

## Pharmacy calculations II: Isotonicity

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### What is isotonicity?

For a solution to be termed isotonic (equal tone) it must have the same osmotic pressure as a specific bodily fluid. The easiest way to calculate the osmotic pressure of a solution is to utilise the more easily measured property of the freezing point depression as they are proportional to one another. In pharmacy, isotonicity calculations are most often performed for parenteral and ophthalmic solutions which must have a freezing point depression of  $0.52^{\circ}\text{C}$  for them to be isotonic with blood plasma and tears. Therefore a solution is considered to be isotonic if it has a freezing point<sup>1</sup> of  $-0.52^{\circ}\text{C}$ .

### Why is it important?

It is important for a solution to be isotonic with a bodily fluid to prevent irritation and cell damage, and to maximise drug efficacy. If a hypotonic solution (with lower osmotic pressure than that of a bodily fluid) is administered intravenously water will pass into the red blood cells, causing them to swell and possibly burst (haemolysis). If a hypertonic solution (with higher osmotic pressure than that of a bodily fluid) is administered intravenously then water is drawn from the cells in an attempt to dilute the solution, causing them to shrink (crenation).

### Method

A hypotonic solution can be made isotonic by adding an adjusting substance, usually sodium chloride; the exact amount of this substance to add is to be calculated. The basic formula used to do this is

$$W = \frac{0.52 - a}{b}$$

where  $W$  = Weight of the added substance (g/100ml);  
 $a$  = Freezing point depression of the unadjusted hypotonic solution;  
 $b$  = Freezing point depression of a 1% w/v solution of the adjusting substance.

Ensuring consistent units in this equation highlights an important point. The 0.52 in the top line of the fraction is measured in  $^{\circ}\text{C}$  so the term  $a$  must also be measured in  $^{\circ}\text{C}$ . Reference texts such as *The Pharmaceutical Codex* usually quote freezing point depression values for one particular concentration of a pharmaceutical preparation, usually 1% w/v. If the isotonic solution being prepared has a different concentration — say 2% w/v — then the value of  $b$  must be adjusted accordingly.<sup>2</sup>

<sup>1</sup>Confusing 'freezing point' and 'freezing point depression' is a common source of error in isotonicity. For example, a solution with freezing point depression  $0.5^{\circ}\text{C}$  has freezing point  $-0.5^{\circ}\text{C}$  as 'depression' indicates a decrease in value.

<sup>2</sup>Pursuing this a little further,  $W$  is measured in g/100ml. For the units on the two sides of the equation to agree the bottom line in the fraction must be measured in  $^{\circ}\text{C}$  per g/100ml — that is, in  $^{\circ}\text{C}$  per 1% w/v concentration. If the available data for  $b$  refer to a different concentration then the value of  $b$  used in any calculation must also be adjusted.



**Example** The freezing point depression of a 1% w/v solution of morphine sulfate is 0.08°C and that of 1% w/v sodium chloride solution is 0.576. How many grams each of morphine sulfate and sodium chloride are required to prepare 50ml of a 1% w/v morphine sulfate solution isotonic with blood plasma?

**Solution**

The freezing point of (a 1% w/v solution of) morphine sulfate is -0.08°C. The required freezing point is 0.52°C, therefore the freezing point must be lowered by: 0.52°C - 0.08°C = 0.44°C. A 1% w/v sodium chloride solution produces a freezing point depression of 0.576°C, therefore the weight of sodium chloride required to produce a depression of 0.44°C is:

$$\begin{aligned}
 W &= \frac{0.52 - a}{b} \\
 &= \frac{0.52 - 0.08}{0.576} \\
 &= 0.7638\text{g}/100\text{ml}
 \end{aligned}$$

The quantities needed to make a 50ml solution will be:

1. Morphine sulfate: (1g/100ml) × 50ml = 0.5g
2. Sodium chloride: (0.7638g/100ml) × 50ml = 0.3819g

**Example** A pharmacist receives a prescription for 10ml of isotonic 0.5% w/v chloramphenicol eye drops, what weight of sodium chloride is required to make the solution isotonic with tears?

**Solution** From *The Pharmaceutical Codex* a 1% w/v solution of chloramphenicol has a freezing point depression of 0.06°C. Therefore a 0.5% w/v solution has a freezing point depression of 0.06°C × 0.5 = 0.03°C. The required freezing point is -0.52°C, therefore the freezing point must be lowered by: 0.52°C - 0.03°C = 0.49°C. 1% w/v sodium chloride produces a freezing point depression of 0.576°C, therefore the weight of sodium chloride required to produce a depression of 0.49°C is:

$$\begin{aligned}
 W &= \frac{0.52 - a}{b} \\
 &= \frac{0.52 - 0.03}{0.576} \\
 &= 0.8507\text{g}/100\text{ml}
 \end{aligned}$$

As the prescription requests 10ml of eye drops we require (0.8507 × 10)/100 = 0.08507g = 85.07mg of sodium chloride.

**Exercises**

1. How many grams each of lidocaine hydrochloride (i) and sodium chloride (ii) are required to prepare 150ml of a 2% w/v solution of lidocaine hydrochloride isotonic with blood plasma? Freezing point depression of a 1% w/v lidocaine hydrochloride solution is 0.063°C and that of sodium chloride is 0.576°C.
2. A pharmacist receives a prescription for 10ml of isotonic 1% w/v atropine sulfate eye drops. What weight of sodium chloride is required to make the solution isotonic with tears?

**Solutions**

1. (i) 3g (ii) 1.026g
2. 78.125mg

