Chapter 11

Isotonic solutions

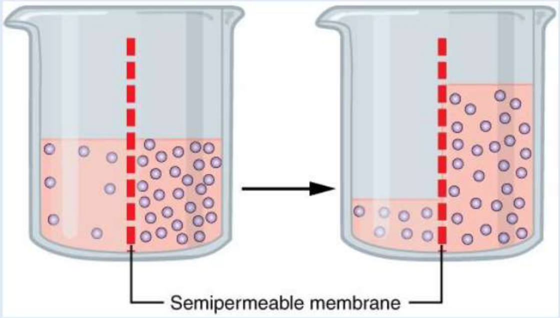
Objectives

Upon successful completion of this chapter, the student will be able to:

1. **Calculate the dissolution factor (i) of a chemical agent .**
2. **Calculate the sodium chlorid equivealnt (E- valu) of a chemical agent .**
3. **Perform calculation required in the preparation of isotonic solution .**

Lecture 3

When a **solvent** passes through a semipermeable membrane ***from*** a **dilute solution** ***into*** a **more concentrated one**, the **concentrations become equalized** and the phenomenon is known as **osmosis**.



Osmosis

The **pressure responsible** or this phenomenon is termed **osmotic pressure** and ***varies*** with the **nature of the solute.**

- If the solute is a **nonelectrolyte**, its solution contains only molecules and the **osmotic pressure varies with the concentration o the solute.**
- If the solute is an **electrolyte**, its solution contains ions and the **osmotic pressure varies with both the concentration of the solute and its degree o dissociation**.

Thus, **solutes that dissociate** present a greater number of particles in solution and **exert a greater osmotic pressure** than undissociated molecules.

Two solutions that have the **same osmotic pressure** are termed **isosmotic**

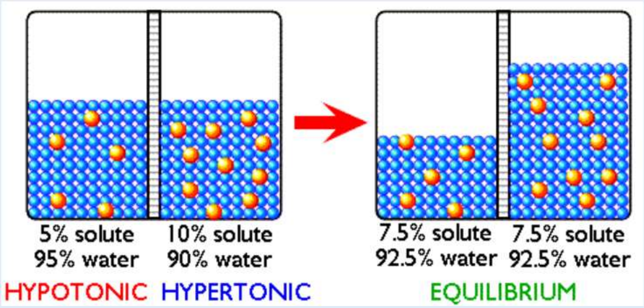
Many solutions intended to be mixed with body fluids are designed to have the same osmotic pressure for greater patient comfort, efficacy, and safety.

A solution having the **same osmotic pressure** as a ***specific*** **body fluid** is termed **isotonic** (meaning of equal tone) with *that* specific body fluid.

Solutions of ***lower*** **osmotic pressure** than that of a body fluid are termed **hypotonic**.

A solution having a ***higher*** **osmotic pressure** than that of a body fluid are termed **hypertonic**.

Pharmaceutical dosage forms intended to be added directly to the blood or mixed with biological fluids of the eye, nose, and bowel are of principal concern to the pharmacist in their preparation and clinical application.



Special Clinical Considerations of Tonicity

It is generally accepted that for ophthalmic and parenteral administration, isotonic solutions are better tolerated by the patient than those at the extremes of hypo- and hypertonicity.

With the administration of an **isotonic solution**, there is a **homeostasis with the body's intracellular fluids.** Thus, *in most instances*, preparations that are isotonic, or nearly so, are preferred.

However, there are ***exceptions***, as in instances in which **hypertonic solutions** are used to **"draw" fluids out of edematous tissues** and into the administered solution.

Most **ophthalmic preparations** are:

1. Formulated to be isotonic, or approximately isotonic, to duplicate ophthalmic tears or the comfort of the patient.
2. These solutions are also prepared and buffered at an appropriate pH.

Both to reduce the likelihood of irritation to the eye's tissues and to maintain the stability o the preparations.

Injections that are not isotonic should be **administered slowly and in small quantities** to minimize tissue irritation, pain, and cell fluid imbalance.

