

6

Solutions

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Introduction and overview

Solutions are one of the oldest dosage forms used in the treatment of patients and afford rapid and high absorption of soluble medicinal products. Therefore, the compounding of solutions retains an important place in therapeutics today. Owing to the simplicity and hence the speed of preparation of an ad hoc formulation, they are of particular use for individuals who have difficulty in swallowing solid dosage forms (for example paediatric, geriatric, intensive care and psychiatric patients), where compliance needs to be checked on administration (for example in prisons or psychiatric pharmacy) and in cases where precise, individualised dosages are required.

Essentially a solution is a homogeneous liquid preparation that contains one or more dissolved medicaments. Since, by definition, active ingredients are dissolved within the vehicle, uniform doses by volume may be obtained without any need to shake the formulation. This is an advantage over some other formulation types (e.g. suspensions, see Chapter 7).

In general, water is chosen as the vehicle in which medicaments are dissolved, as it is non-toxic, non-irritant, tasteless, relatively cheap, and many drugs are water soluble. Problems may be encountered where active drugs are not particularly water soluble or suffer from hydrolysis in aqueous solution. In these cases it is often possible to formulate a vehicle containing water mixed with a variety of other solvents.

In the British Pharmacopoeia (BP), oral solutions are defined as ‘Oral Liquids containing one or more active ingredients dissolved in a suitable vehicle’.

Solutions provide a number of distinct advantages and disadvantages compared with other dosage forms. The advantages of solutions as pharmaceutical products are that:

- The drug is immediately available for absorption. When solid dosage forms are taken orally, the drug needs to dissolve before absorption into the body can take place. By providing the drug in a solution, the dissolution phase of the absorption process can be bypassed, providing quicker absorption.
- Flexible dosing is possible. The active ingredient within the solution will be present in a certain concentration per unit volume. If alterations to the quantity of active ingredient to be administered are required, a simple alteration to the quantity of solution to be taken is all that is required.
- They may be designed for any route of absorption. Although when discussing solutions the oral route of administration is often considered, solutions can be administered via a number of other routes. Parenteral preparations (injections), enemas for rectal use, topical (for use on the skin) preparations and ophthalmic preparations can all be solutions.
- There is no need to shake the container. Unlike some liquid preparations (e.g. suspensions), as the active ingredient is dissolved within the vehicle there is no need to shake the container to ensure a uniform dose is measured.
- They facilitate swallowing in difficult cases. Some patients may find it hard to swallow traditional solid dosage forms (e.g. infants or the elderly). In these situations, it may be easier for the patient to take a liquid dosage form.

The disadvantages of solutions as pharmaceutical products are that:

- Drug stability is often reduced in solution by solvolysis, hydrolysis or oxidation. The stability of the active ingredient needs to be taken into consideration when formulating a solution. For this reason, it is common for solutions to attract a shorter expiry date than equivalent solid dosage forms.

- It is difficult to mask unpleasant tastes. Although liquid dosage forms may be ideal for small children who are unable to swallow solid dosage forms, many drugs taste unpleasant when formulated into a solution. It is possible to attempt to mask any unpleasant tastes by the addition of a flavouring, but this will not always be successful.
- They are bulky, difficult to transport and prone to breakages. A major disadvantage of all liquid dosage forms is that they are always much larger and more bulky than their comparable solid formulation. This makes them heavier and more difficult to transport. Coupled with this is the fact that, traditionally, pharmaceutical liquids are packed in glass bottles. These are obviously prone to breakage which can be hazardous and cause the loss of the preparation.
- Technical accuracy is needed to measure the dose on administration. Although the dose can be titrated without the need to produce additional preparations (see point 2 from the advantages above), patient accuracy in measuring a dose is required. It is accepted that patients’ abilities to measure an accurate dose can vary considerably and this needs to be taken into consideration when preparing a liquid preparation. This is especially important when the volume of liquid to be administered is very small, where small changes in the volume administered may result in large increases or decreases in dose.
- Some drugs are poorly soluble. The solubility of a drug needs to be taken into consideration when preparing a solution to ensure that the final volume produced is not excessive. In some cases it may be necessary to alter the vehicle or drug form (for example the free alkaloid or its salt) in order to be able to formulate a convenient preparation.
- A measuring device is needed for administration. Although not a major disadvantage, it must be borne in mind that a measuring device will need to be supplied to the patient in order for them to be able to measure an accurate dose (this will have cost implications), and in addition the patient will need counselling on the use of the measuring device.

