



National university of Pharmacy Technology of drugs department



Discipline “Pharmacy-based technology of drugs”

The topic of the lecture :

ISOTONIC AND INFUSION SOLUTIONS. SOLUTIONS FOR INJECTIONS OF THERMOLABILE SUBSTANCES. SUSPENSIONS FOR INJECTIONS



a lecture for English students of 3rd course
in the speciality “Pharmacy” for foreign students

Lecturer: associate professor Yuryeva A.B.

Plan of the lecture

- 1. Classification of solutions for injections.**
- 2. Method of calculation of isotonic concentration.**
- 3. Formulation of isotonic solutions.**

QUESTIONS FOR SELF-STUDY

- 1. Principle of selection isotonic substances and general technological methods of preparation of isotonic solutions.**
- 2. Nomenclature of most frequently used plasma-replacing and antishock solutions in the form of ready medicinal forms.**

REFERENCES:

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2. Tikhonov A.I., Yarnykh T.G., Yuryeva A.B., Gaydukova Ye.A., Oleynik S.V., Kovalyova O.A. **Sterile medicines and medicines requiring aseptical conditions of preparation.** lectures for English students in the speciality “Pharmacy”/ edited by acad.A.I.Tikhonov. – Kh.: NUPh, 2010. – 164 p.
3. **Dry, liquid and soft medicinal forms.** A textbook for English students in speciality “Pharmacy” / A.I. Tikhonov, T.G. Yarnykh, A.B. Yuryeva, L.N. Podorozhna, S.S. Zuykina; Ed. by A.I. Tikhonov. – Kharkiv: NUPh; Original, 2011. – 208 p.
4. Tikhonov A.I., Yarnykh T.G., Yuryeva A.B., Podorozhna L.N., Zuykina S.S. **Biopharmaceutics.** Lectures for English students on the speciality “Pharmacy”: a handbook for the out-of-class work of students/ edited by acad. A.I. Tikhonov. – Kharkiv: NUPh, Original, 2011. – 140 p.

1. CLASSIFICATION OF SOLUTIONS FOR INJECTIONS

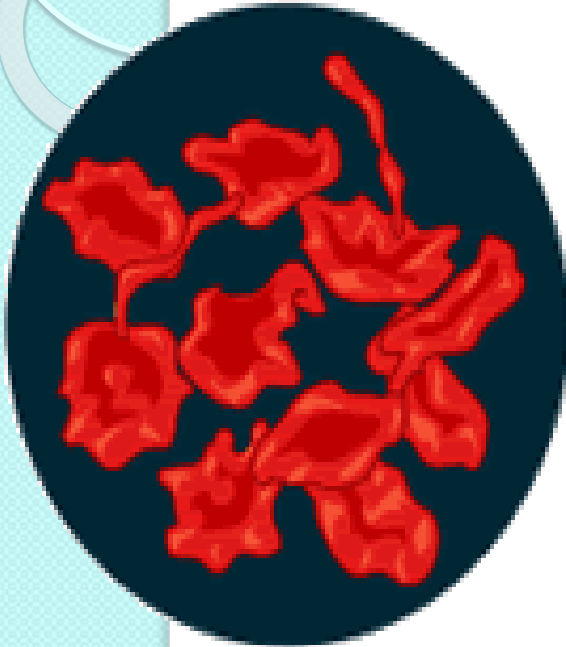
ISOTONIC SOLUTIONS

(from, Greek. isos – equal; tonus - pressure)

***Solutions, which has osmotic pressure equal to osmotic pressure of the body fluids (blood, plasma, lymph),
i.e. – 7.4 atm.***