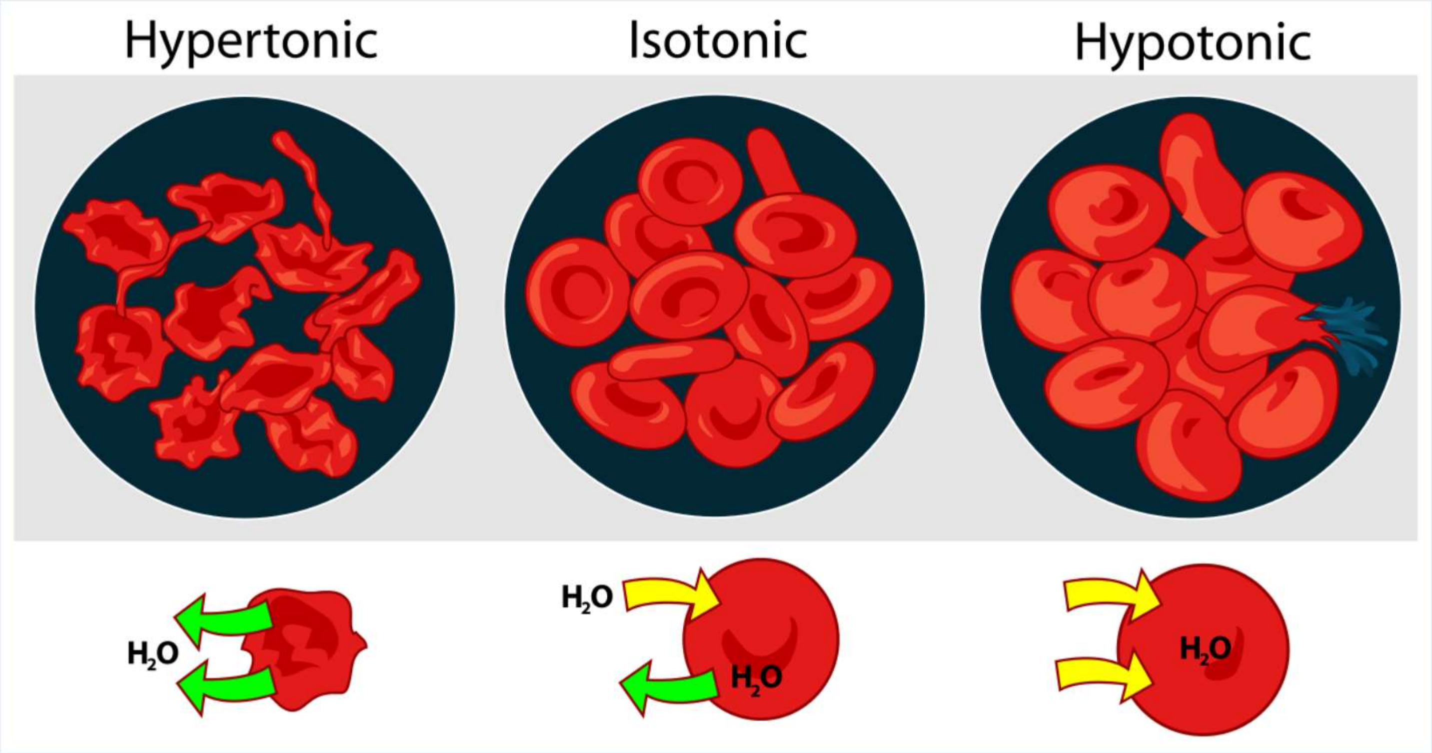
- The tonicity of small volume injections is generally unimportant when added to large-volume parenteral infusions because of the presence of tonic substances, such as sodium chloride or dextrose in the large-volume infusion, which serve to adjust the tonicity o the smaller added volume.

