NATIONAL UNIVERSITY OF PHARMACY
Technology of Drugs Department

Discipline “Pharmacy-based technology of drugs”

The topic of the lecture :

SOLUTIONS FOR INJECTIONS REQUIRING STABILIZATION

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

Lecturer: associate professor Yuryeva A.B.

THE PLAN OF THE LECTURES

- 1. Stability and its types
- 2. The methods of stabilization
- 3. Stabilizers
- 4. Stabilization of hydrolizable solutions
- 5. Stabilization of solutions of easily oxidizable substances
- 6. Characteristics of antioxidants

QUESTIONS FOR SELF-STUDY

1. Characteristics of stabilizers of used for preparation of injection solution
2. Classification of stabilizers
3. Antioxidants and their classification

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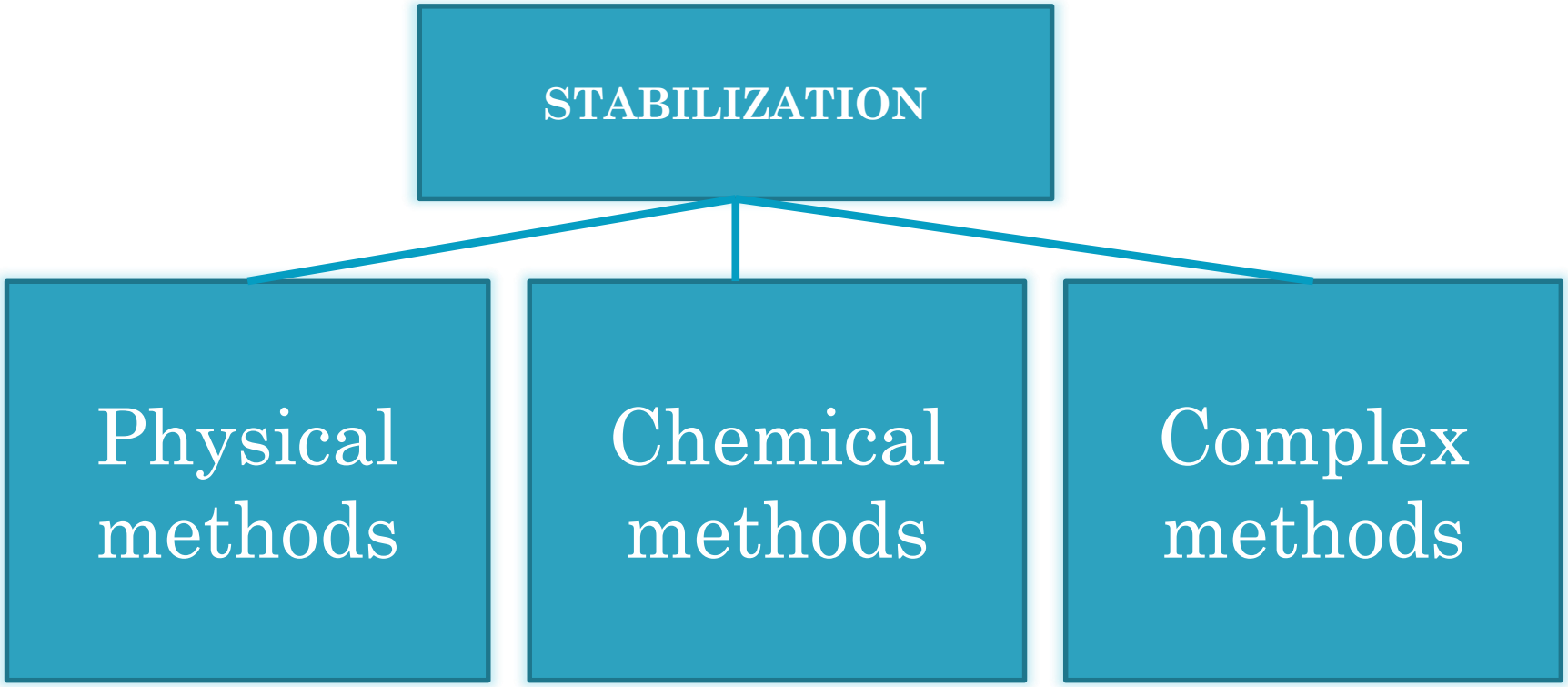
1. STABILITY AND ITS TYPES



1. STABILITY AND ITS TYPES

Stability is ability of medicines to preserve their physical and chemical properties and pharmacological activity during some definite term of their storage stipulated by the requirements of normative documentation.

