CHAPTER 8
BUFFER
AND
ISOTONIC SOLUTION

Pharmaceutical buffers

- **1- Gifford buffer:**
- $H_3BO_3/Na_2CO_3.H_2O$ pH = 5 – 9
- **2- Sörensen buffer:**
- NaH_2PO_4/Na_2HPO_4 pH= 6 -8
- **3- Clark and Lubs buffers:**
- a- HCl/KCl pH= 1.2 – 2.2
- b- HCl/ K_2HPO_4 pH= 2.2 – 4
- c- NaOH/ K_2HPO_4 pH= 4.2 - 5.8
- d- NaOH/ KH_2PO_4 pH =5.8 – 8
- e- H_3BO_3.NaOH/ KCl pH= 8 - 10

Isotonic solution

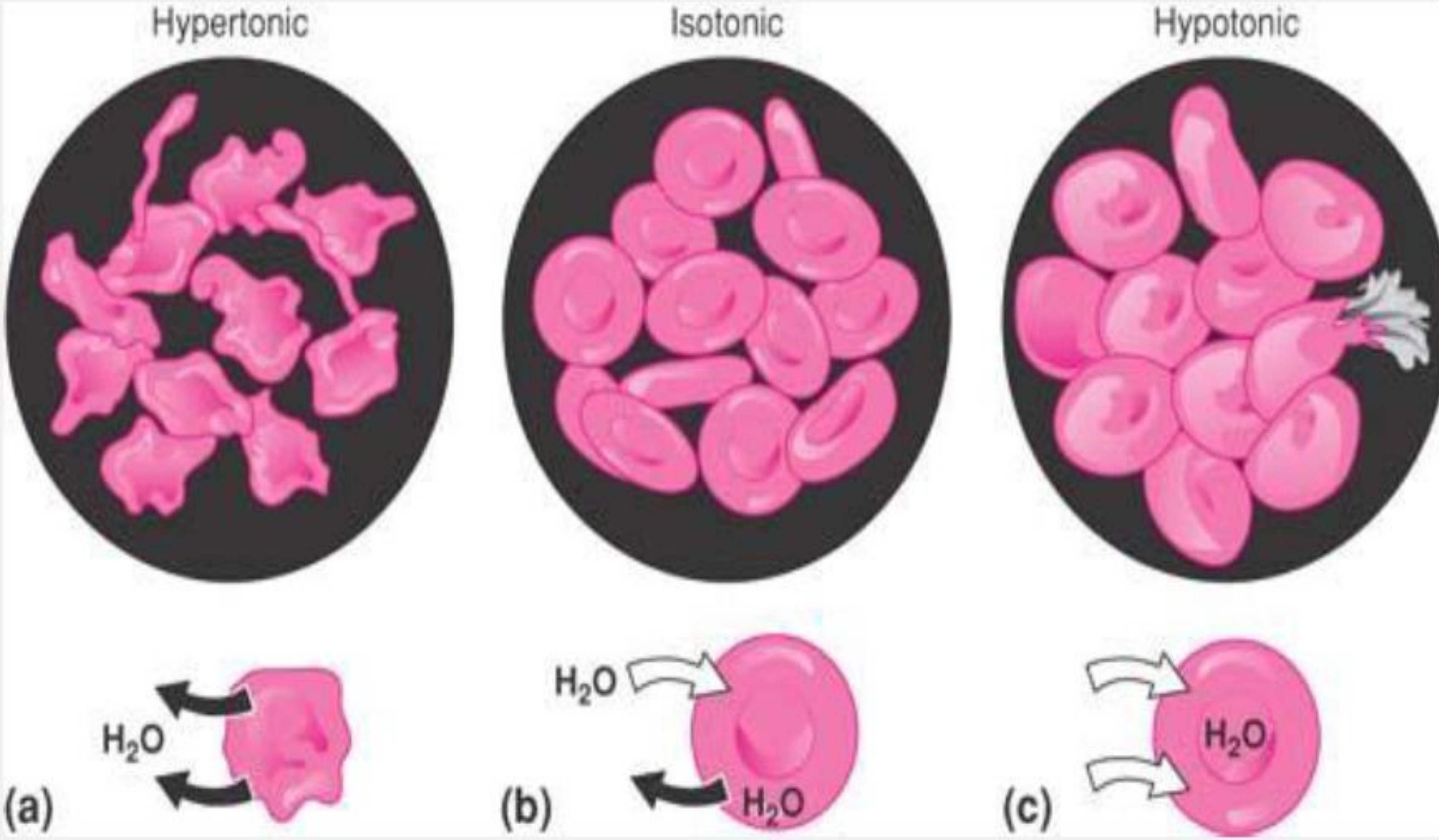
- The solution which has the same salt concentration of cell contents, or has the same osmotic pressure (π) as the cell contents.
- **0.9** g of NaCl per 100 mL is Isotonic solution of red blood cell