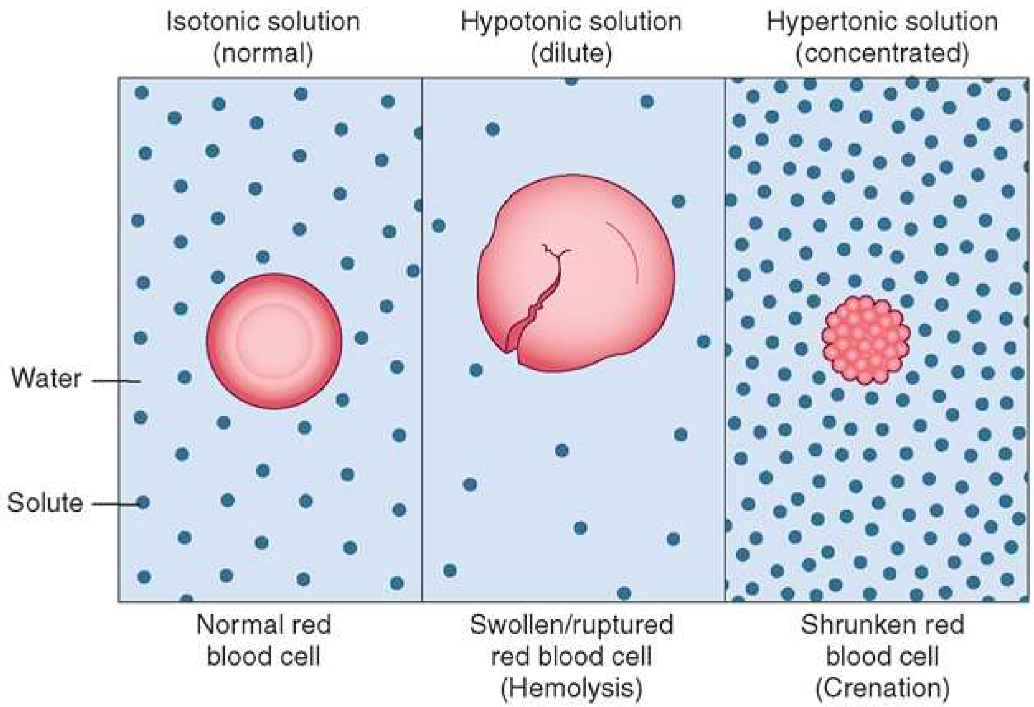
Intravenous infusions, which are hypotonic or hypertonic, can have profound adverse effects because they generally are administered in large volumes.

- Large volumes of ***hypertonic*** infusions containing dextrose, or example, can result in hyperglycemia, osmotic diuresis, and excessive loss of electrolytes.

- Excess infusions of ***hypotonic*** *f*luids can result in the osmotic hemolysis of red blood cells and surpass the upper limits of the body's capacity to safely absorb excessive fluids.

- ***Isotonic*** *fluids*, when in used intravenously in ***excessive volumes or at excessive rates***, can be deleterious due to an overload of fluids placed into the body's circulatory system.


Hypertonic
Isotonic
Hypotonic
H_2O
H_2O
H_2O
H_2O



Isotonic solution
(normal)
Hypotonic solution
(dilute)
Hypertonic solution
(concentrated)
Water
Solute
Normal red
blood cell
Swollen/ruptured
red blood cell
(Hemolysis)
Shrunken red
blood cell
(Crenation)

Physical/Chemical Considerations in the Preparation of Isotonic Solutions

The calculations involved in preparing isotonic solutions may be made in terms of data relating to the colligative properties of solutions.

Theoretically, any one of these properties may be used as a basis or determining tonicity.
Practically and most conveniently, a comparison of freezing points is used or this purpose.

It is generally accepted that −0.52°C is the freezing point of both blood serum and lacrimal fluid.

Nonelectrolyte

When **1g** molecular weight of any **nonelectrolyte**, that is, a substance with negligible dissociation, such as boric acid, is dissolved in **1000 g** of water, the freezing point of the solution is about **1.86°C** below the freezing point of pure water.

By simple proportion, therefore, we can calculate the weight of any **nonelectrolyte** that should be dissolved in each 1000 g of water in the solution is to be isotonic with body fluids.

Boric acid, or example, has a **molecular weight of 61.8**; thus (in theory), 61.8 g in 1000 g of water should produce a freezing point of **−1.86°C**. There ore:

$$\frac{1.86\ (°C)}{0.52\ (°C)} = \frac{61.8\ (g)}{x\ (g)}$$

$$x = 17.3\ g$$

In short, 17.3 g of boric acid in 1000 g o water, having a weight-in-volume strength o approximately 1.73%, should make a solution isotonic with lacrimal fluid.

Electrolyte

With **electrolytes**, because osmotic pressure depends more on the number of particles, substances that dissociate have a tonic effect that increases with the degree of dissociation; ***the greater the dissociation***, ***the smaller the quantity required*** to produce any given osmotic pressure.