Stability of medicines depends on:

- *temperature of storage;*
- *light intensity;*
- *environmental composition;*
- *method of preparation;*
- *auxiliary substances;*
- *type of medicinal form (especially the aggregate state);*
- *packing.*

2. THE METHODS OF STABILIZATION

- **PHYSICAL METHODS OF STABILIZATION**

  1. Protection of a medicinal substances from unfavorable effect of the environment

  2. Application of medicinal and auxiliary substances with a high degree of purification

  3. Application of modern technological

  4. Application of results of scientific research

2. THE METHODS OF STABILIZATION

CHEMICAL METHODS OF STABILIZATION

Chemical stability of solutions depends on:

- *properties of solvents and medicinal substances;*
- *class and sort of bottles glass;*
- *presence of oxygen in water and in solutions;*
- *pH of solutions;*
- *temperature and time of sterilization;*
- *presence of ions of heavy metals;*
- *terms of storage of medicines.*

2. THE METHODS OF STABILIZATION

CHEMICAL METHODS OF STABILIZATION

The choice of stabilizers depends on:

- *nature of medicinal substances;*
- *description of processes, which take place in the solutions*

Chemical methods involve the increase in the stability of medicinal substances and medicines on the whole by adding the substances – stabilizers.

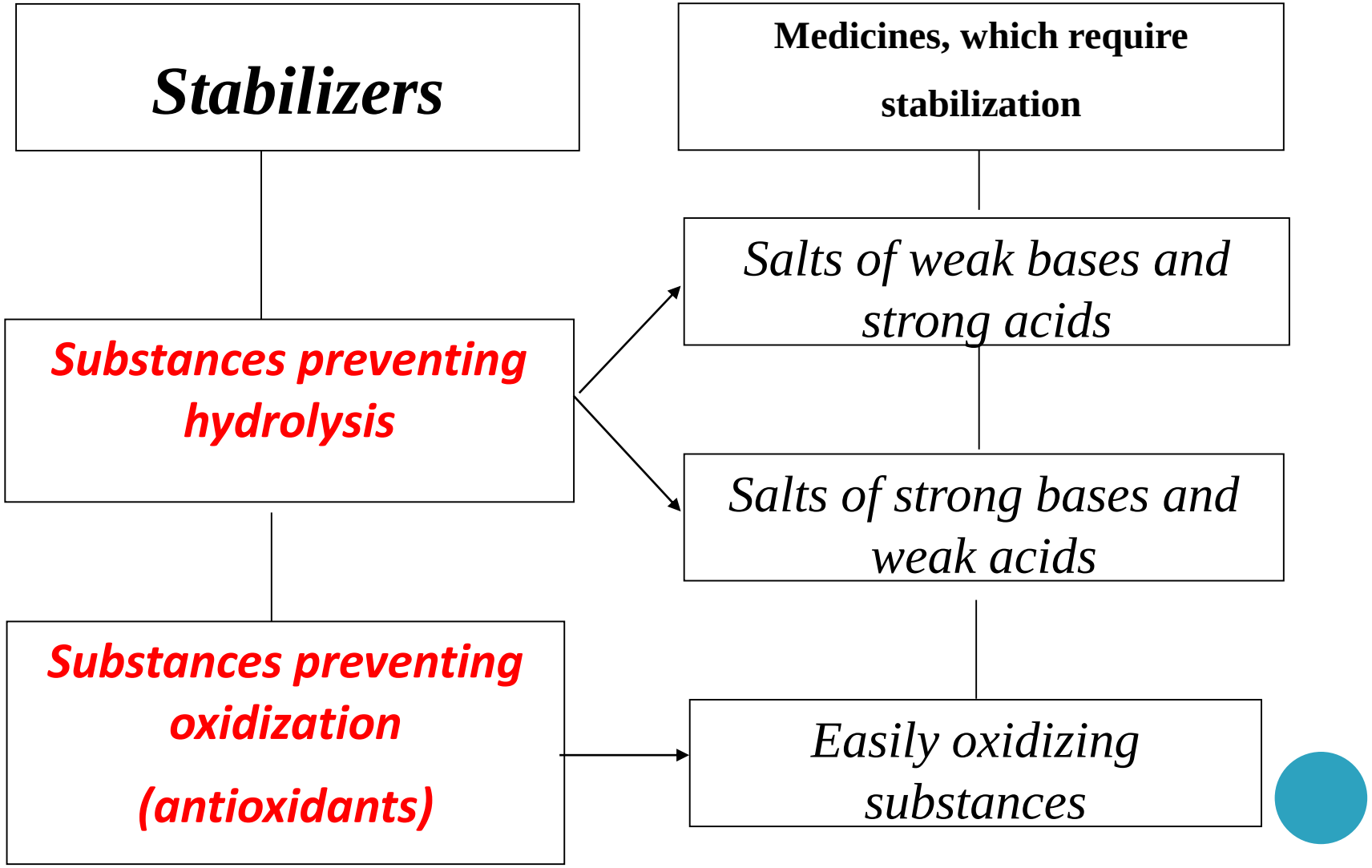
3. STABILIZERS

Stabilizers are the substances increasing chemical stability of medicinal substances in solutions for injections.

Requirements to a stabilizer:

- ***it must be safe for the patient both in its pure state and in combination with the components of medicines (pharmacological indifference);***
- ***it must be approved for application in medical practice;***
- ***it must be effective in the applied concentrations (to perform its functional purpose);***
- ***chemical purity;***
- ***availability.***

3. STABILIZERS