HYPERTONIC SOLUTION

- The solution which has concentration of salt more than of cell and causes to passes the water from the cell membrane
- the cell will be shrinking and causes Osmotic pressure (π) cell larger than inside the cell.
- **2%** NaCl is an Hypertonic solution will respect to the blood

Key Concept

Tonicity



Hypotonic solution

- The solution which has a salt concentration lass of the cell.
- The water passes to the cell through the cell membrane because of Osmotic pressure (π) inside the cell is larger than outside
- The cell will be swell and finally burst.
- This phenomena is known hemolysis.
- **0.2%** NaCl is an Hypotonic solution with respect to the blood
- Finally:
  - **0.2 %** **0.9%** **2%**
  - **Hypo** **iso** **Hyper**

Measurement of tonicity

- 1- By hemolytic method
- 2- By determine Colligative properties:
  - $\Delta T_f = L_{iso} C$

Calculation tonicity using L_{ISO} values

- $\Delta T_f = L_{iso}\, C$
- C: Isotonic concentration with body fluid.
- ΔT_f: Isotonic freezing temperature depressing = 0.52 ^{0}C for NaCl Isotonic concentration.
- L_{iso}: for NaCl = 3.4 from table
- $C = \Delta T_f / L_{iso}$ = 0.52/3.4 = 0.154 M of NaCl (Isotonic concentration
- We have:

Isotonic C of NaCl = 0.9%

M = W*1000/(Mw*V) = 0.9x1000/(58.5x100) = 0.154 M

Table 8-3 Average L_{iso} Values for Various Ionic Types*

Type	L_{iso}	Examples
Nonelectrolytes	1.9	Sucrose, glycerin, urea, camphor
Weak electrolytes	2.0	Boric acid, cocaine, phenobarbital
Di-divalent electrolytes	2.0	Magnesium sulfate, zinc sulfate
Uni-univalent electrolytes	3.4	Sodium chloride, cocaine hydrochloride, sodium phenobarbital

Uni-divalent electrolytes	4.3	Sodium sulfate, atropine sulfate
Di-univalent electrolytes	4.8	Zinc chloride, calcium bromide
Uni-trivalent electrolytes	5.2	Sodium citrate, sodium phosphate
Tri-univalent electrolytes	6.0	Aluminum chloride, ferric iodide
Tetraborate electrolytes	7.6	Sodium borate, potassium borate

*From J. M. Wells, J. Am. Pharm. Assoc. Pract. Ed. **5,** 99, 1944.

Method for adjusting

Tonicity and pH

CLASS 1 METHODS

- By calculation the quantity of NaCl or other substance is add to the solution of drug to render them Isotonic by using ΔT_f.
- **NaCl method:**
- $\Delta T_f = 0.52\ ^0C$ make Isotonic with body fluids
- $\Delta T_f = L_{iso(drug)}$ *1g/Mw $_{(drug)}$ ……….1
- $\Delta T_f = L_{iso(NaCl)}$ *E(g)/58.45 $_{(NaCl)}$ ……2
- E(g) of NaCl add to **1** g of drug to make Isotonic
- From 1 and 2
- So, $\Delta T_f = \Delta T_f$, equation 1 = equation 2 = 3.4 C
  - **E= 17 $L_{iso(drug)}$ /Mw $_{(drug)}$**
  - E, g of NaCl to adjusting tonicity

[†] The full table is available at the book's companion website at thepoint.lww.com/Sinko6e.

