4

Concentrations

Learning objectives

By the end of this chapter you will be able to:

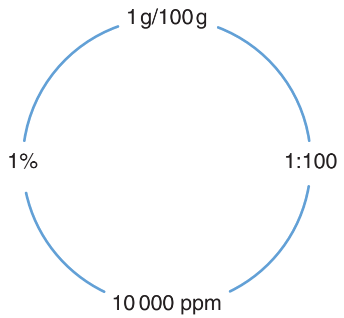
- state the relationship between the different methods of expressing the concentration of a pharmaceutical preparation
- convert one expression of concentration to another
- calculate the amount of ingredient required to make a product of a stated strength

Introduction

Pharmaceutical preparations consist of a number of different ingredients in a vehicle to produce a product. The ingredients and vehicles used in a product can be solid, liquid or gas.

Concentration is an expression of the ratio of the amount of an ingredient to the amount of product. It can be expressed in several ways:

- In the case of a solid ingredient in a liquid vehicle the ratio is expressed as a weight in volume, denoted by w/v (for example sugar granules dissolved in a cup of coffee)
- For a liquid ingredient in a solid vehicle the ratio is expressed as a volume in weight, denoted by v/w (for example lemon juice drizzled on the top of a cake)
- If both ingredient and vehicle are liquids the ratio is expressed as a volume in volume, denoted by v/v (for example milk added to a cup of coffee)
- When the ingredient and vehicle are both solid the ratio is expressed as a weight in weight, denoted by w/w (for example the blueberries as a proportion of the whole blueberry muffin)



- The concentration of pharmaceutical preparations usually describes the strength of the drug in the preparations. In practice it is important that the patient receives the correct amount of the drug
- If a patient receives too much of the drug they are likely to experience side-effects; side-effects are often dose-related, so the higher the amount of the drug the stronger the side-effect
- If a patient receives too little of the drug, then their treatment is likely to be less effective than the prescriber intended. This can lead to a deterioration in the health of the patient.

We know that rational numbers can be expressed as ratios, fractions, decimals or percentages. As concentrations are expressions of ratios, they can also be expressed in different forms. The forms traditionally used are those of amount strengths, ratio strengths, parts per million and percentage strength.

Each of these four forms can be expressions of w/w, v/v, w/v or v/w, depending on whether solids or liquids are involved.

For ratio strengths, parts per million and percentage strengths in w/w or v/v the amounts of ingredients and product must be expressed in the same units:

- a ratio of 7 mL to 12 mL is the ratio 7 : 12 v/v
- a ratio of 3 mg to 5 mg is the ratio 3 : 5 w/w.

As long as the units used are the same, they lead to the same ratio.

For a concentration of 3 mg to 5 g, we need to change to the same units before we can express the w/w ratio.

Converting 5 g to milligrams:

	g	–	–	mg	
5 g =	5	0	0	0	= 5000 mg

The ratio becomes 3 mg to 5000 mg, which is the ratio 3 : 5000 w/w.

In the case of w/v and v/w there is an agreed convention that states that weight is expressed in grams and volume is expressed in millilitres.

Let us now examine each of the traditional ways of expressing concentrations in more detail.

Amount strengths

Amount strengths can appear in any of the four forms, w/w, v/v, w/v or v/w. The amount strength is a ratio of the quantities and any units can be used, i.e. g/mL, mg/mL, mg/g, mL/mL, g/g, g/mL, etc. The units are stated in all cases.

Keep out of the reach and sight of children		
100 g Menthol 1% w/w in aqueous cream		
Apply as directed		
For external use only		
Mrs A Patient 08.01.15		
The Pharmacy 2 The Road, The Town 0123 45678	Disp	Chkd

Let us first consider a solid dissolved in a liquid to produce a solution.

Example 4.1

A preparation contains 900 mg of sodium chloride dissolved in water to produce 100 mL of solution. Express the concentration of the solution as an amount strength.

The concentration of this solution can be expressed as an amount strength in units of mg/100 mL, mg/mL, g/100 mL, g/L and so on.

To convert the above concentration of sodium chloride solution into these different representations we use proportional sets. The solution contains the same concentration of sodium chloride irrespective of whether we have 100 mL, 50 mL or 1 mL. The ratio of sodium chloride to product is constant.

Let us consider how the concentration could be expressed as the ratio mg/mL and as the ratio g/mL.