The advantages and disadvantages of solutions as dosage forms are summarised in Box 6.1.

Box 6.1 Advantages and disadvantages of solutions as dosage forms

Advantages

Drug available immediately for absorption
Flexible dosing
May be designed for any route of administration
No need to shake container
Facilitates swallowing in difficult cases

Disadvantages

Drug stability often reduced in solution
Difficult to mask unpleasant tastes
Bulky, difficult to transport and prone to container breakages
Technical accuracy needed to measure dose on administration
Measuring device needed for administration
Some drugs poorly soluble

General principles of solution preparation

Historically, a range of solutions have been developed in order to fulfil a wide variety of pharmaceutical functions. It is therefore common to find solutions classified according to their intended use (e.g. oral internal, topical, ophthalmic, nasal or parenteral), by the nature of their formulation (e.g. simple or complex), or to be categorised by a traditional name that relates to the solvent system used and/or their intended function (e.g. spirits, tinctures, aromatic waters, syrups and elixirs).

Although the precise characteristics of different types of solution may vary, the essential principles governing their preparation remain similar. The two key characteristics that need to be considered when compounding solutions are solubility and stability.

Solubility

The following points relating to the solubility of the drug element(s) of the formulation need to be taken into consideration:

- Will the drug(s) dissolve in the solvent or a component of the solvent system?
- What quantity of drug will dissolve?
- How long will dissolution take?
- Will the drug(s) remain in solution and for how long?

- What is the pH of solvent required for dissolution?

Answers to many of the above questions will require the compounder to perform a solubility calculation, as described in Chapter 4.

When preparing a solution, the solid(s) will need to go through a dissolution phase. During compounding, it is worth remembering that dissolution rates generally increase with:

- smaller particle sizes
- effective stirring
- lower viscosities
- increased temperature.

Stability

In addition to the solubility of the drug element(s) of the formulation, other considerations regarding the physical stability of the preparation will need to be taken into consideration (e.g. temperature variation, photosensitivity, etc.), as will the chemical stability and time period, and the microbiological stability and need for a preservative.

General method

The following general method should be used in the preparation of a solution:

- 1 Write out the formula either from the prescription (unofficial) or from an official text (official).
- 2 Calculate the quantities required for each ingredient in the formula to produce the required final volume. Remember, it is not usual to calculate for an overage of product in the case of solutions as it is relatively easy to transfer the entire final contents of the conical measure. Also, as far as is practically possible, the product will be assembled in the final measure, thus reducing any transference losses.
- 3 Complete all sections of the product worksheet (see Chapter 5, page 70).
- 4 Prepare a suitable label (see Chapter 5, page 91).
- 5 Weigh all solids.
- 6 Identify the soluble solids and calculate the quantity of vehicle required to fully dissolve the solids. If more than one solid is to be dissolved,

they are dissolved one by one, in order of solubility (i.e. the least soluble first, see Chapter 4, page 62). In almost all cases, dissolution will take place in a glass (or occasionally plastic) beaker, not a conical measure. Remember that the solubility of the soluble solids will be dependent on the vehicle used.

- 7 Transfer the appropriate amount of vehicle to a glass beaker.
- 8 If necessary, transfer the solid to a glass mortar and use the glass pestle to reduce particle size to aid dissolution.
- 9 Transfer the solid to the beaker and stir to aid dissolution. If a mortar and pestle have been used to reduce particle size, ensure that the mortar is rinsed with a little vehicle to ensure complete transfer of the powders.
- 10 When all the solid(s) have dissolved, transfer the solution to the conical measure that will be used to hold the final solution.
- 11 Rinse out the beaker in which the solution was made with a portion of the vehicle and transfer the rinsings to the conical measure.
- 12 Add any remaining liquid ingredients to the conical measure and stir.
- 13 Make up to final volume with remaining vehicle.
- 14 Transfer to a suitable container, label and dispense to the patient.