Example 8-13

Sodium Chloride Equivalents

Calculate the approximate *E* value for a new amphetamine hydrochloride derivative (molecular weight 187).

Because this drug is a uni-univalent salt, it has an L_{iso} value of 3.4. Its *E* value is calculated from equation (8-45):

$$E = 17\frac{3.4}{187} = 0.31$$

Calculations for determining the amount of sodium chloride or other inert substance to render a solution

Alternative isotonic agent

- Mannitol, propylene glycol (glycerin) also Isotonic agent alternative to NaCl.
- The concentration of these agents for Isotonicity calculated by :
  - $X = Y/E$
- X: g of Isotonic agent to adjust Isotonicity
- Y: g added of NaCl for Isotonicity

CLASS 2 METHODS

WHIT- VINCENT METHOD

- By addition of water to the drugs to make an Isotonic solution, followed by addition of an Isotonic solution or Isotonic buffer to bring the solution to final volume of V.
- V= w* E* 111.1
- W: g of drug
- V: mL of Isotonic soln. that maybe prepared by mixing the drug with water.
- 111.1 = 100/0.9 (NaCl Isotonic concentration)
- E from Table 8-4
- We can calculate V for each w to reach Isotonic
- V for 0.3 g of drug reported in table 8-4

Table 8-4 Isotonic Values*, †

Substance	MW	E	V	$\Delta T_f^{1\%}$	L_{iso}
Alcohol, dehydrated	46.07	0.70	23.3	0.41	1.9
Aminophylline	456.46	0.17	5.7	0.10	4.6
Amphetamine sulfate	368.49	0.22	7.3	0.13	4.8
Antipyrine	188.22	0.17	5.7	0.10	1.9
Apomorphine hydrochloride	312.79	0.14	4.7	0.08	2.6
Ascorbic acid	176.12	0.18	6.0	0.11	1.9
Atropine sulfate	694.82	0.13	4.3	0.07	5.3
Diphenhydramine hydrochloride	291.81	0.20	6.6	0.34	3.4
Boric acid	61.84	0.50	16.7	0.29	1.8
Caffeine	194.19	0.08	2.7	0.05	0.9
Dextrose·H_2O	198.17	0.16	5.3	0.09	1.9
Ephedrine hydrochloride	201.69	0.30	10.0	0.18	3.6
Ephedrine sulfate	428.54	0.23	7.7	0.14	5.8
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]

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To complete the isotonic solution, enough isotonic sodium chloride solution, another isotonic solutio

an isotonic-buffered diluting solution is added to make 30 mL of the finished product.

When more than one ingredient is contained in an isotonic preparation, the volumes of isotonic solu

obtained by mixing each drug with water, are additive.

Example 8-16

Isotonic Solutions

Make the following solution isotonic with respect to an ideal membrane:

Phenacaine hydrochloride	0.06 g
Boric acid	0.30 g
Sterilized distilled water, enough to make	100.0 mL

$$V = [(0.06 \times 0.20) + (0.3 \times 0.50)] \times 111.1$$

$$V = 18\,\text{mL}$$

The drugs are mixed with water to make 18 mL of an isotonic solution, and the preparatio

brought to a volume of 100 mL by adding an isotonic diluting solution.

SPROWL'S METHOD

- This method is modification of White-Vincent
- By choosing w = **0.3** g of drug in 1% solution using Ophthalmic and parenteral solution.
- So the volume **V** of each drug is calculated in table 8-4

solution is finally brought to the specified volume with the desired isotonic or isotonic buffered diluting solutions.

Chapter Summary

Buffers are compounds or mixtures of compounds that, by their presence in solution, resist changes in pH upon the addition of small quantities of acid or alkali. The resistance to a change in pH is known as *buffer action*. If a small amount of a strong acid or base is added to water or a solution of sodium chloride, the pH is altered considerably; such systems have no buffer action. In this chapter, the theory of buffers was introduced as were several formulas for making commonly used buffers. Finally, the important concept of tonicity was introduced. Pharmaceutical buffers must usually be made isotonic so that they cause no swelling or contraction of biological tissues, which would lead to discomfort in the patient being treated.

Practice problems for this chapter can be found at thePoint.lww.com/Sinko6e.

References