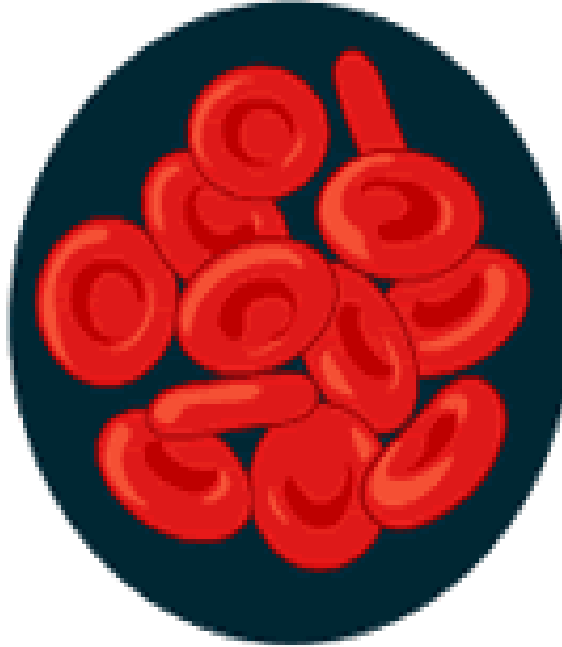
1. CLASSIFICATION OF SOLUTIONS FOR INJECTIONS

HYPOTONIC

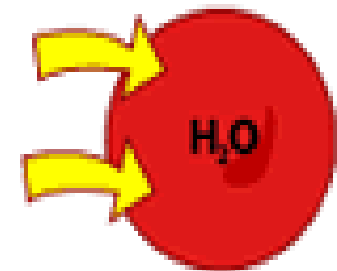
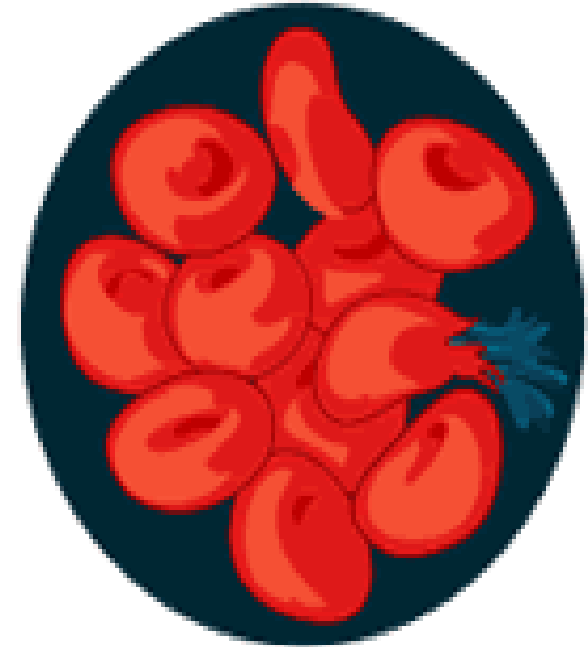


