chapter 2
Solutions

Overview

Upon completion of this chapter, you should be able to:
- prepare a solution from first principles
- select an appropriate container in which to package a solution
- prepare an appropriate label for a solution
- understand the differing calculations used in the preparation of solutions, including:
  - Basic strength calculations
  - Tailored strength calculations
  - Percentage calculations
  - Parts calculations
  - Millimolar calculations.

Introduction and overview of solutions

Solutions are traditionally 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 therefore 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.

Generally, water is chosen as the vehicle in which medicaments are dissolved, since 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.

British Pharmacopoeia (BP) definition (oral solutions)
Oral solutions are oral liquids containing one or more active ingredients dissolved in a suitable vehicle.
Key Points

**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
- Some drugs poorly soluble
- Measuring device needed for administration

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**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. Additionally, 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.
4. Prepare a suitable label.
5. Weigh all solids.
6. Identify the soluble solids and calculate the quantity of vehicle required to dissolve the solids fully. 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). 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 (Figure 2.1).
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) has/have dissolved, transfer the solution to the conical measure that will be used to hold the final solution.

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**Key Points**

**Dissolution will normally take place in a glass beaker, not a conical measure, for a number of reasons.**
- Firstly, owing to the shape of the conical measure, any solid added to a conical measure 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.
- Secondly, the action of the stirring rod may scratch the inside of the glass conical measure, permanently altering the internal volume of the measure.
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**

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 time-saving. If stirring devices are used to assist dissolution (e.g. rod, magnetic stirrers), remember to remove them before adjusting to final volumes.

**Tips**

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:**

1. To aid dissolution, high-viscosity liquid components should be added to those of lower viscosity.

2. Completely dissolve salts in a small amount of water prior to the addition of other solvent elements.

3. In complex solutions, organic components should be dissolved in alcoholic solvents and water-soluble components dissolved in aqueous solvents.

4. 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.

**Worked examples**

**Example 2.1**

**The preparation of Alkaline Gentian Mixture BP**

You receive a prescription in your pharmacy with the following details:

| Patient: | Mr David Shaw, 5 Longmeadow, Astonbury |
| Age:     | 56 |
| Prescription: | Mist Gent Alk |
| Directions: | 10mL tds ac ex aq |
| Mitte:   | 150mL |
1. **Use of the product**

   Gentian is used as a bitter to stimulate appetite (*British Pharmacopoeia 2007*, p 949).

2. **Is it safe and suitable for the intended purpose?**

   This is an official preparation, therefore the formula is safe and suitable for purpose. Note that if the dose of an oral liquid is specified as 5 mL or 10 mL, the dose regimen would be 5 mL or 10 mL three or four times daily by convention.

3. **Calculation of formula for preparation**

   Prepare 150 mL of Alkaline Gentian Mixture BP.

   **Product formula**

   *(from the British Pharmacopoeia 2007, p 2616):*

<table>
<thead>
<tr>
<th></th>
<th>Master</th>
<th>100 mL</th>
<th>50 mL</th>
<th>150 mL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Concentrated Compound</td>
<td>100 mL</td>
<td>10 mL</td>
<td>5 mL</td>
<td>15 mL</td>
</tr>
<tr>
<td>Gentian Infusion BP</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sodium Bicarbonate BP</td>
<td>50 g</td>
<td>5 g</td>
<td>2.5 g</td>
<td>7.5 g</td>
</tr>
<tr>
<td>Double Strength Chloroform Water BP</td>
<td>500 mL</td>
<td>50 mL</td>
<td>25 mL</td>
<td>75 mL</td>
</tr>
<tr>
<td>Potable water</td>
<td></td>
<td>to 1000 mL</td>
<td>to 50 mL</td>
<td>to 150 mL</td>
</tr>
</tbody>
</table>

   **Interim formula for Double Strength Chloroform Water BP**

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

4. **Method of preparation**

   a. **Solubility where applicable**

      Sodium Bicarbonate BP is soluble 1 in 11 in water (*British Pharmacopoeia 1988*, p 509). Therefore to dissolve 7.5 g Sodium Bicarbonate BP, a minimum of $7.5 \times 11 = 82.5$ mL of water would be required. As this is greater than 50% of the mixture, a solution of Double Strength Chloroform Water BP and water would be used for dissolution.

   b. **Vehicle/diluent**

      Double Strength Chloroform Water BP and potable water would be used as the vehicle as per the product formula.

   c. **Preservative**

      Double Strength Chloroform Water BP is included in this product as the preservative as per the product formula.

   d. **Flavouring when appropriate**

      No extra flavouring is required. In addition to preservative action Double Strength Chloroform Water BP will give some flavouring and act as a sweetener, therefore helping to counteract the bitter taste of the Concentrated Compound Gentian Infusion BP.
The following method would be used to prepare 150 mL of Alkaline Gentian Mixture BP from the formula above:

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).