If we assume that **sodium chloride** in weak solutions is about **80% dissociated**, then each 100 molecules yields 180 particles, or 1.8 times as many particles as are yielded by 100 molecules of a nonelectrolyte

- This **dissociation factor**, commonly symbolized by the letter ***i***, must be included in the proportion when we seek to determine the strength of an isotonic solution of sodium chloride (m.w. 58.5):

$$\frac{1.86\ (^{\circ}\text{C}) \times 1.8}{0.52\ (^{\circ}\text{C})} = \frac{58.5\ (\text{g})}{\text{x}\ (\text{g})}$$

$$\text{x} = 9.09\ \text{g}$$

Hence, 9.09 g of sodium chloride in 1000 g of water should make a solution isotonic with blood or lacrimal fluid.

In practice, a 0.9% w/v sodium chloride solution is considered isotonic with body fluids.

Simple isotonic solutions may then be calculated by using this formula:

$$\frac{0.52 \times \text{molecular weight}}{1.86 \times \text{dissociation}\ (i)} = \text{g of solute per 1000 g of water}$$

The value of ***i*** for many medicinal salts has not been experimentally determined. Some salts are exceptional (such as zinc sulfate, with only 40% dissociation and an ***i*** value therefore of 1.4), but most medicinal salts approximate the dissociation of sodium chloride in weak solutions.

If the number of ions is known, we may use the following values, lacking better information:

- ✓ Nonelectrolytes and substances of slight dissociation: 1.0
- ✓ Substances that dissociate into 2 ions: 1.8
- ✓ Substances that dissociate into 3 ions: 2.6
- ✓ Substances that dissociate into 4 ions: 3.4
- ✓ Substances that dissociate into 5 ions: 4.2

Example Calculations of the *i* Factor

***Zinc sulfate is a 2-ion electrolyte, dissociating 40% in a certain concentration. Calculate its dissociation (i) factor*.**

On the basis of 40% dissociation, 100 particles of zinc sulfate will yield:

40 zinc ions
40 sulfate ions
60 undissociated particles
or 140 particles

Because 140 particles represent 1.4 times as many particles as were present before dissociation, the dissociation (*i*) factor is **1.4**.

***Zinc chloride is a 3-ion electrolyte, dissociating 80% in a certain concentration. Calculate its dissociation (i) factor*.**

On the basis of 80% dissociation, 100 particles of zinc chloride will yield:

80 zinc ions
80 chloride ions
80 chloride ions
20 undissociated particles
or 260 particles

Because 260 particles represents 2.6 times as many particles as were present before dissociation, the dissociation (*i*) factor is **2.6**.

Lecture 4

Sodium chloride equivalent

A special problem arises when a prescription directs us to make a solution isotonic by adding the proper amount of a tonicity agent (such as sodium chloride or boric acid) to the solution containing the active ingredient.

- Given a 0.5% w/v solution of sodium chloride, we may easily calculate that :

0.9 g − 0.5 g = 0.4 g of additional sodium chloride that should be contained in each 100 mL if the solution is to be made isotonic with a body fluid.

But how much sodium chloride should be used in preparing 100 mL of a 1% w/v solution of atropine sulfate, which is to be made isotonic with lacrimal fluid?

The answer depends on ***how much sodium chloride is in effect represented by the atropine sulfate*.**

The relative tonic effect of two substances that is, the quantity of one that is equivalent in tonic effects to a given quantity of the other may be calculated if the **quantity of one having a certain effect in a specified quantity of solvent is divided by the quantity of the other having the same effect in the same quantity of solvent**

For example, we calculated that 17.3 g of boric acid per 1000 g of water and 9.09 g of sodium chloride per 1000 g of water are both instrumental in making an aqueous solution isotonic with lacrimal fluid.

If, however, 17.3 g of boric acid are equivalent in tonicity to 9.09 g of sodium chloride, then 1 g of boric acid must be the equivalent of

17.3 g 9.09 g

1 g x

X= 9.09 g ÷ 17.3 g or 0.52 g of sodium chloride.

Similarly, 1 g of sodium chloride must be the “tonicic equivalent” of 17.3 g ÷ 9.09 g or 1.9 g of boric acid.