Hemolysis

ISOTONIC

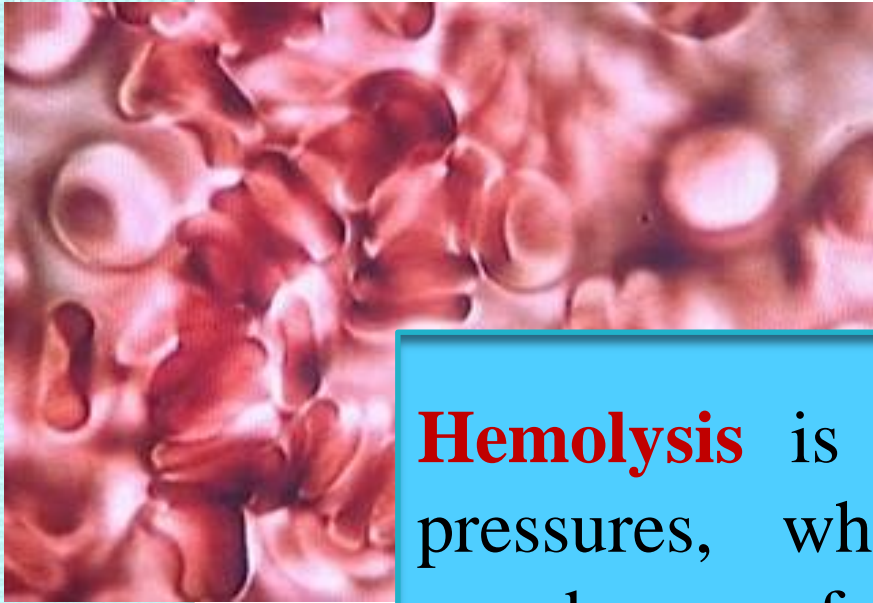


HYPERTONIC



Plasmolysis

1. CLASSIFICATION OF SOLUTIONS FOR INJECTIONS



HYPOTONIC SOLUTIONS

Hemolysis is a wide difference in osmotic pressures, which causes breaking of the membranes of erythrocytes.

When introducing liquid penetrates inside erythrocytes causing their swelling.

Hypotonic solutions are prepared only if it is indicated in the prescription by a doctor (in rare cases).

1. CLASSIFICATION OF SOLUTIONS FOR INJECTIONS



HYPERTONIC SOLUTIONS

Plasmolysis is the loss of shape by erythrocytes. When introducing water from the erythrocytes gets into the plasma before the osmotic pressure is equalized. Erythrocytes shrink.

Hypertonic solutions are prepared only if the exclamation mark in a prescription is present.

2. Methods of calculating the isotonic concentration of solutions

Methods of calculating the isotonic concentration of solutions

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graph TD; A[Methods of calculating the isotonic concentration of solutions] --> B[Based on the gas laws: using Van't Hoff, Avogadro, Gerhardt, on the Mendeleyev-Clapeyron equation]; A --> C[Pharmacopoeian method: using sodium chloride isotonic equivalents]; A --> D[Cryoscopic method: by the Raoult's law]; A --> E[Graphic methods];
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Based on the gas laws: using Van't Hoff, Avogadro, Gerhardt, on the Mendeleyev-Clapeyron equation

Pharmacopoeian method:
using sodium chloride isotonic equivalents

Cryoscopic method:
by the Raoult's law

Graphic methods

2. Methods of calculating the isotonic concentration of solutions

THE CALCULATION OF ISOTONIC CONCENTRATIONS OF SOLUTIONS FOR NON-ELECTROLYTES BASED ON THE GAS LAWS THE CALCULATION BY THE VAN'T-HOFF EQUATION

1 g/mol – at 0° C or 273 K and 1 atm occupies the volume of 22.4 l

The amount of water for dissolving 1 g/mol of a substance is:

$$22.4 / 7.4 = 3.03 \text{ l}$$

Correction to the temperature of the human body:

$$273 \text{ K} + 37 \text{ K} = 310 \text{ K}$$

$$273 \text{ K} - 3.03 \text{ l}$$

$$310 \text{ K} - x \text{ l} \qquad x = 3.44 \text{ l}$$

To prepare of 1 litre of the solution:

$$1 \text{ g/mol} - 3.44 \text{ l}$$

$$x \text{ g/mol} - 1 \text{ l} \qquad x = 0.29 \text{ g/mol}$$

$$m = 0.29xM$$

where:

m – is the mass of a substance, g;

0.29 – is the isotonicity factor of a non-electrolyte;

M – is the molecular weight of a substance.

2. Methods of calculating the isotonic concentration of solutions

THE CALCULATION OF ISOTONIC CONCENTRATIONS OF SOLUTIONS USING OF SODIUM CHLORIDE ISOTONIC EQUIVALENTS

Sodium chloride isotonic equivalent (E) – is the quantity of sodium chloride, which at equal conditions creates the osmotic pressure that is equal to the osmotic pressure created by 1.0 g of a medicinal substance.

2. Methods of calculating the isotonic concentration of solutions

***Advantages of the method
(it is the Pharmacopoeian method):***

- universal;
- accurate;
- the most frequently applied in the pharmacy practice.