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.

Noting that Sodium Bicarbonate BP is soluble 1 in 11 with water, a minimum of 11 mL of water would be required to dissolve 1 g of Sodium Bicarbonate BP.

The final volume of Alkaline Gentian Mixture BP required (150 mL) will contain 7.5 g of Sodium Bicarbonate BP. As 1 g of Sodium Bicarbonate BP 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 dissolve the solute initially. When choosing the amount of vehicle to use for...
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. Equally, it would also be incorrect to dissolve the Sodium Bicarbonate BP in 90 mL of water as the final volume of the preparation will contain less than 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).

3. Weigh 7.5 g Sodium Bicarbonate BP on a Class II (Figure 2.2) 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).
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 medical bottle with a child-resistant closure and label.

5. **Choice of container**
   A plain amber bottle with a child-resistant closure would be most suitable as the preparation is a solution for internal use.

6. **Labelling considerations**
   a. **Title**
      The product is official, therefore the following title would be suitable: ‘Alkaline Gentian Mixture BP’.
   b. **Quantitative particulars**
      Quantitative particulars are not required as the product is official.
   c. **Product-specific cautions (or additional labelling requirements)**
      Not applicable.
   d. **Directions to patient – interpretation of Latin abbreviations where necessary**
      ‘Take TWO 5 mL spoonfuls THREE times a day before food in water’.
   e. **Recommended British National Formulary cautions when suitable**
      Not applicable.
   f. **Discard date**
      *The British Pharmacopoeia* (2004, p 2453) states that this product should be recently prepared, therefore it will attract a 4-week discard date. Alternatively, a 2-week discard date could be assigned as the product also contains an infusion.
   g. **Sample label** (you can assume 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):

<table>
<thead>
<tr>
<th>Alkaline Gentian Mixture BP</th>
<th>150 mL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Take TWO 5 mL spoonfuls THREE times a day before food in water.</td>
<td></td>
</tr>
<tr>
<td>Do not use after (2 weeks)</td>
<td></td>
</tr>
<tr>
<td>Mr David Shaw</td>
<td>Date of dispensing</td>
</tr>
</tbody>
</table>

7. **Advice to patient**
   The patient would be advised to mix two 5 mL spoonfuls with an equal volume of water to dilute the bitter taste three times a day before food. In addition, the discard date would be highlighted to the patient.
Example 2.2
The preparation of Ammonium Chloride Mixture BP
You receive a prescription in your pharmacy with the following details:

<table>
<thead>
<tr>
<th>Patient:</th>
<th>Mr James Watson, 4 Arrow Ave, Astonbury</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age:</td>
<td>42</td>
</tr>
<tr>
<td>Prescription:</td>
<td>Ammonium Chloride Mixture BP</td>
</tr>
<tr>
<td>Directions:</td>
<td>10 mL tds prn</td>
</tr>
<tr>
<td>Mitte:</td>
<td>50 mL</td>
</tr>
</tbody>
</table>

1. **Use of the product**
   Used as an expectorant to treat chesty coughs (*Martindale* 35th edn, p 1399).

2. **Is it safe and suitable for the intended purpose?**
   This is an official preparation, therefore the formula is safe and suitable for purpose. The dose of 10 mL three times a day when required is consistent with the adult standard dosage for official oral liquids (of 10 mL) three to four times a day by convention.

3. **Calculation of formula for preparation**
   Prepare 50 mL of Ammonium Chloride Mixture BP.

**Product formula**
*(from the *British Pharmacopoeia* 2007, p 2317)*

<table>
<thead>
<tr>
<th></th>
<th>Master</th>
<th>500 mL</th>
<th>50 mL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ammonium Chloride BP</td>
<td>100 g</td>
<td>50 g</td>
<td>5g</td>
</tr>
<tr>
<td>Aromatic Ammonia Solution BP</td>
<td>50 mL</td>
<td>25 mL</td>
<td>2.5 mL</td>
</tr>
<tr>
<td>Liquorice Liquid Extract BP</td>
<td>100 mL</td>
<td>50 mL</td>
<td>5 mL</td>
</tr>
<tr>
<td>Potable water</td>
<td>to 1000 mL</td>
<td>to 500 mL</td>
<td>to 50 mL</td>
</tr>
</tbody>
</table>

4. **Method of preparation**
   a. **Solubility where applicable**
      Ammonium Chloride BP is soluble 1 in 2.7 in water (*British Pharmacopoeia* 1988, p 36). Therefore to dissolve 5 g of ammonium chloride a minimum of 5 × 2.7 = 13.5 mL of water would be required.
   b. **Vehicle/diluent**
      Potable water would be used as the vehicle as per the product formula.
   c. **Preservative**
      No additional preservative is required as per the product formula.
   d. **Flavouring when appropriate**
Liquorice Liquid Extract BP, although a mild expectorant, is mainly included for its flavouring and sweetening properties and its ability to disguise the taste of the Ammonium Chloride BP.

