2
1g x 100 ml / 0.1g = 1000 mL

Concentration and Dilution

- Stock solutions are concentrated bulk solutions from which more dilute solutions can be quickly prepared
- These solutions can be used with a ratio strength or percentage strengths
- General formula for solving: V1 X S1 = V2 X S2
- V1= the quantity or the amount of the original preparation
- S1= the % strength of the original preparation expressed as a decimal or percent
- V2= the quantity or amount of the wanted preparation
- S2= the % strength of the wanted preparation expressed as a decimal or percent

Concentration and Dilution

- Example: if 500 ml of a 15% solution are diluted to 1500 ml, what will be the percent strength ?

500 ml (V1) X 15% (S1)= 1500 ml (V2) X S2

S2=5%

$500 \times 15\% = 1500 \times S_2$

$S_2 = \frac{500 \times 15\%}{1500} = 5\%$

- If 1000 ml of a 20% solution are diluted to 5000 ml what will be the percent strength?

1000 ml(V1)X 20% (S1) = 5000 ml (V2) X S2

S2= 4%

$1000 \times 20\% = 5000 \times S_2$

$S_2 = \frac{1000 \times 20\%}{5000} = 4\%$

Concentration and Dilution

- Solve:

1. How many milliliters of a 25% solution can be prepared from 750ml of a 65% solution? $25\% \times S_2 = 750 \times 65\%$

Answer:1950 ml $S_2 = \frac{750 \times 65\%}{25\%} = 1950\,mL$

2. If 30 gm of a 45% powder was diluted to make a 30% powder, how many grams will the new preparation weigh?

$30 \times 45\% = M_2 \times 30\%$

Answer: 45 gm $M_2 = 45\,gm$

3. If 20 ml of a 1:200 solution of a chemical is diluted to 500 ml, what is the ratio strength? $\frac{1}{200} = 0.005$

Answer: 1:5000

$20 \times 0.005 = 500 \times M_2$

$M_2 = \frac{20 \times 0.005}{2500} = \frac{5}{\frac{10000}{25}} = \frac{5}{25000} = \frac{1}{5000}$

Reducing and Enlarging formulas

- Determine the total weight or volume of ingredients and convert to the required quantity. The quantity in the original and new formulas will have the same ratio

1. Total Weight or Volume of ingredients (orginal).
2. Convert to the required quantity.
3. X or ÷ every ingridient at equal ratio.

Reducing and Enlarging formulas

- Calculate the amount needed for 50 ml strong sodium salicylate mixture

Sodium salicylate 10g

Sodium metabisulfate 1 g

D.S. chloroform water 525 ml

Water q.s. 1000 ml

Answer:

Sodium salicylate 0.5g

Sodium metabisulfate 0.05g

D.S. chloroform water 26.25 ml

Water q.s to 50 ml

نضيف ماء حتى يصبح الحجم النهائي 1000

① $\frac{50}{1000} = 0.05$ reducing ratio

② نضرب كل مكون في ratio

$10 \times 0.05 = 0.5$ g

$1 \times 0.05 = 0.05$ g

$525 \times 0.05 = 26.25$ ml

Reducing and Enlarging formulas

- Calculate the amounts needed for 100 ml peppermint water?

Peppermint water:

Peppermint 2 ml

Talc 15gm

Purified water q.s. 1000 ml

Answer:

Peppermint 0.2 ml

Talc 1.5 gm

Purified water q.s. 100 ml

$\frac{100}{1000} = 0.1$ Reducing ratio

$2 \times 0.1 = 0.2$

$15 \times 0.1 = 1.5$

- What is the percentage of alcohol in the following mixture ?

Alcohol 2% 5ml (0.1 ml)

Alcohol 4% 10 ml (0.4 ml)

Answer:

0.1+0.4=0.5

0.5/(5+10)=0.0333

X= 3.33%

2% x 5 = 0.1 ml

4% x 10 = 0.4 ml

total alcohol qauntity = 0.1 + 0.4 = 0.5 ml

total alcohol volume = 10 + 5 = 15

$$\text{Percentage} = \frac{0.5}{15} = 0.033$$

$$\% \Rightarrow \frac{33}{1000} \times 100 = 3.3$$

Alligation method

How many parts of an 20% w/v solution and 8% w/v solution are needed to produce an 10% w/v solution?