(*continued*)

Let the number of milligrams of sodium chloride in 1 mL of water be z. Setting up proportional sets:

sodium chloride (mg)	900	z
water (mL) to	100	1

The reason that we write *to* 100 mL rather than *in* 100 mL is that the sodium chloride is dissolved in water and made up to 100 mL with water; 900 mg of sodium chloride and 100 mL of water will produce more than 100 mL of solution, so the amount of water required to make 100 mL of solution will be less than 100 mL because of the displacement caused by the sodium chloride. We consider the concept of displacement and displacement values later. In addition, some drugs, such as strong concentrations of alcohol, may cause a contraction in volume when dissolved in water. For this reason, in pharmacy we always make up *to* volume.

From the proportional sets, it can be spotted that $z = 9$, so the concentration of sodium chloride in this solution can be represented by an amount strength of 9 mg/mL.

Sodium chloride in water is a solid in a liquid and is therefore expressed as milligrams (a weight) in millilitres (a volume). This is a w/v ratio. We can also convert 9 mg to grams:

	g	–	–	mg	
9 mg =	0	0	0	9	= 0.009 g

The concentration of sodium chloride, which was earlier expressed as 9 mg/mL, can therefore also be represented by an amount strength of 0.009 g/mL.

Ratio strengths

Ratio strength is expressed as a ratio in the form 1 in r. The corresponding fraction would have a numerator of 1.

The agreed convention states that, when ratio strength represents a solid in a liquid involving units of weight and volume, the weight is expressed in grams and the volume in millilitres.

1 in 500 potassium permanganate in water is a solid in a liquid and is therefore a weight in volume (w/v) ratio strength. This means that the solution contains 1 g of potassium permanganate made up to 500 mL with water.

Example 4.2

2 L of an aqueous solution contains 50 mL of ethanol. Express this as a ratio strength.

As this solution is a volume in volume we need to convert to the same units before we can express this as a ratio.
Converting 2 L into millilitres:

	L	–	–	mL	
2 L =	2	0	0	0	= 2000 mL

Let the volume of product in millilitres containing 1 mL of ethanol be r.
Setting up proportional sets:

ethanol (mL)	50	1
product (mL)	2000	r

By 'spotting', $r = 40$, so the ratio strength is 1 in 40 v/v.

Example 4.3 illustrates the calculation of a ratio strength for a solid in a solid.

Example 4.3

5 g of product contains 250 mg of sulfur in yellow soft paraffin. Express this as a ratio strength.

This is a weight in weight product because both the sulfur and the yellow soft paraffin are solid. The weights must be converted to the same units before the concentration can be stated as a ratio strength.
Converting 250 mg to grams:

	g	–	–	mg	
250 mg =	0	2	5	0	= 0.25 g

(*continued*)

Let the weight in grams of product containing 1 g of sulfur be *r*. Setting up proportional sets:

sulfur (g)	0.25	1
product (g)	5	*r*

Corresponding pairs are in the same ratio, therefore:

$$\frac{5}{0.25} = \frac{r}{1}$$

Solving for the unknown:

$$r = \frac{5}{0.25}$$

$$r = 20$$

The ratio strength is 1 in 20 w/w.

Parts per million

Parts per million (ppm) is used to denote concentrations in cases when the ratio of ingredient to product is very small. It is equivalent to a ratio in the form of *p* in 1000 000 or a fraction in which the denominator is 1000 000.

By the agreed convention, 1 ppm weight in volume is 1 g in 1000 000 mL; 1 ppm weight in weight is 1 mg per 1000 000 mg or 1 g per 1000 000 g. In volume in volume it is 1 mL in 1000 000 mL or 1 L in 1000 000 L.

Example 4.4

Fluoride in a water supply is expressed as parts per million w/v. Fluoride supplements should not be taken if the amount of fluoride in the water supply exceeds 0.7 parts per million w/v according to the British National Formulary *(BNF). Express this ratio in mg/L.*

By convention, 0.7 ppm can be represented as 0.7 g in 1000 000 mL.

→

Converting 0.7 g to milligrams:

	g	–	–	mg	
0.7 g =	0	7	0	0	= 700 mg

Converting 1000 000 mL into litres:

	L	–	–	mL				
1000 000 mL =	1	0	0	0	0	0	0	= 1000 L

0.7 ppm w/v = 700 mg per 1000 L = 0.7 mg/L.
Therefore, it can be seen that part per million is the same as mg/L. These representations of the concentrations of fluoride appear to be used interchangeably in documentation. In the BNF fluoride levels are expressed as ppm and micrograms/L.