**Method of compounding**

1. Calculate the quantity of ingredients required to produce the final volume needed. As with Example 2.1, this calculation is best attempted in stages.
2. Weigh 5 g Ammonium Chloride BP accurately on a Class II or electronic balance.
3. Measure approximately 15 mL potable water and transfer to a beaker.
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.

**5. Choice of container**

A plain amber bottle with a child-resistant closure would be the most suitable as the preparation is a solution intended for internal use.

**6. Labelling considerations**

a. **Title**

The product is official, therefore the following title would be suitable: ‘Ammonium Chloride Mixture BP’.

b. **Quantitative particulars**

Quantitative particulars are not required as the product is official.

c. **Product-specific cautions (or additional labelling requirements)**

No product-specific cautions are applicable, although the patient could be advised to take the product in water (to dilute

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**Tips**

As Ammonium Chloride BP 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, for example, 15 mL.

The solution should be gently stirred to reduce the likelihood of frothing that can occur upon the addition of Liquorice Liquid Extract BP. Any resultant frothing will make the accurate reading of the final meniscus difficult.

Note that the syringe will not need rinsing as it is designed to deliver a measured volume.
the taste) or in warm water (to dilute the taste but also to improve the expectorant action by hastening the release of the ammonia, which is the main expectorant in the mixture).

d. **Directions to patient – interpretation of Latin abbreviations where necessary**
   ‘Take TWO 5 mL spoonfuls THREE times a day when required’.

e. **Recommended British National Formulary cautions when suitable**
   Not applicable.

f. **Discard date**
   The *British Pharmacopoeia* (2004, p 2181) states that this product should be recently prepared, therefore it will attract a 4-week discard date.

g. **Sample label (you can assume 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):**

<table>
<thead>
<tr>
<th>Ammonium Chloride Mixture BP</th>
<th>50 mL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Take TWO 5 mL spoonfuls THREE times a day when required.</td>
<td></td>
</tr>
<tr>
<td>Do not use after (4 weeks)</td>
<td></td>
</tr>
<tr>
<td>Mr James Watson</td>
<td>Date of dispensing</td>
</tr>
</tbody>
</table>

7. **Advice to patient**
   The patient would be advised to take two 5 mL spoonfuls three times a day when required. In addition, the discard date and the fact that the solution may be taken diluted with an equal volume of warm water would be highlighted.

**Example 2.3**

**The preparation of Sodium Chloride Compound Mouthwash BP**

You receive a prescription in your pharmacy with the following details:

| Patient: | Mrs Avril Asker, 21 Station Road, Astonbury |
| Age:     | 36 |
| Prescription: | Sodium Chloride Compound Mouthwash BP |
| Directions: | Use 20 mL qqh prn |
| Mitte:    | 150 mL |

1. **Use of the product**
   Used as a mouthwash to cleanse and freshen the mouth, suitable for treatment of superficial infections if used frequently (*British National Formulary* 61st edn, p 697).
2. **Is it safe and suitable for the intended purpose?**
   This is an official preparation, therefore the formula is safe and suitable for purpose. The dose of 20 mL every 4 hours when required is consistent with the recommended dosage (*British National Formulary* 61st edn, p 698).

3. **Calculation of formula for preparation**
   Prepare 150 mL of Sodium Chloride Compound Mouth wash BP.

### Product formula
*(from the *British Pharmacopoeia* 2007, p 2911)*

<table>
<thead>
<tr>
<th>Product formula</th>
<th>Master</th>
<th>100 mL</th>
<th>50 mL</th>
<th>150 mL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium Bicarbonate BP</td>
<td>10 g</td>
<td>1 g</td>
<td>500 mg</td>
<td>1.5 g</td>
</tr>
<tr>
<td>Sodium Chloride BP</td>
<td>15 g</td>
<td>1.5 g</td>
<td>750 mg</td>
<td>2.25 g</td>
</tr>
<tr>
<td>Concentrated Peppermint Emulsion BP</td>
<td>25 mL</td>
<td>2.5 mL</td>
<td>1.25 mL</td>
<td>3.75 mL</td>
</tr>
<tr>
<td>Double Strength Chloroform Water BP</td>
<td>500 mL</td>
<td>50 mL</td>
<td>25 mL</td>
<td>75 mL</td>
</tr>
<tr>
<td>Potable water</td>
<td>to 1000 mL</td>
<td>to 100 mL</td>
<td>to 50 mL</td>
<td>to 150 mL</td>
</tr>
</tbody>
</table>