4. STABILIZATION OF HYDROLIZABLE SOLUTIONS

Hydrolysis is a reaction of ion exchange between different substances (salts, esters, etc.) and water

Salts of solutions of strong bases and weak acids are stable

When adding (as a stabilizer) sodium hydrocarbonate or 0.1 M sodium hydroxide solution

Solutions:

- ***Sodium thiosulphate;***
- ***Sodium caffeine benzoate;***
- ***Sodium nitrite.***

4. STABILIZATION OF HYDROLIZABLE SOLUTIONS

The solution of sodium caffeine benzoate is stabilized by 0.1 M sodium hydroxide solution in the amount of 4 ml per 1 litre of the solution

Rp.: Sol. Coffeini-Natrii benzoatis 10 % 50 ml
Sterilisa!
D. S. 2 ml 2 times a day.

WCP (reverse side)

Sodium caffeine benzoate:
10.0 / 2 = 5.0
0.1M sodium hydroxide solution
1000 ml – 4 ml
50 ml – X X = 0.2 ml
1 ml – 20 drops
0.2 ml – X X=4 drops
Water for injections up to 50 ml

WCP (front side)

Date № Pr.
Coffeini-Natrii benzoatis 5.0
Sol. Natrii hydroxydi 0.1M gtts. IV
(1 ml – 20 drops)
Aquae pro injectionibus ad 50 ml
V_{total}= 50 ml
Sterilis
Prepared by: (signature)
Checked by: (signature)

4. STABILIZATION OF HYDROLIZABLE SOLUTIONS

Solutions of the weak base salt and the strong acid are stable

<u>Without adding the stabilizers</u>

Solutions:

- Dimedrol
- Papaverine hydrochloride
- Trimecain
- Emetine hydrochloride
- Ephedrine hydrochloride

When adding 0.1 M hydrochloric acid solution

Solutions:

- Atropine sulphate
- Dibasol
- Dicain (0.1%; 0.2%; 0.3%)
- Novocain (0.25%; 0.5%; 1%; 2%)
- Scopolamine hydrobromide
- Spasmolithin
- Strychnine nitrate

When adding 0.1 M hydrochloric acid solution and antioxidants

Solutions:

- Apomorphine hydrochloride
- Novocain (5%; 10%)

4. STABILIZATION OF HYDROLIZABLE SOLUTIONS

Novocain solutions are stabilized by 0.1 M hydrochloric acid solution to adjust pH 3.8-4.5. The amount of it depends on the concentration of novocain in the solution.