 See Solutions video for a demonstration of the preparation of a solution.

Key points from the method

- Dissolution will normally take place in a glass beaker, not a conical measure, for a number of reasons. First, owing to the shape of the conical measure, any solid added will tend to 'cake' at the bottom of the measure and hamper any attempt to stir the solid around with the stirring rod, which aids dissolution. Second, the action of the stirring rod may scratch the inside of the glass, permanently altering the internal volume of the measure.
- During the dissolution phase, solutions should be stirred gently and uniformly to avoid air entrapment, which may result in foaming of the solution. If available, automatic stirring devices may be useful in assisting the production of a

uniform product and can be timesaving. If stirring devices are used to assist dissolution (e.g. rod, magnetic stirrers), remember to remove them before adjusting to final volume.

- It is best to stir continuously when combining ingredients into a solution (either liquid or solid ingredients). By stirring continually during incorporation, high concentration planes within the fluid body, which might increase the likelihood of incompatibilities, will be avoided.

Further considerations during the preparation of a solution:

- To aid dissolution, high-viscosity liquid components should be added to those of lower viscosity.
- Completely dissolve salts in a small amount of water prior to the addition of other solvent elements.
- In complex solutions, organic components should be dissolved in alcoholic solvents and water-soluble components dissolved in aqueous solvents.
- Aqueous solutions should be added to alcoholic solutions with stirring to maintain the alcohol concentration as high as possible – the reverse may result in separation of any dissolved components.

Oral solutions

This section describes the different types of pharmaceutical solution that are used orally. Although all are prepared using the same general techniques highlighted above, there are important differences between the different solution types.

Elixirs

An elixir is a liquid oral preparation that usually contains either potent or unpleasant-tasting drugs. The formulation is clear and generally contains a high proportion of sugar or other sweetening agent, included to mask offensive or nauseating tastes. Paediatric elixirs are usually formulated with a fruit syrup as a base flavouring agent.

In general, non-aqueous solvents (alcohol, glycerin or propylene glycol) form a significant proportion of the vehicle used in elixirs, or alternatively solubilising agents are included.

Linctuses

A linctus is a liquid oral preparation that is chiefly used for a demulcent, expectorant or sedative purpose, principally in the treatment of cough. As such, a linctus is intended to be sipped slowly and allowed to trickle down the throat in an undiluted form. Consequently, linctuses are formulated as viscous solutions which contain sugars.

Syrups

A syrup is a concentrated, viscous solution containing one or more sugar components, chiefly sucrose, and is described in more detail in Chapter 2, page 29.

Mixtures

Simple liquid preparations intended for oral use containing dissolved medicaments may be described as oral solutions or mixtures, although the term 'mixture' may also be applied to a suspension.

Draughts

A draught is an older term used to describe a liquid preparation formulated as a single dose, in a volume which is larger than generally utilised in traditional mixture formulations. Each draught was usually supplied in a 50 mL unit dose container.

Spirits

Spirits are solutions containing one or more active medicaments dissolved in either absolute or dilute ethanol.

Paediatric drops

These are an oral liquid formulation of potent drugs usually in solution, intended for administration to paediatric patients, though they may be useful in other patients with swallowing difficulties. The formulation is designed to have very small dose volumes which must be administered with a calibrated dropper.

Gargles and mouthwashes

Gargles and mouthwashes are aqueous solutions that are intended for treatment of the throat (gargles) and mouth (mouthwashes) and are generally formulated in a concentrated form.

These preparations must be diluted before use and care should be taken to ensure that appropriate instructions are included on the label and that the container used will be easily distinguishable from those containing preparations intended to be swallowed.

Enemas and douches

These liquid preparations are often formulated as solutions (though they may be presented as an emulsion or suspension) and are intended for instillation into the rectum (enema) or other orifice, such as the vagina or nasal cavity (douche). The volumes of these preparations may vary from 5 mL to much larger volumes. When the larger volumes are used it is important that the liquid is warmed to body temperature before administration.