### Interim formula for Double Strength Chloroform Water BP

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

4. **Method of preparation**
   
   **a. Solubility where applicable**
   Sodium Bicarbonate BP is soluble 1 in 11 parts of water (*British Pharmacopoeia* 1988, p 509). Therefore to dissolve 1.5 g of Sodium Bicarbonate BP a minimum of $1.5 \times 11 = 16.5$ mL water would be required. Sodium Chloride BP is soluble 1 in 3 parts of water (*British Pharmacopoeia* 1988, p 512). Therefore to dissolve 2.25 g of Sodium Chloride BP a minimum of $2.25 \times 3 = 6.75$ mL water would be required.

   **b. Vehicle/diluent**
   Double Strength Chloroform Water BP and potable water would be used as the vehicle as per the product formula.

   **c. Preservative**
   Double Strength Chloroform Water BP is included in this product as the preservative as per the product formula.

   **d. Flavouring when appropriate**
   Concentrated Peppermint Emulsion BP is added to this product as a flavouring as per the product formula. In addition the Double Strength Chloroform Water BP will also sweeten and flavour the product. The following method would be used...
to prepare 150 mL of Sodium Chloride Compound Mouthwash BP from the formula above:

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).

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.

Note that Sodium Bicarbonate BP is soluble 1 in 11 with water, a minimum of 11 mL of water would be required to dissolve 1 g of Sodium Bicarbonate BP.

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 BP is soluble in 11 mL, 1.5 g is soluble in 16.5 mL (1.5 × 11 = 16.5 mL).

The Sodium Chloride BP 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 BP.

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 BP is soluble in 2.8 mL, 2.25 g is soluble in 6.3 mL (2.25 × 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 BP and a minimum of 6.3 mL of vehicle would be required to dissolve the 2.25 g of Sodium Chloride BP in this example.
For ease of compounding, choose a convenient volume of vehicle, for example, 30 mL, in which to dissolve the solute initially.

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 bottle and label.

5. **Choice of container**
   As this is an extemporaneously prepared mouthwash, the container of choice would be an amber fluted medical bottle with child-resistant closure.

6. **Labelling considerations**
   a. **Title**
      The product is official, therefore the following title would be suitable: ‘Sodium Chloride Compound Mouthwash BP’.
   b. **Quantitative particulars**
      Quantitative particulars are not required as the product is official.
   c. **Product-specific cautions**
      As the product is a mouthwash, ‘Not to be taken’, ‘Do not swallow in large amounts’ and ‘Dilute with an equal volume of water before using’ would all be required on the product label.
   d. **Directions to patient – interpretation of Latin abbreviations where necessary**
      ‘Use 20 mL as a mouthwash every four hours when required’.

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.
e. Recommended British National Formulary cautions when suitable
   The British National Formulary has no specific labelling cautions for this product but does advise dilution with an equal volume of warm water.

f. Discard date
   The product is a mouthwash containing a preservative and so will attract a 4-week discard date.

g. Sample label (you can assume 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 150mL**
   Use 20mL as a mouthwash every four hours when required.
   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)

   Mrs Avril Asker Date of dispensing

7. Advice to patient
   The patient would be advised that 20mL of mouthwash should preferably be diluted with an equal volume of warm water and used every 4 hours when required. In addition, the discard date and the fact that, although the mouthwash should not be swallowed, it is not harmful to swallow small amounts would be highlighted.

**Example 2.4**
**The preparation of a magistral formulation from a doctor’s prescription**
You receive a prescription in your pharmacy with the following details:

<table>
<thead>
<tr>
<th>Patient:</th>
<th>Mr Gary Murray, 12 Bishop Road, Astonbury</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age:</td>
<td>49</td>
</tr>
<tr>
<td>Prescription:</td>
<td>Potassium Permanganate Solution 0.2%</td>
</tr>
<tr>
<td>Directions:</td>
<td>Dilute 1 in 20 and use as a wet dressing alt die</td>
</tr>
<tr>
<td>Mitte:</td>
<td>150mL</td>
</tr>
</tbody>
</table>

1. Use of the product
   Used for cleansing wounds and deodorising suppurating eczematous reactions and wounds (British National Formulary 61st edn, p 744).
2. **Is it safe and suitable for the intended purpose?**
   It is commonly used as a solution at a strength of 1 in 10 000 (*British National Formulary* 61st edn, p 744). When the prepared solution is diluted as indicated it will provide a 1 in 10 000 solution.
   