Example 4.5

If the concentration of fluoride is 0.25 ppm w/v, how many litres would contain 1 mg of fluoride?

0.25 ppm w/v means 0.25 g per 1000 000 mL.
Converting 0.25 g to milligrams:

	g	–	–	mg	
0.25 g =	0	2	5	0	= 250 mg

Let the amount of product in millilitres containing 1 mg of fluoride be y. Setting up proportional sets:

fluoride (mg)	250	1
product (mL)	1000 000	y

Corresponding pairs of values are in the same ratio so:

$$\frac{1000\ 000}{250} = \frac{y}{1}$$

(*continued*)

Solving for the unknown in the proportional sets:

$$y = \frac{1000\ 000}{250}$$

$$y = 4000$$

Hence 4000 mL contains 1 mg of fluoride.
Converting 4000 mL to litres:

	L	–	–	mL	
4000 mL =	4	0	0	0	= 4 L

4 L therefore contains 1 mg of fluoride.

Percentage concentration

In terms of parts, a percentage is the amount of ingredient in 100 parts of the product. In the w/v and v/w cases, using the convention, the units are grams per 100 mL and millilitres per 100 g.

Example 4.6

A cream contains 12 g of drug X made up to 100 g with cream base. What is the percentage concentration?

From the information above the percentage concentration is the units in grams in 100 g.

As the amount in grams is 12 g in 100 g, it is 12% w/w.

Example 4.7

Express 1 in 500 w/v solution of potassium permanganate as a percentage.

Let the number of grams of potassium permanganate in 100 mL of product be x. Setting up proportional sets:

→

potassium permanganate (g)	1	x
product (mL)	500	100

We can spot that we divide 500 by 5 to get 100, so we divide 1 by 5 to get $\frac{1}{5}$ and therefore $x = 0.2$ and the percentage of potassium permanganate is 0.2% w/v.

Example 4.8

Express 900 mg of sodium chloride made up to 100 mL with water as a percentage.

To express the value as a percentage, we need to convert the number of milligrams in 100 mL to grams in 100 mL:

	g	–	–	mg	
900 mg =	0	9	0	0	= 0.9 g

There is 0.9 g of sodium chloride in 100 mL of solution. The percentage is 0.9% w/v.

Example 4.9

A morphine sulfate injection contains 10 mg/mL. What is the percentage concentration?

To express the value as a percentage, we need to convert the number of milligrams in 1 mL to grams in 100 mL:

	g	–	–	mg	
10 mg =	0	0	1	0	= 0.01 g

There is 0.01 g of morphine sulfate in 1 mL of solution.

Which means that there is 0.01×100 g = 1 g in 100 mL.

The percentage is 1% w/v.

Converting expressions of concentration from one form to another

Let us consider a general case. Let the amount of the ingredient be *a* and the amount of product be *b*. Let *p* be the amount in 100 parts (the percentage concentration), 1 in *r* be the ratio strength and *m* be the number of parts per million.

We can set up the following proportional sets:

	amount	*percentage*	*ratio strength*	*ppm*
ingredient	*a*	*p*	1	*m*
product	*b*	100	*r*	1000 000

This table shows the relationship between the different expressions of concentration. By using the proportional sets of the known expression of concentration and the required expression of concentration, it is possible to convert from one expression to another.

Example 4.10

A solution contains 20 mL of ethanol in 500 mL of product. Express the concentration as a ratio strength and as a percentage strength.

Let *p* be the percentage strength and let the ratio strength be 1 in *r*. Setting up proportional sets as above:

	volume	*ratio*	*percentage*
ethanol (mL)	20	1	*p*
product (mL)	500	*r*	100

Corresponding pairs of values are in the same ratio so:

$$\frac{500}{20} = \frac{r}{1}$$

Solving for the unknown in the proportional sets:

$$r = \frac{500}{20}$$

$$r = 25$$

→

By 'spotting' we can see that $p = \frac{20}{5} = 4$, so the mixture can be expressed as the ratio strength 1 in 25 v/v or as the percentage strength 4% v/v.

Example 4.11

A solid ingredient mixed with a solid vehicle has a ratio strength of 1 in 40. Find the percentage strength and the amount strength expressed as grams per gram.