We have seen that one quantity of any substance should in theory have a constant tonic effect if dissolved in 1000 g of water: **1 g molecular weight of the substance divided by its *i* or dissociation value.**

Hence, the relative quantity of sodium chloride that is the tonicic equivalent of a quantity of boric acid may be calculated by these ratios:

$$\frac{58.5 \div 1.8}{61.8 \div 1.0} \text{ or } \frac{58.5 \times 1.0}{61.8 \times 1.8}$$

and we can formulate a convenient rule: ***quantities of two substances that are tonicic equivalents are proportional to the molecular weights of each multiplied by the*** **i** ***value of the other*****.**

To return to the problem involving 1 g of atropine sulfate in 100 mL of solution:
Molecular weight of sodium chloride = 58.5; i = 1.8
Molecular weight of atropine sulfate = 695; i = 2.6

$$\frac{695 \times 1.8}{58.5 \times 2.6} = \frac{1 \text{ (g)}}{x \text{ (g)}}$$

x = 0.12 g of sodium chloride represented by 1 g of atropine sulfate

Therefore, the sodium chloride equivalent, or *E*-value, of atropine sulfate is 0.12.

Because a solution isotonic with lacrimal fluid should contain the equivalent of 0.9 g of sodium chloride in each 100 mL of solution, the difference to be added must be

0.9 g − 0.12 g = 0.78 g of sodium chloride.

Rearranging the information for calculating the *E*-value of boric acid or atropine sulfate, the following equation can be used to calculate the sodium chloride equivalent of any substance:

$$\frac{\text{Molecular weight of sodium chloride}}{i \text{ Factor of sodium chloride}} \times \frac{i \text{ factor of the substance}}{\text{Molecular weight of the substance}} = \text{Sodium chloride equivalent}$$

Substance	molecular Weight	Ions	Sodium Chloride equivalent (e-value)[a]
Antipyrine	188	1	0.17
Atropine sulfate·H_2O	695	3	0.12
Benoxinate hydrochloride	345	2	0.17
Benzalkonium chloride	360	2	0.16
Benzyl alcohol	108	1	0.17
Boric acid	61.8	1	0.52
Brimonidine tartrate	442	2	0.13
Chlorobutanol	177	1	0.24
Cocaine hydrochloride	340	2	0.17
Cromolyn sodium	512	2	0.14
Cyclopentolate hydrochloride	328	2	0.18
Demecarium bromide	717	3	0.12
Dextrose (anhydrous)	180	1	0.18
Dextrose·H_2O	198	1	0.16
Ephedrine hydrochloride	202	2	0.29
Ephedrine sulfate	429	3	0.2
Epinephrine bitartrate	333	2	0.18
Fluorescein sodium	376	3	0.31

Table 11.1 gives the sodium chloride equivalents (E values) of each of the substances listed. These values were calculated according to the rule stated previously.

If the number of grams of a substance included in a prescription is multiplied by its sodium chloride equivalent, the amount of sodium chloride represented by that substance is determined.

Example Calculations of the Sodium Chloride Equivalent (E-values)

Papaverine hydrochloride **(m.w. 376)** ***is a 2-ion electrolyte, dissociating 80% in a given concentration. Calculate its sodium chloride equivalent*****.**

Because papaverine hydrochloride is a 2-ion electrolyte, dissociating 80%, its *i* factor is 1.8.

$$\frac{\text{Molecular weight of sodium chloride}}{i \text{ Factor of sodium chloride}} \times \frac{i \text{ factor of the substance}}{\text{Molecular weight of the substance}} = \text{Sodium chloride equivalent}$$

$$\frac{58.5}{1.8} \times \frac{1.8}{376} = 0.16$$

Calculate the sodium chloride equivalent for glycerin, a nonelectrolyte with a molecular weight of 92**.**

Glycerin, *i* factor = 1.0

$$\frac{58.5}{1.8} \times \frac{1.0}{92} = 0.35$$

Calculate the sodium chloride equivalent or timolol maleate (TIMOPTIC), which dissociates into two ions and has a molecular weight of 432.

Timolol maleate, *i factor* = 1.8

$$\frac{58.5}{1.8} \times \frac{1.8}{432} = 0.14$$

Calculate the sodium chloride equivalent or fuorescein sodium, which dissociates into three ions and has a molecular weight of 376.

Fluorescein sodium, *i factor* = 2.6

$$\frac{58.5}{1.8} \times \frac{2.6}{376} = 0.22$$

Note that the calculated value differs from the value in Table 11.1 (0.31). This is most likely due to using the general dissociation factor of 2.6 rather than the specific dissociation factor or fluorescein sodium. The value reported in Table 11.1 is an experimentally determined value.