   0.2% w/v solution is the same as a 1 in 500 solution which, when diluted 20 times, becomes a 1 in 10 000 solution.

3. **Calculation of formula for preparation**
   Prepare 150 mL of Potassium Permanganate Solution 0.2% w/v.
   
   0.2% w/v is equal to 0.2 g in 100 mL. Therefore there is 200 mg of Potassium Permanganate BP in every 100 mL of solution.

<table>
<thead>
<tr>
<th>Product formula</th>
<th>Master</th>
<th>50 mL</th>
<th>150 mL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Potassium Permanganate BP</td>
<td>200 mg</td>
<td>100 mg</td>
<td>300 mg</td>
</tr>
<tr>
<td>Freshly boiled and cooled purified water</td>
<td>to 100 mL</td>
<td>to 50 mL</td>
<td>to 150 mL</td>
</tr>
</tbody>
</table>

4. **Method of preparation**
   
   a. **Solubility where applicable**
      Potassium Permanganate BP is soluble 1 in 16 in cold water and freely soluble in boiling water (*British Pharmacopoeia* 1988, p 455).
   
   b. **Vehicle/diluent**
      Freshly boiled and cooled purified water would be used as the vehicle, as no preservative will be added and the solution is intended for application to a wound.
   
   c. **Preservative**
      No preservative is to be added to this product.
   
   d. **Flavouring when appropriate**
      Not applicable as the solution is for external use.

   The following method would be used to prepare 150 mL of Potassium Permanganate BP 0.2% w/v from the formula above:
   
   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 under water into a powder.
   3. Transfer the solution to a 250 mL conical measure.

---

Tips

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. Using this method, the compounder is less likely to make a calculation error.
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 medical bottle with a child-resistant closure and label.

5. Choice of container
A fluted amber bottle with a child-resistant closure would be most suitable as the preparation is a solution for external use.

6. Labelling considerations
a. Title
The product is unofficial, therefore the following title would be suitable: 'Potassium Permanganate Solution 0.2% w/v'.

b. Quantitative particulars
The product is unofficial, therefore it is necessary to put the quantitative particulars on the label. As the product is intended for external use, the quantitative particulars would be expressed per container.

**This container contains:**
Potassium Permanganate BP 0.2%
Freshly boiled and cooled purified water to 100%
or

**This container contains:**
Potassium Permanganate BP 300 mg
Freshly boiled and cooled purified water to 150 mL

The quantitative particulars for a product for external use may be expressed in percentage terms instead of actual quantities; either would be correct.

c. Product-specific cautions (or additional labelling requirements).
'For external use only.'

d. Directions to patient – interpretation of Latin abbreviations where necessary
'Dilute ONE capful with NINETEEN capfuls of water and use as a wet dressing every other day.'

e. Recommended British National Formulary cautions when suitable

**Tips**

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. In addition, a glass mortar is always used for grinding as crystalline substances can scratch a porcelain mortar.
The *British National Formulary* has no specific labelling cautions for this product but does advise that solutions of Potassium Permanganate BP stain skin and clothing. Therefore, a suitable caution could be added to the final label.

f. **Discard date**
   The product would attract a 2-week discard date as there is no preservative and the product is being applied to an open wound.

g. **Sample label** (you can assume 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  150mL

Dilute ONE capful with NINETEEN capfuls of water and use as a wet dressing every other day.
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%