12 parts

- Solution of Highest Concentration: 20% w/v
- Solution of Lowest Concentration: 8% w/v
- Solution of Desired Concentration: 10% w/v
- Subtracting the lower concentration (8 w/v) from the desired concentration (10% w/v) = 2 (higher concentration ratio value)
- Subtract the desired concentration (10 w/v) from the higher concentration (20% w/v) = 10 (lower concentration ratio value)

This gives us a ratio of 2:10 (higher concentration : lower concentration)

Let's suppose that the question asked us to produce 500mL of 10% w/v solution.

In this case, we know the ratio – 2:10

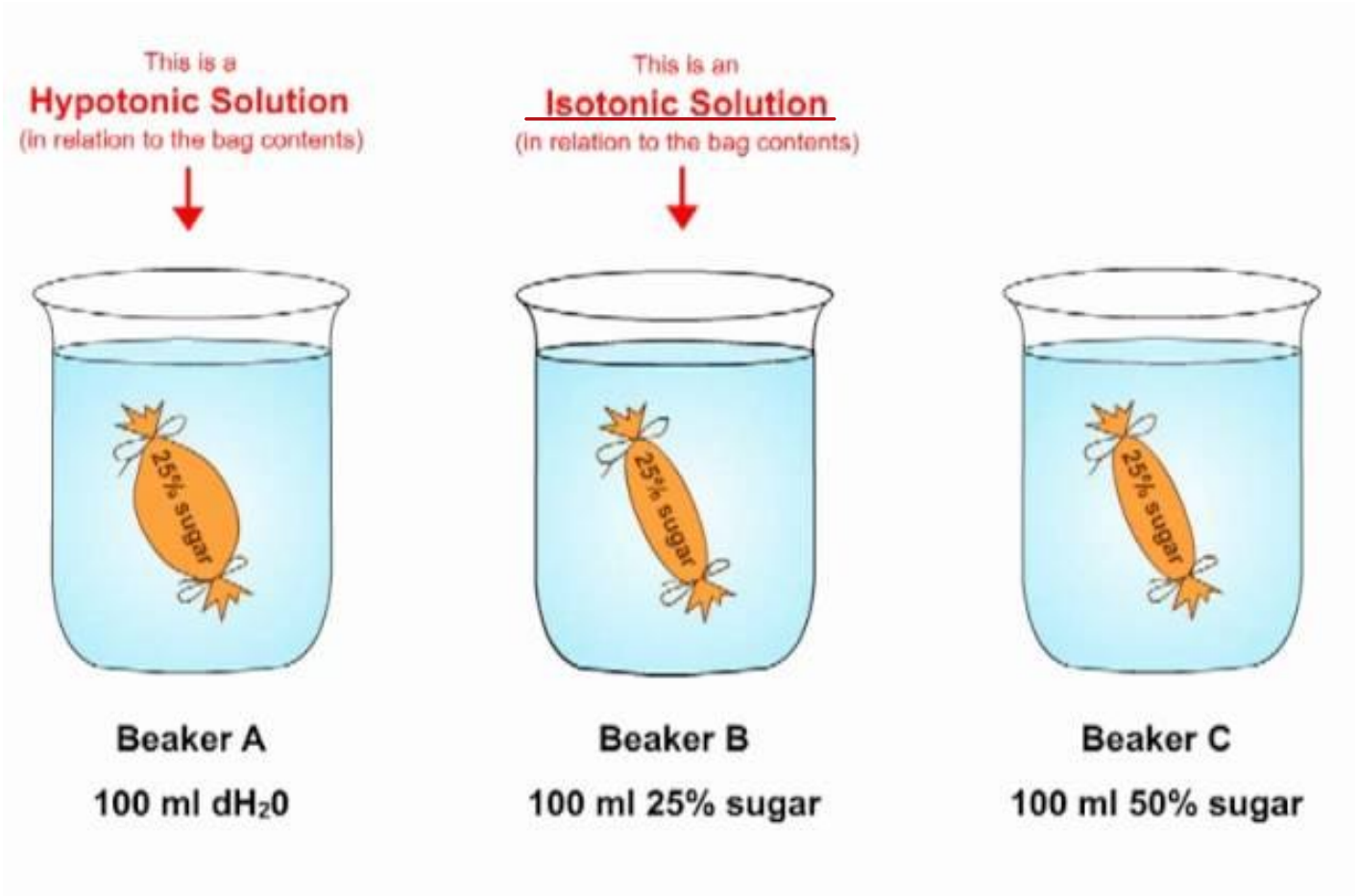
In other words, 2 parts higher concentration to 10 parts lower concentration.