External solutions

As with internal solutions, owing to the versatility of the solution, a number of different preparation types have been developed for external use.

Lotions

Lotions are solutions, but may also be suspensions or emulsions, that are intended to be applied to the skin without friction on a carrier fabric such as lint and covered with a waterproof dressing. In some cases lotions are applied to the scalp, where the vehicle for the medication is alcohol based, allowing for rapid drying of the hair and thus making the product more acceptable to the patient (e.g. Salicylic Acid Lotion 2% BPC). In these cases, problems of flammability are addressed by suitable labelling.

Liniments

A liniment is a liquid preparation intended to be rubbed with friction and massaged onto the skin to obtain analgesic, rubefacient or generally stimulating effects. Liniments should not be used on broken skin. They are usually solutions of oils, alcohols or soaps, but may be formulated as emulsions.

Applications

Applications are solutions, though they may also be suspensions or emulsions, intended to be applied without friction to the skin and to be used without any dressing or covering material.

Collodions

These are principally solutions of pyroxylin in a vehicle of ether and alcohol that are intended to be painted onto the skin and left to dry. When dry, the collodion leaves a flexible film of cellulose on the skin which may

be used to seal minor injuries or retain a dissolved drug in contact with the skin for an extended period.

Collodions are highly volatile and highly flammable and care should be taken to label any preparation appropriately.

Worked examples



Example 6.1 Preparation of 150 mL of Alkaline Gentian Mixture BP

Example label (we have assumed that the name and address of the pharmacy and the words 'Keep out of the reach and sight of children' are pre-printed on the label):

Gentian Alkaline Mixture BP	150 mL
Product directions.	
Do not use after (2 weeks)	
Name of patient	Date of dispensing

Product formula (British Pharmacopoeia 1988, page 736):

	1000 mL	100 mL	50 mL	150 mL
Concentrated Compound Gentian Infusion BP	100 mL	10 mL	5 mL	15 mL
Sodium Bicarbonate BP	50 g	5 g	2.5 g	7.5 g
Double Strength Chloroform Water BP	500 mL	50 mL	25 mL	75 mL
Potable water	to 1000 mL	to 100 mL	to 50 mL	to 150 mL

Interim formula for Double Strength Chloroform Water BP (see Chapter 2, page 32):

Concentrated Chloroform 5 mL
Water BPC 1959
Potable water to 100 mL

Method:

- Using the master formula from the British Pharmacopoeia for 1000 mL of final product, calculate the quantity of ingredients required to produce the final volume needed (150 mL).

Point of clarity – Step 1

Rather than attempt this conversion in one stage, it may be simpler to take the calculation through a number of stages. In the example given here, the quantities in the master formula are first divided by 10 to give a product with a final volume of 100 mL. These quantities are then halved to give a product with a final volume of 50 mL. The quantities in the 100 mL product and 50 mL product are then added together to give the quantities of ingredients in a product with a final volume of 150 mL. By using this method, the compounder is less likely to make a calculation error.

**Example 6.1 Continued**

- 2 Calculate the composition of a convenient quantity of Double Strength Chloroform Water BP, sufficient to satisfy the formula requirements but also enabling simple, accurate measurement of the concentrated component. To compound Double Strength Chloroform Water BP:
 - a In this case, 75 mL of Double Strength Chloroform Water BP is required and so it would be sensible to prepare 100 mL. To prepare 100 mL Double Strength Chloroform Water BP, measure 5 mL of Concentrated Chloroform water BPC 1959 accurately using a 5 mL conical measure.
 - b Add approximately 90 mL of potable water to a 100 mL conical measure (i.e. sufficient water to enable dissolution of the concentrated chloroform component without reaching the final volume of the product).
 - c Add the measured Concentrated Chloroform Water BPC 1959 to the water in the conical measure.
 - d Stir gently and then accurately make up to volume with potable water.
 - e Visually check that no undissolved chloroform remains at the bottom of the measure.



See Solutions video for a demonstration of the preparation of Double Strength Chloroform Water BP.