Mr Gary Murray  Date of dispensing
```

7. **Advice to patient**
   The patient would be advised to dilute one capful of the solution with 19 capfuls of water and use as a wet dressing every other day. In addition, the discard date and the following cautions would be highlighted to the patient:
   - For external use only.
   - The preparation may stain hair, skin and fabrics.
   - With prolonged use nails may also be stained.
   - Discontinue use if the skin becomes dry.

**Self-assessment**

**Basic strength calculations**
The simplest way to express the strength of a solution is to specify the amount of solute to be dissolved in a stated amount of solvent.

If the solute is a solid dissolved in a liquid, the strength of the solution may often be expressed as mg/mL, mg/100mL, g/100mL, mg/L or g/L. Similarly, if the solute is a liquid, the strength could be expressed as mL/10mL, mL/100mL or mL/L.
Example 2.5
You are asked to prepare a 100 mL solution containing Sodium Chloride BP 9 mg/mL

<table>
<thead>
<tr>
<th>Sodium Chloride BP</th>
<th>9 mg</th>
<th>90 mg</th>
<th>900 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Potable water</td>
<td>to 1 mL</td>
<td>to 10 mL</td>
<td>to 100 mL</td>
</tr>
</tbody>
</table>

Therefore the amount required would be 900 mg (= 0.9 g).

Similarly, the request could be to prepare 100 mL of a solution containing Sodium Chloride BP 0.009 g/mL

<table>
<thead>
<tr>
<th>Sodium Chloride BP</th>
<th>0.009 mg</th>
<th>0.09 mg</th>
<th>0.9 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Potable water</td>
<td>to 1 mL</td>
<td>to 10 mL</td>
<td>to 100 mL</td>
</tr>
</tbody>
</table>

Therefore the amount required would be 0.9 g (= 900 mg).

Questions
1. How much solid would be required in order to produce 500 mL of a 15 mg/10 mL solution?
   a. 75 mg
   b. 150 mg
   c. 750 mg
   d. 1500 mg
   e. 7500 mg

2. If 30 mg of an ingredient was dissolved in 1.5 mL of solvent, what would be the strength of the resulting solution expressed as mg/mL?
   a. mg/mL
   b. 15 mg/mL
   c. 20 mg/mL
   d. 30 mg/mL
   e. 200 mg/mL

3. A patient requires a dose of 1 mg of atropine sulphate. Ampoules containing 600 micrograms/mL are available. If a 2 mL syringe graduated to 0.1 mL is available, which of the following provides the nearest dose?
   a. 1.5 mL
   b. 1.6 mL
   c. 1.7 mL
   d. 1.8 mL
   e. 1.9 mL

4. A paediatric vitamin drop contains 0.25 mg of vitamin D in each millilitre. How many micrograms of vitamin D are contained in 0.2 mL of this preparation?
   a. 50 micrograms
   b. 75 micrograms
   c. 100 micrograms
   d. 150 micrograms
   e. 250 micrograms
5. **What weight of sodium bicarbonate (in grams) would be required to make 150 mL of a 6 g/L solution?**

a. 0.5 g  

b. 0.6 g  

c. 0.75 g  

d. 0.9 g  

e. 1 g

**Tailored strength calculations**

Often this type of calculation is required if you are attempting to give a tailored dose to a patient using existing pre-prepared stock mixtures.

**Example 2.6**

A common dose seen in paediatric prescribing is 62.5 mg phenoxymethylpenicillin four times a day. This is the recommended dose for a child 1 month–1 year. The readily available mixture is 125 mg/5 mL. Therefore to provide a dose of 62.5 mg we give 2.5 mL of a 125 mg/mL mixture.

\[
\text{Volume required} = \frac{\text{strength required}}{\text{stock strength}} \times \text{volume of stock solution}
\]

\[
= \frac{62.5}{125} \times 5 \text{ mL}
\]

\[
= \frac{62.5}{125} \times 5 \text{ mL}
\]

\[
= \frac{312.5}{125}
\]

\[
= 2.5 \text{ mL}
\]

**Questions**

6. A patient requires a dose of 5 mg of a drug. The available stock solution contains 25 mg/5 mL. How much of this stock solution would be required to deliver this dose?

7. A baby requires a dose of 37.5 mg chloroquine base each week to prevent infection with malarial parasite. The solution available for you to dispense contains 50 mg/5 mL chloroquine base. How much of this stock solution should be given to the baby each week?

8. A 5-year-old child needs a dose of 125 mg cimetidine four times a day. The stock solution of cimetidine available contains 200 mg/5 mL. How many millilitres of this stock solution will be administered for each dose?

**Percentage calculations**

Percentages are also commonly used to express the strength of solutions. Usually these solutions are not intended for the oral route of administration. As a
percentage this can have four different meanings and in order to make clear the intention the following terms are used:

- % w/w percentage weight in weight. This expresses the amount in grams of solute in 100 g of product.