In other words, there are 12 parts (2 parts + 10 parts):

- 2/12 x 500mL = 83.33mL
- 10/12 x 500mL = 416.66mL

Iso-osmoticity and Isotonicity

- Osmosis is a phenomenon that occur when a semipermeable membrane (permeable only to solvent molecules) is used to separate solutions of different solute concentrations
  - The solvent molecules cross the membrane from lower to higher concentration to establish a concentration equilibrium
  - The pressure driving this movement called osmotic pressure
- Osmotic pressure is governed by the number of particles of solute in solution
- Iso-osmotic solutions: solutions containing the same concentration of particles and thus exert equal osmotic pressure



In the final experiment, watch what happens when a bag containing 25% sugar is placed in a beaker containing 50% sugar. In this case, the solute concentration of the beaker is higher than that of the bag.

Isotonic Solution ← IV (Intravenous) * المحاليل الوريدية

* تسمية المحاليل بنسبة لتركيز المذاب solute *

↓ Solute ← Hypo *

↑ Solute ← Hyper *

* المحلول المحيط بالخلية عالي التركيز ← داخل الخلية أقل تركيز

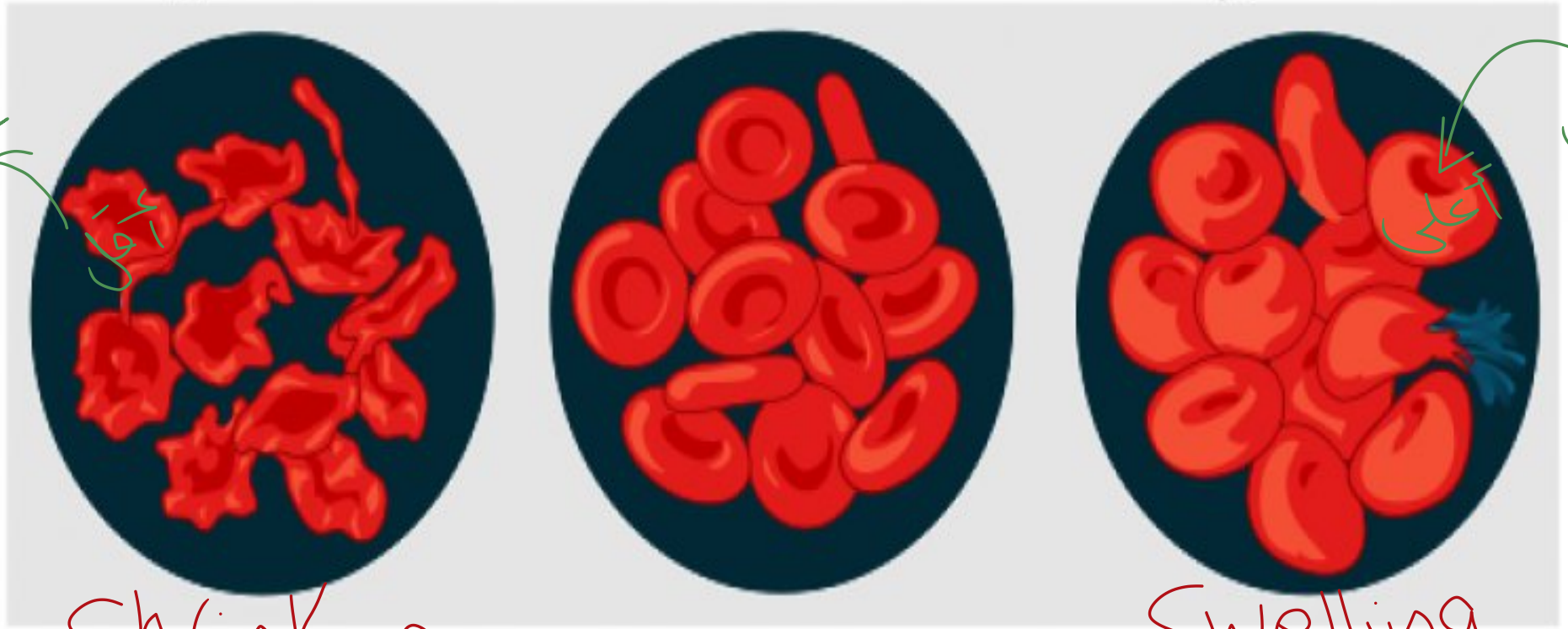
* المحلول المحيط بالخلية أقل تركيز ← الخلية أعلى تركيز