Noting that sodium bicarbonate is soluble 1 in 11 with water, a minimum of 11 mL of water would be required to dissolve 1 g of sodium bicarbonate. The final volume of Gentian Alkaline Mixture BP required (150 mL) will contain 7.5 g of Sodium Bicarbonate BP. As 1 g of sodium bicarbonate is soluble in 11 mL, 7.5 g is soluble in 82.5 mL ($7.5 \times 11 = 82.5$ mL). Therefore a minimum of 82.5 mL of vehicle would be required to dissolve the 7.5 g of Sodium Bicarbonate BP in this example. For ease of compounding choose a convenient volume of vehicle, say 90 mL, in which to initially dissolve the solute. When choosing the amount of vehicle to use for dissolution, it is important to consider the total amount of each liquid ingredient in the preparation to ensure that only the correct amounts are added or the final product does not go over volume.

- 3 Weigh 7.5 g Sodium Bicarbonate BP on a Class II or electronic balance.
- 4 Accurately measure 75 mL Double Strength Chloroform Water BP using a 100 mL measure. To this add approximately 15 mL potable water in order to produce 90 mL of vehicle which should be poured into a beaker (in order to produce sufficient volume to dissolve the 7.5 g Sodium Bicarbonate BP).

Point of clarity – Step 4

As discussed above, in this example 90 mL of vehicle is required to dissolve the Sodium Bicarbonate BP. It is important to consider the total amount of each liquid ingredient in the product to ensure that only the correct amounts are added. In this example, it would be incorrect to dissolve the Sodium Bicarbonate BP in 90 mL of Double Strength Chloroform Water BP as the final volume of the preparation only contains 75 mL. In this case, all the Double Strength Chloroform Water BP is used (75 mL) along with enough potable water to reach the desired volume (approximately 15 mL).

**Example 6.1 Continued**

- 5 The Sodium Bicarbonate BP (7.5 g) should be added to the vehicle, thus following the principle of adding solutes to solvents.
- 6 Stir to aid dissolution.
- 7 Transfer the solution to a 250 mL conical measure.
- 8 Rinse the beaker with potable water, adding the rinsings to the Sodium Bicarbonate BP solution.
- 9 Accurately measure 15 mL of Concentrated Compound Gentian Infusion BP in an appropriately sized conical measure and add to the Sodium Bicarbonate BP solution in the 250 mL measure. Rinse out the small conical measure with potable water and add the rinsings to the mixture.
- 10 Make up to volume (150 mL) accurately with potable water and stir.
- 11 Transfer the solution to a 150 mL amber flat medicine bottle with a child-resistant closure and label.



See Solutions video for a demonstration of the preparation of a solution.

**Example 6.2 Preparation of 50 mL Ammonium Chloride Mixture BP**

Example label (we have assumed that the name and address of the pharmacy and the words 'Keep out of the reach and sight of children' are pre-printed on the label):

Ammonium Chloride Mixture BP 50 mL	
Product directions.	
Do not use after (4 weeks)	
Name of patient	Date of dispensing

Product formula (British Pharmacopoeia 1988, page 720):

	1000 mL	500 mL	50 mL
Ammonium Chloride BP	100 g	50 g	5 g
Aromatic Ammonia Solution BP	50 mL	25 mL	2.5 mL
Liquorice Liquid Extract BP	100 mL	50 mL	5 mL
Potable water	to 1000 mL	to 500 mL	to 50 mL

Method:

- 1 Calculate the quantity of ingredients required to produce the final volume needed. As with Example 6.1, this calculation is best attempted in stages.
- 2 Weigh 5 g Ammonium Chloride BP accurately on a Class II or electronic balance. As ammonium chloride is soluble 1 part in 2.7 parts of water, the 5 g required for this product would only dissolve in a minimum initial volume of 13.5 mL aqueous vehicle. Therefore we should choose a convenient volume of vehicle to dissolve the solute, say 15 mL.
- 3 Measure approximately 15 mL potable water and transfer to a beaker.