The agent brimonidine tartrate (ALPHAGAN P) has a molecular weight of 442 and dissociates into two ions when in solution. It is used as a 0.1% ophthalmic solution in the treatment of glaucoma. Calculate

(a) the sodium chloride equivalent of brimonidine tartrate

(b) whether, without additional formulation agents, a 0.1% solution would be isotonic, hypotonic, or hypertonic with tears.

(a) $\frac{58.5}{1.8} \times \frac{1.8}{442} = \mathbf{0.13}$ **sodium chloride equivalent**

(b) Arbitrarily select a volume of solution as a basis or the calculation.
The commercial product is available in **10-mL** containers, so that volume would be a good choice.
For isotonicity, a 10-mL volume would require the following amount of sodium chloride or its equivalent:
10 mL × 0.9% w/v = 0.09 g sodium chloride or its equivalent
A 10-mL volume of a 0.1% w/v solution of brimonidine tartrate would contain
10 mL × 0.1% w/v = 0.01 g brimonidine tartrate
Applying the sodium chloride equivalent (0.13):
0.01 g brimonidine tartrate × 0.13 = 0.0013 g of sodium chloride equivalence
Thus, this solution would be **hypotonic**.

If 1 g of epinephrine bitartrate, when dissolved in water, prepares 20 mL of an isotonic solution, calculate its sodium chloride equivalent.

20 mL of an isotonic *sodium chloride* solution would be calculated by

20 mL × 0.9% w/v = 0.18 g sodium chloride (in 20 mL of solution)

Therefore, 1 g of epinephrine bitartrate is equal in tonic effect to 0.18 g sodium chloride, and thus, its sodium chloride equivalent is 0.18.

The procedure for the ***calculation of isotonic solutions with sodium chloride equivalents*** may be outlined as follows:

Step 1. Calculate the amount of sodium chloride *represented* by each ingredient in a prescription by **multiplying the amount of each ingredient by its sodium chloride equivalent.**

Step 2. Calculate the amount of sodium chloride, alone, that would be contained in an isotonic solution of the volume specified in the prescription, namely, ***the amount of sodium chloride in a 0.9% solution of the specified volume*.**

Step 3. Subtract the amount of sodium chloride represented by the ingredients in the prescription (*Step 1*) from the amount of sodium chloride, alone, that would be represented in the specific volume of an isotonic solution (*Step 2*). T he answer represents the amount of sodium chloride to be added to make the solution isotonic.

Step 4. If an agent other than sodium chloride, such as boric acid, dextrose, or mannitol, is to be used to make a solution isotonic, divide the amount of sodium chloride (*Step 3*) by the sodium chloride equivalent of the other substance.

Example Calculations of Tonicic Agent Required

How many grams of sodium chloride should be used in compounding the following prescription?

℞ Homatropine hydrobromide 0.6 g
Sodium chloride qs
Purif ed water ad 30 mL
Make isoton. sol.
Sig. for the eye

Step 1

$$0.6\text{ g} \times \frac{1000\text{ mg}}{1\text{ g}} \times 0.17 \text{ (from Table 11.1)}$$

= 102 mg of sodium chloride represented by the homatromine HBr

Step 2

$$30\text{ mL} \times \frac{0.9\text{ g}}{100\text{ mL}} \times \frac{1000\text{ mg}}{1\text{ g}}$$

= 270 mg of sodium chloride in 30 mL of an isotonic sodium chloride solution

Step 3

270 mg (from *Step 2*) − 102 mg (from *Step 1*) = **168 mg of sodium chloride to be used**

How many grams of boric acid should be used in compounding the following prescription?

Rx	Proparacaine hydrochloride	0.5%
	Pilocarpine hydrochloride	2%
	Boric acid	qs
	Purif ed water ad	60 mL
	Make isoton. sol.	
	Sig. one drop in each eye	

Step 1

Proparacaine HCl:

$$\frac{0.5\text{ g}}{100\text{ mL}} \times \frac{1000\text{ mg}}{1\text{ g}} \times 60\text{ mL} = 300\text{ mg} \times 0.15 = 45\text{ mg of sodium chloride represented}$$

Pilocarpine HCl:

$$\frac{2\text{ g}}{100\text{ mL}} \times \frac{1000\text{ mg}}{1\text{ g}} \times 60\text{ mL} = 1200\text{ mg} \times 0.24 = 288\text{ mg of sodium chloride represented}$$