exp: RBC's

Hypertonic

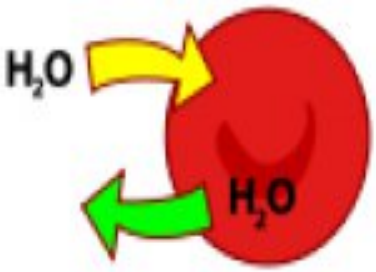
Isotonic

Hypotonic

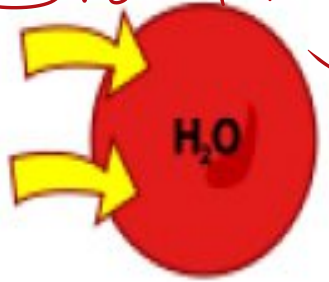


Shrinking

* تنكمش وتنحل *



Swelling



* تنتفخ وتنفجر *

Lysis

iso-osmotic = isotonic

Iso-osmoticity and Isotonicity

- A 0.9% solution of sodium chloride (normal saline) is iso-osmotic with blood

osmatic pressure NaCl = Osmatic Pressure Blood

- Isotonic means equal tone and sometimes is used interchangeably with the term iso-osmotic

same osmatic pressure

- The importance of using isotonic or iso-osmotic solutions is to assure that there is no tissue damage or pain when the formulation is administered

- Hypotonic solutions produce painful swelling of tissues
- Hypertonic solutions produce painful shrinking of tissues

Methods used to adjust the isotonicity of compounded solutions:

1. Sodium chloride equivalent method:

- the most widely used
- The NaCl equivalent (E) is the amount of NaCl that has the same osmotic effect (based on the number of particles) as 1gm of drug
- Tables of (E) for various drugs are available in standard references

2. Cryscopic method
3. Isotonic solution V values

Sodium Chloride Equivalent Method:

- Example: Calculate the amount of NaCl required to make the following ophthalmic solution isotonic:

Atropine Sulfate 2%

NaCl q.s.

Aqua. Dist. q.s. ad. 30 ml

* each gram of atropine sulfate can be replaced by 0.13 g of NaCl

0.9 gm → 100 mL

X → 30 mL

X = 0.27 gm of NaCl

1gm of Atropine Sulfate = 0.13gm of NaCl حسب التالي

Sodium Chloride Equivalent Method:

1. Determine the amount of NaCl to make 30 ml of an isotonic solution:

- 0.9g of sodium chloride in 100 ml of water will make an isotonic solution
- 0.9gm 100 ml
- X 30 ml
- X= 0.27 gm

* NaCl Isotonic 0.9 %

* محلول ملحي

Sodium Chloride Equivalent Method:

2. Calculate the contribution (تأثير) of atropine sulfate to the osmotic pressure of the solution (the sodium chloride equivalent for atropine sulfate (E)= 0.13):

- 30 ml X 2g/100 ml= 0.6 g atropine sulfate will be present in the formulation
- 0.6g X 0.13= 0.078 gm will be the sodium chloride equivalent contribution of atropine sulfate

2 gm → 100 ml

X → 30 ml

X = 0.6 gm of atropine sulfate

amount X E = 0.6 X 0.13 = 0.078

needed to make solution isotonic

Sodium Chloride Equivalent Method:

3. Determine the amount of NaCl to add to the formulation:

- The sodium chloride needed to make the final solution isotonic is calculated by:

0.27 gm- 0.078g= 0.192 gm ⇒ NaCl should be added.