2. Methods of calculating the isotonic concentration of solutions

THE CALCULATION OF ISOTONIC CONCENTRATIONS OF SOLUTIONS USING RAOULT'S LAW (Cryoscopic method)

Raoult's law

Pressure of vapour over the solution is proportional to the molar fraction of the dissolved substance

The conclusion from the Raoult's law:

decrease in the freezing temperature (depression) is proportional to the decrease in the vapour pressure and proportional to the concentration of the dissolved substance in the solution;

isotonic solutions of different substances freeze at the same temperature, i.e. have identical temperature depression of 0.52°C (depression of the blood serum).

2. Methods of calculating the isotonic concentration of solutions

Depression (decrease) in the freezing temperature point of 1 % solution of a medicinal substance (Δt) shows how many degrees the freezing temperature point 1 % solution of a medicinal substance decreases in comparison with the freezing temperature point of a solvent.

1. Formulation of isotonic solutions

Rp.: Sol. Glucosi 100 ml isotonicae

Sterilisa!

D. S. For intravenous introduction.

Doctor's seal

Doctor's signature

Control of isotonicity:

1) by sodium chloride **isotonic equivalent** of glucose:

$$E_{\text{glucose/NaCl}} = 0.18$$

sodium chloride isotonic concentration 0.9% (0.9 NaCl for 100ml)

$$0.18 \text{ NaCl} - 1.0 \text{ of glucose}$$

$$0.9 - x \quad x = 5.0$$

i.e. the isotonic concentration of glucose - **5 %** (5.0 glucose for 100 ml)

2) by the **Raoult's law**: isotonic concentration of glucose

$$1\% - 0.104^\circ\text{C}$$

$$x - 0.52^\circ\text{C} \quad x = \mathbf{5\%}$$

3) by the **van't-Hoff equation**: $m = 0.29 \times M$; $M = 180$

$$m = 0.29 \times 180 = 52 \text{ g/l}$$

i.e. the isotonic concentration of the glucose solution – **5.2%**

Calculations of the sodium chloride amount for isotonic solution preparation

Rp.: Sol. Glucosi 3% 100 ml isotonicae

Sterilisa!

D. S. For intravenous introduction.

Doctor's seal

Doctor's signature

WCP (RS)

Amount of NaCl for 100 ml 0.9

Amount of glucose for 100 ml 3.0

Sodium chloride isotonic equivalent of glucose:

$$E_{\text{glucose/NaCl}} = 0.18$$

1.0 of glucose – 0.18 NaCl

3.0 of glucose – x

$$x = 0.54$$

$$\text{Sodium chloride } 0.9 - 0.54 = 0.36$$

Calculations of the sodium chloride amount for isotonic solution preparation

Rp.: Sol. Glucosi 3% 100 ml isotonicae.

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WCP (RS)

Amount of NaCl for 100 ml 0.9

Amount of glucose for 100 ml 3.0

Isotonic concentration of glucose

1% – 0.104 °C

x – 0.52 °C

x = **5 %**

The volume isotonised by 3.0 g of glucose

5.0 – 100 ml

3.0 – x

x = 60 ml

The volume of water without isotonisation: 100 – 60 = 40 ml

Sodium chloride 0.9 – 100 ml

x – 40 ml

x = **0.36**

Technology

In aseptic conditions place 3.3 g of glucose (humidity 9 %) and 0.36 g of sodium chloride into a sterile 100 ml volumetric flask, add one part of water for injections and dissolve, then add 5 ml of the Weybel stabilizer, mix, and dilute with water for injections.

Perform the quantitative and qualitative analysis, filter the substance and cork with a rubber cap. After that check the presence of particulate matters, cork the bottle by aluminium cover and sterilize at 120°C for 8 minutes immediately after preparation.

After sterilization perform the secondary quality control.

Then register the medicine for dispensing by the number of prescription and labels «For injections» and «Sterile».



Conclusions:

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- 1. Classification of solutions for injections have been generalized.**
- 2. Method of calculation of isotonic concentration have been studied.**
- 3. Formulation of isotonic solutions has been generalized.**

**Thank you for your
attention!**