- % w/v percentage weight in volume. This expresses the amount in grams of solute in 100 mL of product.
- % v/v percentage volume in volume. This expresses the number of millilitres of solute in 100 mL of product.
- % v/w percentage volume in weight. This expresses the number of millilitres of solute in 100 g of product.

The strength of solutions of solids in liquids is usually expressed as % w/v, whereas that of liquids in liquids is expressed as % v/v. When the type of percentage is not specified by convention the above rule will apply. For example, % solid in liquid is interpreted as % w/v.

**Example 2.7**

Prepare 50 mL potassium permanganate solution 2.8%.

As Potassium Permanganate BP is a solid this would mean: prepare a solution containing potassium permanganate 2.8% w/v.

This means that there would be 2.8 g of Potassium Permanganate BP dissolved in every 100 mL of solution.

<table>
<thead>
<tr>
<th>Potassium Permanganate BP</th>
<th>2.8 g</th>
</tr>
</thead>
<tbody>
<tr>
<td>Freshly boiled and cooled purified water</td>
<td>to 100 mL</td>
</tr>
</tbody>
</table>

**Questions**

What quantities would be required for the following?

9. 500 mL of a 0.1% w/v solution using a 20% w/v solution.

10. 5 L of a 0.9% w/v solution.

11. 20 mL of a 5% solution.

12. How much solid would be required in order to produce 50 mL of a 0.2% w/v solution?
    a. 100 micrograms
    b. 200 micrograms
    c. 10 milligrams
    d. 100 milligrams
    e. 200 milligrams

13. How much solid would be required in order to produce 20 mL of a 5% w/v solution?
    a. 100 mg
    b. 500 mg
14. How much solid would be required in order to produce 300 mL of a 0.01% w/v solution?
   a. 3 micrograms
   b. 3 milligrams
   c. 30 milligrams
   d. 300 milligrams
   e. 3 grams

15. How much solid would be required in order to produce 750 mL of a 15% w/v solution?
   a. 75 mg
   b. 125 mg
   c. 1125 mg
   d. 112.5 g
   e. 750 g

16. How much solid would be required in order to produce 10 litres of a 0.45% solution?
   a. 45 mg
   b. 4.5 g
   c. 9 g
   d. 45 g
   e. 90 g

17. What is the percentage strength when 5 mL of disinfectant concentrate is made up to 1 litre with water?
   a. 0.05% v/v
   b. 0.15% v/v
   c. 0.5% v/v
   d. 1.5% v/v
   e. 5% v/v

18. You have been given the following prescription: Sodium Bicarbonate BP 5% potable water to 10 mL. How much Sodium Bicarbonate BP (in grams) will be needed to prepare the product?
   a. 0.05 g
   b. 0.15 g
   c. 0.5 g
   d. 1.5 g
   e. 5 g
19. How much of a 20% w/v solution would be required to produce 250 mL of a 0.5% w/v solution?
   a. 2.5 mL  
   b. 6.25 mL  
   c. 25 mL  
   d. 62.5 mL  
   e. 125 mL  

20. How much of a 4% w/v solution would be required to prepare 150 mL of a 1% w/v solution?
   a. 2.6 mL  
   b. 3.75 mL  
   c. 26 mL  
   d. 37 mL  
   e. 37.5 mL  

21. How much of a 25% w/v solution would be required to prepare 250 mL of a 0.5% w/v solution?
   a. 0.5 mL  
   b. 1 mL  
   c. 2.5 mL  
   d. 5 mL  
   e. 10 mL  

22. Calculate the amount of stock solution that would be required to make the following solutions.
   a. Half a litre of a 1% v/v solution using a 15% v/v solution  
   b. 250 mL of a 1% v/v solution using a 40% v/v solution  
   c. 500 mL of a 1% v/v solution using a 10% solution  
   d. 1 litre of a 0.5% v/v solution using a 15% solution  
   e. 1 litre of a 0.05% solution using a 4% solution

Parts calculations
The concentration of solutions may also be expressed in terms of ‘parts’. By this we mean ‘parts’ of solute in ‘parts’ of product. This is interpreted as parts by weight (grams) of a solid in parts by volume (millilitres) of the final solution or in parts by volume (millilitres) of a liquid in parts by volume (millilitres) of the final solution. Solubility of ingredients is often expressed in this way.

Example 2.8
Sodium Bicarbonate BP is soluble in 11 parts of water. This means that 1 g of Sodium Bicarbonate BP will dissolve in 11 mL of water. Therefore if you had a formula that required 4 g of Sodium Bicarbonate BP you would need a minimum of 4 × 11 = 44 mL of water in which to dissolve the 4 g of Sodium Bicarbonate BP.
Questions

23. How many millilitres of potable water are required to dissolve 3 g of a solid which is soluble in 2.5 parts of water?
   a. 2.5 mL
   b. 3 mL
   c. 5 mL
   d. 7.5 mL
   e. 8 mL

24. How many millilitres of potable water are required to dissolve 7 g of a solid, which is soluble 1 in 1.5 parts of water?
   a. 1.5 mL
   b. 15 mL
   c. 7.5 mL
   d. 10.5 mL
   e. 75 mL

25. Sodium Bicarbonate BP is soluble 1 in 11. How much Double Strength Chloroform Water BP is needed to dissolve 0.37 kg?