4. What if boric acid is used to adjust isotonicity in ophthalmic solution because of its buffering and anti-infective properties:

- E for boric acid= 0.5 ⇒ 1 gm Boric acid = 0.5 gm NaCl
- 0.192g NaCl X g boric acid
- 0.5 g NaCl 1 g boric acid
- X= 0.38 g

0.5 g → 1 gm

0.192 ← من السؤال السابق → X

$X = \frac{0.192 \times 1}{0.5} = 0.384$ gm

amount of Boric acid that should be added to make solution isotonic

Isotonic Solution V Values

- The V value of a drug is the volume of water to be added to a specified weight of drug to prepare an isotonic solution
- The V values are given in tables constructed for 0.3g and 1.0 g of drug
- The basic principle is to prepare an isotonic solution of the prescribed drug and then dilute this solution to a final volume with a suitable isotonic vehicle

Extra practice

- A physician asks a pharmacist to calculate the dose of a cough syrup so that it may be safely administered dropwise قطرات to a child. The cough syrup contains the active ingredient dextromethorphan HBr, 30mg/15ml, in a 120-ml bottle. Based on the child's weight and literature references, the pharmacist determines the dose of dextromethorphan HBr to be 1.5mg for the child.

The medicine dropper to be dispensed with the medication is calibrated by the pharmacist and shown to deliver 20 drops of the cough syrup per 1 ml.

Calculate the dose, in drops, for the child? (answer 15 drops)

① تركيز الدواء في 1 ml

30 mg → 15 ml

X → 1 mL

$X = \frac{30}{15} = 2$ mg

② كم ml يعطي 1.5mg جرعة

2mg → 1mg

1.5mg → X

X = 0.75 mL

③ تحول ml الى drops

1mL → 20 drops

0.75 → X

X = 15 drops

Extra practice

- The regimen for a drug is as follows: 5 mcg/kg q week x 2, then 7 mcg/kg q2weeks. Calculate the dose in mcg that a 143 lb patient receives in a month. (1 lb = 0.453 kg)

a. 323.9

b. 647.8

c. 1101

d. 453

① تحويل الوزن
1 lb → 0.453 kg
143 lb → x
x = 64.78 kg

② حساب الجرعة الاسبوعية الاولى
5 × 64.78
= 323.9
≈ 324 mcg
لمدة اسبوعين
324 × 2 = 648 mcg

③ الجرعة الثانية
7 × 64.78
= 453.46
≈ 454 mcg
مرة كل أسبوعين

In one month
مرة واحدة أول اسبوعين + في الاسبوعين الثانيين
648 + 454
= 1102 mcg

- How many milligrams of a drug does a 187 lb patient receive over a 4 hour period if the recommended dose is 3.5 mg/kg/h?

a. 296.5

b. 1186

c. 187

d. 2372

e. 595

① تحويل الوزن
1 lb → 0.453 kg
187 → x
x = 84.7 kg

② جرعة خلال ساعة
3.5 × 84.7
= 296.45 mg

③ خلال 4 ساعات
4 × 296.45
= 1185.8 mg

Extra practice

- The pediatric dose for an antibiotic is 10 mcg/kg/day for 5 days. How many micrograms should be given to a 45 lb child for the entire treatment period?

a. 1019
b. 204
c. 2038
d. 90
e. 40.9

① تحويل الوزن
1 lb → 0.453 kg
45 → x
x = 20.385 kg
≈ 20.4 kg

② حساب الجرعة اليومية
10 x 20.4
= 204 mcg/day

③ خلال 5 أيام
5 x 204 = 1020 mcg

- A dose of 2 mg/kg of an antibiotic results in a peak blood serum level of 5 mcg/mL. How many milligrams of the drug should be given to a 143 lb patient if a peak blood serum level of 5.5 mcg/mL is desired?

* المستوى في الدم يتناسب طرديًا مع الجرعة * الجرعة ↑ و تركيز الدواء ↑ في الدم

a. 130
b. 65
c. 286
d. 357.5
e. 143

① تحويل الوزن
1 lb → 0.453 kg
143 → x
x = 64.78 kg
≈ 64.8

② حساب الجرعة الأصلية
2 x 64.8
= 129.6 mg
5 mcg/mL ←

③ حساب الجرعة المطلوبة
5 → 129.6 mg
5.5 → x
x = 142.56 mg

Extra practice

- Pharmaceutical Calculations, Howard Ansel, 31th Edition, 2010 (chapter 7)

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