**Example 6.2 Continued**

- 4 Add the Ammonium Chloride BP to the water in the beaker and stir until dissolved.
- 5 Transfer to a 50 mL conical measure with rinsings.
- 6 Measure 5 mL Liquorice Liquid Extract BP accurately in a 5 mL conical measure and add, with rinsings, to the 50 mL measure containing ammonium chloride solution.
- 7 Measure 2.5 mL Aromatic Ammonia Solution BP accurately in a syringe and transfer to the 50 mL measure containing the composite solution.
- 8 Make up to the final volume of 50 mL with potable water and stir.
- 9 Pack into a 50 mL amber flat medicine bottle and label.



See Solutions video for a demonstration of the preparation of a solution.

**Example 6.3 Preparation of 150 mL of Sodium Chloride Compound Mouthwash BP**

Example label (we have assumed that the name and address of the pharmacy and the words 'Keep out of the reach and sight of children' are pre-printed on the label):

Sodium Chloride Compound Mouthwash BP		150 mL
Product directions.		
Dilute with an equal volume of water before use.		
Do not swallow in large amounts		
Not to be Taken		
Do not use after (4 weeks)		
Name of patient	Date of dispensing	

Product formula (British Pharmacopoeia 1988, page 703):

	1000 mL	100 mL	50 mL	150 mL
Sodium Bicarbonate BP	10 g	1 g	500 mg	1.5 g
Sodium Chloride BP	15 g	1.5 g	750 mg	2.25 g
Concentrated Peppermint Emulsion BP	25 mL	2.5 mL	1.25 mL	3.75 mL
Double Strength Chloroform Water BP	500 mL	50 mL	25 mL	75 mL
Potable water	to 1000 mL	to 100 mL	to 50 mL	to 150 mL

Interim formula for Double Strength Chloroform Water BP (see Chapter 2, page 32):

Concentrated Chloroform Water BPC 1959	5 mL
Potable water	to 100 mL

Method:

- 1 Using the master formula from the British Pharmacopoeia for 1000 mL of final product, calculate the quantity of ingredients required to produce the final volume needed (150 mL).



Example 6.3 Continued

- 2 Calculate the composition of a convenient quantity of Double Strength Chloroform Water BP, sufficient to satisfy the formula requirements but also enabling simple, accurate measurement of the concentrated component. Method of compounding for Double Strength Chloroform Water BP:
 - a In this case, 75 mL of Double Strength Chloroform Water BP is required and so it would be sensible to prepare 100 mL. To prepare 100 mL Double Strength Chloroform Water BP, measure 5 mL of Concentrated Chloroform water BPC 1959 accurately using a 5 mL conical measure.
 - b Add approximately 90 mL of potable water to a 100 mL conical measure (i.e. sufficient water to enable dissolution of the concentrated chloroform component without reaching the final volume of the product).
 - c Add the measured Concentrated Chloroform Water BPC 1959 to the water in the conical measure.
 - d Stir gently and then accurately make up to volume with potable water.
 - e Visually check that no undissolved chloroform remains at the bottom of the measure.



See Solutions video for a demonstration of the preparation of Double Strength Chloroform Water BP.

Noting that sodium bicarbonate is soluble 1 in 11 with water, a minimum of 11 mL of water would be required to dissolve 1 g of sodium bicarbonate. The final volume of Sodium Chloride Compound Mouthwash BP required (150 mL) will contain 1.5 g of Sodium Bicarbonate BP. As 1 g of sodium bicarbonate is soluble in 11 mL, 1.5 g is soluble in 16.5 mL ($1.5 \times 11 = 16.5$ mL). The sodium chloride is soluble 1 in 2.8 with water. Therefore a minimum of 2.8 mL of water would be required to dissolve 1 g of sodium chloride. The final volume of Sodium Chloride Compound Mouthwash BP required (150 mL) will contain 2.25 g of Sodium Chloride BP. As 1 g of sodium chloride is soluble in 2.8 mL, 2.25 g is soluble in 6.3 mL ($2.25 \times 2.8 = 6.3$ mL). Therefore a minimum of 16.5 mL of vehicle would be required to dissolve the 1.5 g of sodium bicarbonate and a minimum of 6.3 mL of vehicle would be required to dissolve the 2.25 g of sodium chloride in this example. For ease of compounding choose a convenient volume of vehicle, say 30 mL, in which to initially dissolve the solute. When choosing the amount of vehicle to use for dissolution, it is important to consider the total amount of each liquid ingredient in the preparation to ensure that only the correct amounts are added or the final product does not go over volume.