Let p represent the percentage strength and let a grams be the weight of ingredient in 1 g of product. Setting up proportional sets:

	ratio strength	*percentage*	*amount strength (g/g)*
ingredient (g)	1	p	a
product (g)	40	100	1

Corresponding pairs of values are in the same ratio so:

$$\frac{1}{40} = \frac{p}{100}$$

Solving for the unknown in the proportional sets:

$$p = \frac{100}{40}$$

$$p = 2.5$$

Corresponding pairs of values are in the same ratio so:

$$\frac{1}{40} = \frac{a}{1}$$

Solving for the unknown in the proportional sets:

$$a = 0.025$$

The concentration of the mixture can be expressed as either 2.5% w/w or 0.025 g/g.

Example 4.12

A solution contains a solid dissolved in a liquid. The ratio strength is 1 in 2000 w/v. What are the percentage strength and the amount concentration expressed as mg/mL?

By convention, a ratio strength 1 : 2000 w/v means 1 g in 2000 mL and the percentage strength is the number of grams of ingredient in 100 mL of product.

Let the percentage strength be p and the amount of solid in grams in 1 mL of product be a. Setting up proportional sets:

	ratio	*percentage*	*amount strength (g/mL)*
solid (g)	1	p	a
product (mL)	2000	100	1

Corresponding pairs of values are in the same ratio so:

$$\frac{1}{2000} = \frac{p}{100}$$

Solving for the unknown in the proportional sets:

$$p = \frac{100}{2000}$$

$$p = 0.05$$

Corresponding pairs of values are in the same ratio so:

$$\frac{1}{2000} = \frac{a}{1}$$

Solving for the unknown in the proportional sets:

$$a = \frac{1}{2000}$$

$$a = 0.0005\,\text{g}$$

→

Converting 0.0005 g to milligrams:

	g	–	–	mg		
0.0005 g =	0	0	0	0	5	= 0.5 mg

The concentration of 1 in 2000 w/v can be expressed as 0.05% w/v or 0.5 mg/mL.

Example 4.13

A liquid ingredient mixed with another liquid vehicle has a concentration of 5% v/v. Find the ratio strength and the amount strength expressed as mL/mL.

5% v/v can be expressed as 5 mL of ingredient in 100 mL of product.

Let the ratio strength be 1 in r and the amount of ingredient in millilitres in 1 mL of product be a. Setting up proportional sets:

	percentage	*ratio*	*amount strength (mL/mL)*
ingredient (mL)	5	1	a
product (mL)	100	r	1

By 'spotting' we can see that:

$$r = \frac{100}{5} = 20$$

$$a = \frac{5}{100} = 0.05$$

The ratio is 1 in 20 v/v and the amount strength in mL/mL is 0.05 mL/mL.

Example 4.14

5 g of solid ingredient is added to 45 g of a base. Find the percentage strength, the ratio strength and the amount strength expressed as g/g.

(*continued*)

Remember that for weight in weight and volume in volume the product is equal to the sum of the vehicle and the ingredient, in this case $5 + 45 = 50$ g.

Let *p* be the percentage strength, 1 in *r* be the ratio strength and *a* grams be the amount in 1 g of product. Setting up proportional sets:

	amount	*percentage*	*ratio*	*amount strength (g/g)*
ingredient (g)	5	*p*	1	*a*
product (g)	50	100	*r*	1

By 'spotting' we can see that:

$$p = \left(\frac{5}{50} \times 100\right) = 10$$

$$r = \left(\frac{50}{5} \times 1\right) = 10$$

$$a = \left(\frac{5}{50} \times 1\right) = 0.1$$

The concentration can therefore be expressed as 10% w/w or 1 in 10 w/w or 0.1 g/g.

Calculating the amount of ingredient required to make up a percentage solution

In the same way as converting from one expression of concentration to another, it is also possible to use the proportional sets to calculate the amount of ingredient required to produce a known amount of a known percentage product.

This can be achieved by using the following proportional sets:

	amount	*percentage*
ingredient	*a*	*p*
product	*b*	100

Values *p* and *b* will be known and, therefore, *a* can be calculated.

Example 4.15

How many milligrams of aluminium acetate are required to prepare 500 mL of a 0.03% w/v solution?

Aluminium acetate is a solid and is expressed as a weight, in this case milligrams. The vehicle is a liquid and is expressed in millilitres. By convention 0.03% w/v means 0.03 g in 100 mL so each 100 mL contains 0.03 g of aluminium acetate.

