

ISOTONIC SOLUTIONS: CONCEPTS AND CALCULATION METHODS

Raxmatillayeva Indira Anvarovna
Oltiyeva Shohista Polvannazirovna
Masharipov Doston Shavkatovich
Urgench branch of Tashkent medical academy

Abstract. Isotonic solutions play a crucial role in pharmaceutical sciences, medical applications, and biological systems. This thesis examines the fundamental concepts of isotonic solutions, explores various methods for calculating isotonic concentrations, and discusses their practical applications. The osmotic pressure relationship between solutions and biological fluids determines the isotonic nature of pharmaceutical preparations.

Introduction. Isotonic solutions are aqueous solutions that have the same osmotic pressure as a reference solution, typically blood serum, tears, or other physiological fluids. The concept of isotonicity is fundamental in pharmaceutical sciences, particularly in the formulation of injectable medications, eye drops, nasal sprays, and other preparations that must be compatible with body fluids to prevent cellular damage and patient discomfort.

The human body maintains a delicate osmotic balance, and introducing solutions with significantly different osmotic pressures can cause cellular dehydration (hypertonic solutions) or cellular swelling and potential lysis (hypotonic solutions). Therefore, achieving isotonicity is critical for patient safety and therapeutic efficacy.

Osmotic pressure and tonicity

Osmotic pressure is a colligative property that depends on the number of dissolved particles in solution rather than their chemical nature. Van't Hoff's equation describes the relationship between osmotic pressure and solution concentration:

$$\pi = iMRT$$

Where:

- π = osmotic pressure
- i = van't Hoff factor (number of particles formed per molecule)
- M = molar concentration
- R = ideal gas constant
- T = absolute temperature

Tonicity specifically refers to the effect of a solution on cell volume when the cell is placed in that solution. While osmolarity measures the total concentration of solute particles, tonicity considers only those solutes that cannot cross the cell membrane.

Physiological reference standards

The standard reference for isotonic solutions in pharmaceutical applications is:

- Blood serum: osmotic pressure equivalent to 0.9% w/v sodium chloride solution

- Tears: osmotic pressure equivalent to 0.9% w/v sodium chloride solution

- Intracellular fluid: varies but generally maintained at physiological osmolarity

Methods for calculating isotonic concentrations

Sodium chloride equivalent method

This method expresses the isotonic concentration in terms of the amount of sodium chloride that would produce the same osmotic effect. The sodium chloride equivalent (E) represents the amount of NaCl that is osmotically equivalent to 1 gram of the drug substance.

Calculation Formula: Amount of NaCl needed = 0.9% - (Drug concentration × E)

Example: For a 1% atropine sulfate solution:

- E value for atropine sulfate = 0.13

- NaCl needed = 0.9% - (1% × 0.13) = 0.9% - 0.13% = 0.77%

Freezing point depression method

This method utilizes the relationship between freezing point depression and osmotic pressure. The freezing point of blood serum (-0.52°C) serves as the reference standard.

Calculation:

- Determine the freezing point depression of the drug solution

- Calculate the additional depression needed to reach -0.52°C

- Add appropriate amount of sodium chloride to achieve this depression

Formula: $\Delta T_f = K_f \times m \times i$

Where:

- ΔT_f = freezing point depression

- K_f = freezing point depression constant for water (1.86°C·kg/mol)

- m = molality

- i = van't Hoff factor

Osmolality method

This method directly measures or calculates the osmolality of the solution and adjusts it to match physiological osmolality (approximately 285-295 mOsm/kg).

Calculation steps:

1. Calculate the osmolality contribution of the active ingredient
2. Determine the deficit to reach physiological osmolality
3. Add appropriate isotonic agent to make up the deficit

White-Vincent method

This graphical method uses isotonic solutions of various concentrations to determine the isotonic concentration of a drug substance through interpolation.

Procedure:

1. Prepare solutions of varying concentrations
2. Measure freezing points or osmotic pressures
3. Plot concentration vs. freezing point depression
4. Determine isotonic concentration by interpolation

Conclusion. Isotonic solutions are fundamental to safe and effective pharmaceutical therapy. Understanding the theoretical principles and practical calculation methods enables pharmaceutical scientists to develop formulations that are compatible with biological systems. The various calculation methods each have specific applications and advantages, and the choice of method depends on the specific formulation requirements, available data, and regulatory considerations.

The importance of isotonic solutions extends beyond basic pharmaceutical compatibility to encompass patient comfort, therapeutic efficacy, and safety. As pharmaceutical technology advances, the principles of isotonicity remain constant while the methods for achieving and validating isotonic solutions continue to evolve.

References

1. Sinko, P. J., & Singh, Y. (2020). *Martin's Physical Pharmacy and Pharmaceutical Sciences: Physical Chemical and Biopharmaceutical Principles in the Pharmaceutical Sciences* (8th ed.). Wolters Kluwer.
2. Florence, A. T., & Attwood, D. (2016). *Physicochemical Principles of Pharmacy: In Manufacture, Formulation and Clinical Use* (6th ed.). Pharmaceutical Press.
3. Aulton, M. E., & Taylor, K. M. G. (2017). *Aulton's Pharmaceutics: The Design and Manufacture of Medicines* (5th ed.). Elsevier.
4. Rawlins, E. A. (2007). *Bentley's Textbook of Pharmaceutics* (8th ed.). Elsevier Health Sciences.
5. Gennaro, A. R. (Ed.). (2020). *Remington: The Science and Practice of Pharmacy* (23rd ed.). Academic Press.

6. Banker, G. S., & Rhodes, C. T. (Eds.). (2017). *Modern Pharmaceutics* (4th ed.). CRC Press.
7. Swarbrick, J. (Ed.). (2019). *Encyclopedia of Pharmaceutical Science and Technology* (4th ed.). CRC Press.
8. Washington, N., Washington, C., & Wilson, C. G. (2021). *Physiological Pharmaceutics: Barriers to Drug Absorption* (3rd ed.). CRC Press.