- 3 Weigh 2.25 g Sodium Chloride BP on a Class II or electronic balance.
- 4 Weigh 1.5 g Sodium Bicarbonate BP on a Class II or electronic balance.
- 5 Measure 75 mL of Double Strength Chloroform Water BP in a 100 mL conical measure.
- 6 Transfer approximately 30 mL of Double Strength Chloroform Water BP to a beaker, add the Sodium Bicarbonate BP and stir to aid dissolution.
- 7 When the Sodium Bicarbonate BP has dissolved, add the Sodium Chloride BP and stir to aid dissolution.
- 8 Transfer the solution from the beaker to a 250 mL conical measure.
- 9 Rinse out the beaker with some Double Strength Chloroform Water BP and add the rinsings to the conical measure.
- 10 Measure 3.75 mL of Concentrated Peppermint Emulsion BP using a 5 mL and a 1 mL syringe.
- 11 Add the Concentrated Peppermint Emulsion BP to the conical measure.
- 12 Make up to volume with the remaining Double Strength Chloroform Water BP and potable water.
- 13 Transfer to a 200 mL amber fluted medicine bottle and label.



See Solutions video for a demonstration of the preparation of a solution.



Example 6.4 Preparation of a magistral formulation (150 mL of Potassium Permanganate Solution 0.2% w/v) from a doctor's prescription

Given that 0.2% w/v is equal to 0.2 g in 100 mL, there are 200 mg of Potassium Permanganate BP in every 100 mL of solution.

Example label (we have assumed that the name and address of the pharmacy and the words 'Keep out of the reach and sight of children' are pre-printed on the label):

Potassium Permanganate Solution 0.2% w/v		150 mL
Product directions.		
Caution: Stains skin, hair and fabric		
Do not use after (2 weeks)		
For External Use Only		
This solution contains:		
Potassium Permanganate BP		0.2%
Freshly boiled and cooled purified water		to 100%
Name of patient		Date of dispensing

Product formula:

	100 mL	50 mL	150 mL
Potassium Permanganate BP	200 mg	100 mg	300 mg
Freshly boiled and cooled purified water	to 100 mL	to 50 mL	to 150 mL

Point of clarity – product formula

Rather than attempt the above conversion in one stage, it may be simpler to take the calculation through a number of stages. In the example given above, the quantities in the master formula are first divided by 2 to give a product with a final volume of 50 mL. The quantities in the 100 mL product and 50 mL product are then added together to give the quantities of ingredients in a product with a final volume of 150 mL. By using this method, the compounder is less likely to make a calculation error.

Method:

Note that Potassium Permanganate is soluble in cold water and freely soluble in boiling water. Freshly boiled and cooled purified water is used as the vehicle as no other preservative is included and the preparation is intended for application to an open wound.

- 1 Weigh 300 mg Potassium Permanganate BP on a Class II or electronic balance.
- 2 Transfer to a glass mortar as the Potassium Permanganate BP is crystalline and for ease of dissolution needs to be ground into a powder.

Point of clarity – Step 2

Potassium Permanganate BP is an oxidising substance therefore there is risk of explosion. To prevent this add approximately 20 mL of freshly boiled and cooled purified water to a glass mortar (Potassium Permanganate BP stains and so a porcelain mortar would not be suitable) and grind under water.

**Example 6.4 Continued**

- 3 Transfer the solution to a 250 mL conical measure.
- 4 Rinse the mortar with freshly boiled and cooled purified water and add the rinsings to the conical measure.
- 5 Make up to volume with freshly boiled and cooled purified water.
- 6 Transfer the solution to a 150 mL amber fluted medicine bottle with a child-resistant closure and label.



See Solutions video for a demonstration of the preparation of a solution.

Summary of essential principles relating to solutions

This section recaps the main principles relating to solutions that have been covered in other sections of the book. To assist compounders in understanding the extemporaneous preparation of solutions, this section contains:

- further notes on the packaging of extemporaneously prepared solutions
- specific points relevant to the expiry of extemporaneously prepared solutions
- additional key points related to the labelling of pharmaceutical solutions.