The amount of 0.1 M hydrochloric acid solution per 1 litre of novocain solution for injections

Concentration of Novocain solution	*The volume of hydrochloric acid, ml*
0.25%	*3 ml*
0.5%	*4 ml*
1%	*9 ml*
2%	*12 ml*

5. STABILIZATION OF SOLUTIONS OF EASILY OXIDIZABLE SUBSTANCES

Oxidation of medicinal substances in the process of preparing solutions for injections takes place in the presence of oxygen contained in water and over the solution. The process of oxidization considerably strengthens under the influence of sensitizing factors:

- ***light;***
- ***warmth;***
- ***value of the pH medium, etc.***

5. STABILIZATION OF SOLUTIONS OF EASILY OXIDIZABLE SUBSTANCES

Antioxidants are auxiliary substances preventing oxidation; in pharmaceutical practice they are applied to stabilize solutions of easily oxidizable substances.

Requirements to antioxidants:

- harmlessness of both antioxidants and products of their metabolism, as well as ingredients formed in the doses applied (absence of non-irritating and allergic effect);
- efficiency at minimal concentrations;
- a good solubility in a dispersion medium.

5. STABILIZATION OF SOLUTIONS OF EASILY OXIDIZABLE SUBSTANCES

PECULIARITIES OF FORMULATION OF *SODIUM HYDROCARBONATE* SOLUTIONS FOR INJECTIONS:

- a substance with the mark «chemically pure», «pure for analysis», «suitable for injections» (amount of calcium and magnesium ions should be less than 0.05 %);
- dissolution is performed at of 15-20° C without shaking thoroughly;
- bottles are filled up to 2/3 of volumes (70 %);
- bottles are sterilized, when they are turned upside-down or when they are in the horizontal position;
- the medicine is used in 2-3 hours after complete cooling with shaking (to dissolve carbon dioxide, which is over the solution).

5. STABILIZATION OF SOLUTIONS OF EASILY OXIDIZABLE SUBSTANCES

GLUCOSE SOLUTIONS

- *Stabilization of glucose solutions is carried out by adjusting the solution, which consists of sodium chloride, hydrochloric acid and purified water (Weibel liquid), to pH 3.0 – 4.0.*

The content of Weibel liquid	
For volumes less than 1 liter (5 % of the volume of glucose solution)	**For volumes more than 1 liter** (per of the solution)
Sodium chloride 5.2 8.3 % hydrochloric acid 4.4 ml Water for injections up to 1 liter	Sodium chloride 0.26 hydrochloric acid 8.3% 5 ml

100 ml of 0.9% sodium chloride solution were prepared according to the prescription. What sterilization schedule is required for this solution?

A. 100 ºC – 15 min
B. 120 ºC – 12 min
C. 120 ºC – 15 min
D. 120 ºC – 30 min
E. 120 ºC – 8 min

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B. 120 ºC – 12 min
C. 120 ºC – 15 min
D. 120 ºC – 30 min
E. 120 ºC – 8 min

Explanation: according to the rules of sterilization, solutions of volume 1-100 ml are sterilized during 8 min (temperature 120ºC).

A chemist's shop produces solutions for injections which must be apyrogenic. Which solution can be depyrogenised by the method of adsorption with activated carbon?

A. Atropine sulphate
B. Glucose
C. Papaverine hydrochloride
D. Scopolamine hydrobromide
E. Platyphylline hydrotartrate

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Explanation: all other substances are absorbed on the surface of activated carbon.

A pharmacist needs to sterilize 250 ml of glucose solution for injections. During how many minutes should the solution undergo sterilization (autoclave, 120ºC)?

A. 25
B. 8
C. 15
D. 12
E. 30

A pharmacist needs to sterilize 250 ml of glucose solution for injections. During how many minutes should the solution undergo sterilization (autoclave, 120ºC)?

A. 25
B. 8
C. 15
D. 12
E. 30

Explanation: according to the rules of sterilization, solutions of volume 101-500 ml are sterilized during 8-12 min (temperature 120ºC).

An enema can be relieved by means of hypertonic solutions. What phenomenon takes place in the blood cells after injection of such solution?

A. Plasmolysis
B. Hydrolysis
C. Hemolysis
D. Lipolysis
E. Electrolysis

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E. Electrolysis

Explanation: water comes out of the cell in order to equalize the osmotic pressure → erythrocytes lose their shape (plasmolysis).

Conclusions

1. Stability and its types has been generalized
2. The methods of stabilization have been studied
3. Stabilizers and stabilization of hydrolizable solutions have been reviewed
5. Stabilization of solutions of easily oxidizable substances have been analyzed
6. Characteristics of antioxidants have been reviewed.

THANKS FOR ATENTION!