Total: 45 mg + 288 mg = 333 mg of sodium chloride represented by both ingredients

Step 2

$$\frac{0.9\ g}{100\ mL} \times \frac{1000\ mg}{1\ g} \times 60\ mL$$

= 540 mg of sodium chloride in 60 mL of an isotonic sodium chloride solution

Step 3

540 mg (from *Step 2*) − 333 mg (from *Step 1*) = 207 mg of sodium chloride required to make the solution isotonic

But because the prescription calls or boric acid:

Step 4

4. 207 mg ÷ 0.52 = **398.08 mg of boric acid to be used**

How many grams of potassium nitrate should be used to make the following prescription isotonic?

℞	Sol. silver nitrate 1:500 w/v Make isoton. sol. Sig. for eye use	60 mL

Step 1

$$\frac{1\text{ g}}{500\text{ mL}} \times \frac{1000\text{ mg}}{1\text{ g}} \times 60\text{ mL} = 120\text{ mg silver nitrate} \times 0.33$$

$$= 39.6\text{ mg of sodium chloride represented}$$

Step 2

$$\frac{0.9\text{ g}}{100\text{ mL}} \times \frac{1000\text{ mg}}{1\text{ g}} \times 60\text{ mL}$$

= 540 mg of sodium chloride in 60 mL of an isotonic sodium chloride solution

Step 3

540 mg (from *Step 2*) – 39.6 mg (from *Step 1*) = 500.4 mg of sodium chloride required to make solution isotonic

Because, in this solution, sodium chloride is incompatible with silver nitrate, the tonicity agent of choice is potassium nitrate. Therefore,

Step 4

500.4 mg ÷ 0.58 (sodium chloride equivalent of potassium nitrate) = **862.76 mg of potassium nitrate to be used**

How many grams of sodium chloride should be used in compounding the following prescription?

℞	Ingredient X	0.5 g
	Sodium chloride	qs
	Purif ed water ad	50 mL
	Make isoton. sol.	
	Sig. eyedrops	

Let us assume that ingredient X is a new substance or which no sodium chloride equivalent is to be found in Table 11.1 and that its molecular weight is 295 and its *i f*actor is 2.4. The sodium chloride equivalent of ingredient X may be calculated as follows:

$$\frac{58.5}{1.8} \times \frac{2.4}{295} = 0.26, \text{ the sodium chloride equivalent for ingredient X}$$

Step 1

$$0.5 \text{ g} \times \frac{1000 \text{ mg}}{1 \text{ g}} \times 0.26 = 130 \text{ mg of sodium chloride represented by ingredient X}$$

Step 2

$$\frac{0.9\ \text{g}}{100\ \text{mL}} \times \frac{1000\ \text{mg}}{1\ \text{g}} \times 50\ \text{mL}$$

= 450 mg of sodium chloride in 50 mL of an isotonic sodium chloride solution

Step 3

450 mg (from *Step 2*) – 130 mg (from *Step 1*) = **320 mg of sodium chloride to be used**

Use of Freezing Point Data in Isotonicity Calculations

Freezing point data (DT) can be used in isotonicity calculations when the agent has a tonicic effect and does not penetrate the biologic membranes in question (e.g., red blood cells).

As stated previously, the freezing point o both blood and lacrimal fluid is −0.52°C. Thus, a pharmaceutical solution that has a freezing point of −0.52°C is considered isotonic.

Representative data on freezing point depression by medicinal and pharmaceutical substances are presented in Table 11.3.

Table 11.3 • freezIng poInT daTa for SeleCT agenTS

agent	freezing point depression, 1% Solutions ($\Delta T_f^{1\%}$)
Atropine sulfate	0.07
Boric acid	0.29
Chlorobutanol	0.14
Dextrose	0.09
Ephedrine sulfate	0.13
Epinephrine bitartrate	0.10
Glycerin	0.20
Homatropine hydrobromide	0.11
Lidocaine hydrochloride	0.063
Lincomycin	0.09
Morphine sulfate	0.08
Naphazoline hydrochloride	0.16
Physostigmine salicylate	0.09
Sodium bisulfite	0.36
Sodium chloride	0.58
Sulfacetamide sodium	0.14
Zinc sulfate	0.09

Although these data are or solution strengths o 1% (DT %) f1 , data or other solution strengths and or many additional agents may be found in physical pharmacy textbooks and in the literature.