Packaging

The packaging of extemporaneous preparations has been covered in Chapter 5 (page 96). A brief overview of the main considerations for the packaging of solutions will be given here.

When selecting packaging for extemporaneously prepared solutions, consideration should be given to the route or method of administration. Liquid preparations that are intended for the oral route should be packed in plain (smooth) amber bottles. External preparations and preparations that are not intended to be taken internally (e.g. mouthwashes) should be packaged in fluted amber bottles (i.e. amber bottles with vertical ridges or grooves). This will enable simple identification, by

both sight and touch, of preparations that are not to be taken via the oral route.

Pharmaceutical bottles come in a variety of different sizes and it is important to choose a suitably sized container to match the volume of preparation to be dispensed. Obviously it is important not to use a container that is too large for the volume of preparation to be dispensed for both cost and appearance issues (Table 6.1).

Discard dates

Extemporaneously compounded solutions are often relatively unstable for physical, chemical (hydrolysis) and microbiological reasons. The exact impact of such processes on a compounded solution will depend largely upon the storage conditions, the formulation and its intended purpose. Commercially available manufactured products generally have long shelf-lives because of strictly controlled manufacturing environments supported by rigorous quality assurance testing. Because of the lack of complete control of conditions and inability to perform retrospective stability tests on extemporaneously compounded solutions, much shorter shelf-lives must be attributed.

For official preparations, the British Pharmacopoeia employs two definitions that are useful when extemporaneously compounding solutions:

- 'Freshly Prepared' refers to a preparation that has been compounded less than 24 hours prior to issue for use.

Table 6.1 Summary of packaging for pharmaceutical solutions

		Typical sizes	Pharmaceutical product examples include
Oral liquids	Amber flat medical bottle	50 mL, 100 mL, 150 mL, 200 mL, 300 mL, 500 mL	Draughts Elixirs Linctuses Mixtures Spirits Syrups
	Amber round medical bottle with dropper top	10 mL	Paediatric drops
External liquids	Amber fluted medical bottle	50 mL, 100 mL, 200 mL	Applications Collodions Enemas and douches Gargles and mouthwashes Liniments Lotions
	Amber fluted medical bottle with dropper top	10 mL	Ear drops Nose drops

- ‘Recently Prepared’ should be applied to compounded items that are likely to deteriorate if stored for a period greater than four weeks when maintained at 15–25 °C.

In practical terms it is suggested that an expiry date of two weeks is applied to oral solutions that need to be Freshly Prepared or that contain an infusion or other vegetable matter. A four-week expiry should be applied to oral solutions that require to be Recently Prepared.

Remember that because patients frequently misunderstand the term ‘expiry’ it is suggested that a preferred method of indicating shelf-life on the label of extemporaneously compounded products is to apply the term ‘Discard after’ or ‘Do not use after’ followed by a definite date and/or time.

When dealing with unofficial preparations, the compounder must take a number of considerations into account. As a general rule, an expiry of 7–14 days would be given to any of the following preparations:

- a solution that does not contain a preservative

- a solution where there are no stability data available
- a new solution or ad hoc preparation.

Further guidance on expiry dates for pharmaceutical preparations can be found in Chapter 5 (page 92).

Labelling

The labelling of extemporaneous preparations has been covered previously in Chapter 5 (page 91). An overview of the main considerations for the labelling of solutions will be given here.

In addition to the standard requirements for the labelling of extemporaneous preparations, the following points need to be taken into consideration:

- ‘Not to be taken’ and ‘Do not swallow in large amounts’ – This warning must be added to gargles and mouthwashes.

- **'Not to be taken'** – This warning should be added to inhalations and nasal drops.
 - **'For external use only'** – This warning must be added to the label of any other preparation that is not intended for administration via the oral route.
 - **'For rectal use only'** and **'Warm to body temperature before administration'** – These warnings should be added to large-volume enemas.
- Further guidance on auxiliary labelling can be found in Chapter 5 (Table 5.10).