Converting 0.03 g to milligrams:

	g	–	–	mg	
0.03 g =	0	0	3	0	= 30 mg

Let x be the number of milligrams of aluminium acetate in 500 mL. Setting up proportional sets:

aluminium acetate (mg)	x	30
product (mL)	500	100

By 'spotting' it can be seen that:

$$x = 30 \times 5 = 150$$

150 mg of aluminium acetate is required to produce 500 mL of a 0.03% w/v solution.

Calculating the amount of ingredient required to prepare a ratio strength solution

When the final concentration of the product is expressed as a ratio strength, the following proportional sets can be used to calculate the amount of ingredient to produce a known amount of product.

	amount	*ratio*
ingredient	a	1
product	b	r

In this situation, r and b will be known and a will be calculated.

Example 4.16

What is the amount of potassium permanganate in 300 mL of a 1 in 25 solution and what is the percentage strength of the solution?

By convention, a ratio strength of 1 in 25 means 1 g in 25 mL.

Let a be the number of grams of potassium permanganate in 300 mL and p be the percentage strength. Setting up proportional sets:

	ratio	*amount in 300 mL*	*percentage*
potassium permanganate (g)	1	a	p
product (mL)	25	300	100

Corresponding pairs are in the same ratio:

$$\frac{a}{300} = \frac{1}{25}$$

Solving for the unknown:

$$a = \frac{1 \times 300}{25} = 12$$

Amount of potassium permanganate = 12 g.

By 'spotting' we can see that:

$$p = 4$$

The solution therefore contains 4 g potassium permanganate in 100 mL = 4% w/v.

There are 12 g of potassium permanganate in 300 mL of solution and the percentage strength is 4% w/v.

Representation of concentrations

Practice calculations

Answers are given at the end of the chapter.

Q1 Convert the following ratio strengths into percentage strengths:

(a) 1 in 25

(b) 1 in 20

(c) 1 in 50

(d) 1 in 800

(e) 1 in 500

(f) 1 in 2000

(g) 1 in 300

Q2 What is the concentration of the solutions, expressed as percentage strength and ratio strength, when the following amounts of drug Z are dissolved in enough water to produce 125 mL of solution?

(a) 25 g

(b) 50 g

(c) 60 g

(d) 5 g

(e) 7 g

Q3 If the following amounts of drug are made up to 5 g with lactose what is the percentage concentration of the resulting mix?

(a) 100 mg

(b) 150 mg

(c) 200 mg

(d) 300 mg

(e) 500 mg

Q4 How many milligrams of *y* are needed to make 200 mL of a 1 in 500 solution?

Q5 How many millilitres of *y* are needed to produce 400 mL of a 1 in 200 solution?

Q6 How many milligrams of *y* are needed to produce 25 g of a 1 in 5 ointment?

Q7 How many grams of *y* are there in 250 mL of a 1 in 80 solution?

Q8 Potassium permanganate 0.1 g

Purified water to 100 mL

How many millilitres of a 2.5% potassium permanganate solution could be used in place of the 0.1 g in the above formula?

Q9 How many milligrams of *x* are needed to make 5 mL of an 8% solution?

Q10 How many millilitres of *x* are needed to make 600 mL of a 3% solution?

Q11 How many milligrams of *x* are needed to make 200 mL of a 3.4% solution?

Q12 How many milligrams of *x* are there in 100 mL of a 0.01% solution?

Q13 How much calamine is required to produce 250 g of a 3% ointment?

Q14 What volume of 17% w/v solution contains 1.5 g of ingredient?

Q15 What volume of 20% w/v solution contains 5 g of ingredient?

Q16 What volume of 15% w/v solution contains 7 g of ingredient?

Q17 What volume of 34% w/v solution contains 150 g of ingredient?

Answers

A1 **(a)** 4%
(b) 5%
(c) 2%
(d) 0.125%
(e) 0.2%
(f) 0.05%
(g) 0.33%

A2 **(a)** 20%, 1 in 5
(b) 40%, 1 in 2.5
(c) 48%, 1 in 2.1
(d) 4%, 1 in 25
(e) 5.6%, 1 in 17.9

A3 **(a)** 2%
(b) 3%
(c) 4%
(d) 6%
(e) 10%

A4 400 mg

A5 2 mL

A6 5000 mg

A7 3.1 g

A8 4 mL

A9 400 mg

A10 18 mL

A11 6800 mg

A12 10 mg

A13 7.5 g

A14 8.8 mL

A15 25 mL

A16 46.7 mL

A17 441.2 mL