Example Calculations Using Freezing Point Data

How many milligrams each of sodium chloride and lidocaine hydrochloride are required to prepare 30 mL of a 1% solution of lidocaine hydrochloride isotonic with tears?

To make this solution isotonic, the freezing point must be lowered to −0.52°C.

From Table 11.3, it is determined that a 1% solution o lidocaine hydrochloride has a freezing point lowering o 0.063°C. Thus, sufficient sodium chloride must be added to lower the freezing point an additional 0.457°C (0.52°C − 0.063°C).

Also rom Table 11.3, it is determined that a 1% solution o sodium chloride lowers the freezing point by 0.58°C. By proportion:

$$\frac{1\%\ NaCl}{x\%\ NaCl} = \frac{0.58°C}{0.457°C}$$

x = 0.79% sodium chloride needed to lower the freezing point by 0.457°C and, therefore, required to make the solution isotonic

Thus, to make 30 mL of solution,

30 mL × 1% = 0.3 g = **300 mg lidocaine hydrochloride**, and

30 mL × 0.79% = 0.24 g = **236.68 mg sodium chloride**

NOTE: Should a prescription call for more than one medicinal and/or pharmaceutic ingredient, the sum of the freezing points is subtracted from the required value in determining the additional lowering required by the agent used to provide isotonicity.

Isotonisity

- ✓ To calculate the "equivalent tonic effect" to sodium chloride represented by an ingredient in a preparation, multiply its weight by its E-value:

  g × E- value equivalent tonic effect = g, to sodium chloride

- ✓ To make a solution isotonic, calculate and ensure the quantity of sodium chloride and/ or the equivalent tonic effect of all other ingredients to total 0.9% w/v in the preparation:

$$\frac{\text{g (NaCl)} \times \text{g (NaCl tonic equivelant)}}{\text{mL (preparation)}} \times 100 = 0.9\%$$

- ✓ To make an isotonic solution from a drug substance, add sufficient water by the equation:

$$\frac{\text{g (drug substance)} \times \text{E- value (drug substance)}}{0.009} = \text{mL water}$$

This solution may then be made to any volume with isotonic sodium chloride solutionto maintain its isotonicity.

The E-value can be derived from the same equation, given the grams of drug substance and the milliliters of water required to make an isotonic solution.

CaSe In poInT 11.1[a] A local ophthalmologist is treating one of his patients for a post-LAsiK eye infection that is not responding to topical ciprofloxacin. these infections, although rare, can occur after laser in situ keratomileusis (LAsiK) surgery for vision correction.

topical amikacin sulfate has been shown to be effective for the treatment of eye infections due to ciprofloxacin-resistant Pseudomonas,[5,6] Burkholderia ambifaria,[7] Mycobacterium chelonae, and Mycobacterium fortuitum.[8–10]

the ophthalmologist prescribes 60 mL of a 2.5% amikacin sulfate isotonic solution, two drops in the affected eye every 2 hours.

Amikacin sulfate UsP ($c_{22}H_{43}N_5O_{13} \cdot 2H_2sO_2$), m.w., 781.76, is an aminoglycoside-type antibiotic containing three ions.

(a) Determine the weight in grams of amikacin sulfate needed to prepare the solution.
(b) calculate the sodium chloride equivalent (E-value) for amikacin sulfate.
(c) calculate the amount of sodium chloride needed to make the prepared solution isotonic.
(d) How many milliliters of 23.5% sodium chloride injection should be used to obtain the needed sodium chloride?

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[a] case in Point courtesy of W. beach, Athens, GA.

(a) 60 mL × 2.5% w/v = 1.5 g amikacin

(b) NaCl m.w. =58.5
Amikacin m.wt. = 781.76
$i = 2.6$

$$\frac{58.5}{1.8} \times \frac{2.6}{781.76} = E$$

$E = 0.108$

(c) 60 mL × 0.9% w/v = 0.54 g NaCl

(d) 1.5 g (amikacin sulfate)× 0.108 (NaCl equivelant) = 0.162 g
0.54 g – 0.162 g = 0.378 NaCl required for isotonicity

$$\frac{23.5\text{ g}}{100\text{ mL}} = \frac{0.378\text{ g}}{x\text{ mL}}$$

x= 1.61 mL NaCl injection