   a. 3.7 L
   b. 4.07 L
   c. 4090 mL
   d. 4.1 L
   e. 4700 mL

26. How much of a 1 in 150 w/v solution would be required to produce 200 mL of a 0.2% solution?
   a. 3 mL
   b. 15 mL
   c. 25 mL
   d. 30 mL
   e. 60 mL

27. Express 500 micrograms in 2 mL as ‘1 in x’.
   a. 1 in 250
   b. 1 in 400
   c. 1 in 2000
   d. 1 in 2500
   e. 1 in 4000

28. How much Crystal Violet BP is required to prepare 5.4 litres of a 1 in 12 000 solution?
   a. 450 micrograms
   b. 540 micrograms
   c. 4.5 milligrams
   d. 450 milligrams
   e. 540 milligrams
**Millimolar calculations**

The strength of active ingredient within a pharmaceutical preparation can be expressed as the number of millimoles per unit volume or mass of product. The mole is the unit of amount of substance and there are 1000 millimoles in a mole. To calculate the number of millimoles of an ingredient in a medicinal product, you will firstly need to know the molecular weight of the ingredient.

The number of moles of ingredient is the mass of ingredient divided by the molecular mass:

\[
\text{Number of moles} = \frac{\text{Mass in grams}}{\text{Molecular mass}}
\]

For example, the molecular weight quoted for Sodium Chloride BP is 58.44.

Therefore a molar solution of Sodium Chloride BP would contain 58.44 g of Sodium Chloride BP in a litre.

**Example 2.9**

Prepare 100 mL of Sodium Chloride BP solution containing 1.5 mmol per mL.

\[
\begin{align*}
1 \text{ ml} & \text{ contains } 1.5 \text{ mmol} \\
100 \text{ ml} & \text{ contains } 150 \text{ mmol} \\
1 \text{ mole (1000 mmol)} & \text{ of Sodium Chloride BP weighs } 58.44 \text{ g} \\
1 \text{ mmol of Sodium Chloride BP weighs} & \text{ 58.44 g} \\
150 \text{ mmol of Sodium Chloride BP weighs} & \text{ } = \frac{58.44 \times 150}{1000} \text{ = } 8.766 \text{ g (weigh 8.77 g)}
\end{align*}
\]

**Questions**

29. The molecular weight of Sodium Chloride BP is 58.44. How many grams of Sodium Chloride BP would be needed to prepare 1 litre of a molar solution?
   a. 0.2922 g
   b. 0.5844 g
   c. 5.844 g
   d. 29.22 g
   e. 58.44 g

30. The molecular weight of Sodium Bicarbonate BP is 84. How many grams of Sodium Bicarbonate BP would be required to produce 150 mL of 0.5 mmol/mL solution?
   a. 0.63 g
   b. 0.84 g
   c. 6.3 g
   d. 8.4 g
   e. 63 g
31. The molecular weight of Sodium Chloride BP is 58.44. How many grams of Sodium Chloride BP would be required to produce 100 mL of a 2 mmol/mL solution?
   a. 2.92 g
   b. 5.84 g
   c. 11.69 g
   d. 29.20 g
   e. 58.40 g

32. The molecular weight of Sodium Bicarbonate BP is 84. How many grams of Sodium Bicarbonate BP would be required to produce 75 mL of 1 mmol/mL solution?
   a. 0.63 g
   b. 4.2 g
   c. 6.3 g
   d. 8.4 g
   e. 12.6 g

Formulation questions
This section contains details of extemporaneous products to be made in the same way as the examples earlier in this chapter. For each example, provide answers using the following sections:

1. Use of the product
2. Is it safe and suitable for the intended purpose?
3. Calculation of formula for preparation
4. Method of preparation
   a. Solubility where applicable
   b. Vehicle/diluent
   c. Preservative
   d. Flavouring when appropriate
5. Choice of container
6. Labelling considerations
   a. Title
   b. Quantitative particulars
   c. Product-specific cautions (or additional labelling requirements)
   d. Directions to patient – interpretation of Latin abbreviations where necessary
   e. Recommended British National Formulary cautions when suitable
   f. Discard date
   g. Sample label (you can assume 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)
7. Advice to patient
33. You receive a prescription in your pharmacy with the following details.

<table>
<thead>
<tr>
<th>Patient:</th>
<th>Miss Julie Jordan, 21 Fair View, Astonbury</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age:</td>
<td>2 months</td>
</tr>
<tr>
<td>Prescription:</td>
<td>Sodium Bicarbonate Solution 0.5 mmol/mL</td>
</tr>
<tr>
<td>Directions:</td>
<td>10 mL bd with feeds</td>
</tr>
<tr>
<td>Mitte:</td>
<td>200 mL</td>
</tr>
</tbody>
</table>

34. You receive a prescription in your pharmacy with the following details.

<table>
<thead>
<tr>
<th>Patient:</th>
<th>Mrs Sally Burns, 14 Netherton Grove, Astonbury</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age:</td>
<td>45</td>
</tr>
<tr>
<td>Prescription:</td>
<td>Hibitane solution 0.05%</td>
</tr>
<tr>
<td>Directions:</td>
<td>For cleansing the affected area</td>
</tr>
<tr>
<td>Mitte:</td>
<td>150 mL</td>
</tr>
</tbody>
</table>