Ministry of Health of the Russian Federation

Volgograd State Medical University

Department of Pharmaceutical and Toxicological Chemistry

GENERAL PHARMACEUTICAL CHEMISTRY

Redox Titration.

Nitritometry.

Lesson 16

V term

Volgograd, 2022

QUESTIONS FOR THE LESSON

1. Essence of the method
2. Preparation and standardization of sodium nitrite working solution
3. Fixing the titration end point
4. Conditions for nitritometric titration
5. Applications in pharmaceutical analysis

ESSENCE OF THE METHOD

Nitritometry, or nitrite titration, is a method of quantitative determination of substances using a titrant $NaNO_2$ sodium nitrite solution.

The method is based on the use of an acidic reaction medium:

$$NO_2^- + \tilde{e} + 2H^+ \longrightarrow NO + H_2O$$

Since one electron is involved in the given oxidation-reduction half-reaction, the the equivalence factor of sodium nitrite is equal to one, the molar mass of the equivalent is equal to the molar mass, the molar concentration of the equivalent equals the molar concentration of sodium nitrite.

The method is based on

- oxidation-reduction reactions,
- diazotization,
- nitrosation,
- azation.

Sodium nitrite can exhibit the properties of oxidant and reducing agent.

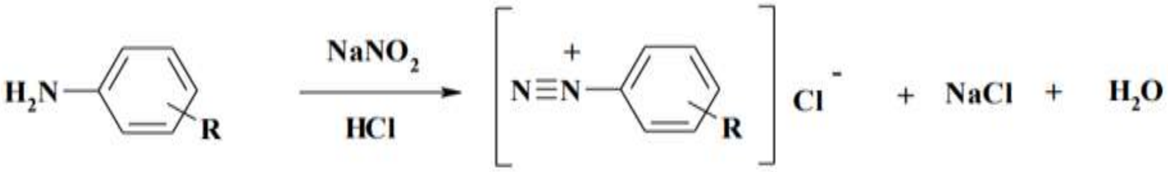
As an ***oxidising agent***, sodium nitrite is used for the determination of the reducing agents tin Sn^{2+}, iron Fe^{2+}, hydrazine and other compounds. At the same time the nitrite is reduced to nitric oxide:

$$HNO_2 + H^+ + \bar{e} \leftrightarrow NO + H_2O$$

As a ***reducing agent,*** sodium nitrite is used for the determination of potassium permanganate, chlorine, potassium iodate and other compounds by reaction:

$$HNO_2 + H_2O - 2\bar{e} \leftrightarrow NO_3^- + 3H^+$$

The most often used reaction is diazotation, which takes place with primary aromatic amines in an acidic medium:



PREPARATION AND STANDARDIZATION OF SODIUM NITRITE WORKING SOLUTION

The method titrant sodium nitrite ($NaNO_2$) is usually used as an aqueous solution with a concentration of 0.1 or 0.5 M.

The solution is prepared in an ***approximate concentration*** as sodium nitrite is unstable during storage and can oxidise to nitrate.

Standardisation of sodium nitrite is carried out according to the reaction that to be used for the determination.

If $NaNO_2$ is used

- as an oxidizing agent, it is standardized for iron(II), arsenic(III), hydrazine,
- as a reducing agent, it is standardized for potassium permanganate (secondary standard), potassium dichromate,
- in diazotization reactions, it is standardized for sulphanilic acid, p-minobenzoic acid, p-aminoethylbenzoate.

FIXING THE TITRATION END POINT

Instrumental method. The end of the titration in nitrite titration is most often recorded electrometrically by a potentiometric titration.

Indicators. In the indicator fixing of the titration end-point in nitrite titration, two groups of indicators are used two groups of indicators: *internal* and *external*.

Internal indicators. Redox indicators such as tropeolin 00 (colour change from red to yellow), its mixture with methylene blue (colour change from crimson to blue), neutral red (colour change from red-purple to blue) are used internally.

External indicators._ Starch-iodide paper is commonly used as an external indicator. It is a filter paper soaked in starch and potassium iodide solution and then dried.

The titration process is monitored by periodically taking a drop of the titrated solution and apply it to starch-iodide paper. Until the equivalence point is reached there is no oxidizing agent - nitrite ions - in the titrated solution. Therefore, when a drop of this solution is applied to starch-iodide paper, the iodide ions are not oxidized, no iodine is formed and the paper does not turn blue.

Once the equivalence point has been reached, the addition of one drop of the excess titrant already leads to the appearance of nitrite ions in the solution, so when a drop of this solution is applied to starch-iodide paper, the iodide ions are oxidized to iodine by the nitrite ions:

$$2I^- + 2NO_2^- + 4H^+ = I_2 + 2NO + 2H_2O$$

The iodine produced in the presence of starch turns the paper blue.

CONDITIONS FOR NITRITOMETRIC TITRATION

1. Titration is carried out in an acidic medium (usually HCl).
2. It is necessary to work at 15-20 °C (in some cases with cooling down to 0-5 °C). Because at higher temperatures the resulting reaction products (diazonium salts) may be destroyed, and at lower temperatures the interaction speed of the titrant with the substance to be determined may decrease.
3. The titrant must be added slowly because the reaction goes through several intermediate stages.
4. KBr catalyst is used to speed up the reaction.

APPLICATIONS IN PHARMACEUTICAL ANALYSIS

Nitritometric titration is used for the determination of

- inorganic substances (tin(II), arsenic (III), iron (II), hydrazine and its derivatives)
- organic compounds containing
  - ✓ a primary or secondary aromatic amino group,
  - ✓ aromatic nitro derivatives (after prior reduction of the nitro group to an amino group), and hydrazides.

Determination of iron (II) salts

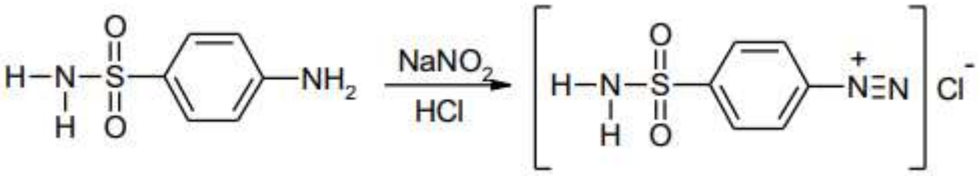
Thus, the nitritometric determination of iron (II) is based on reaction:

$$Fe^{2+} + NO_2^- + 2H^+ = Fe^{3+} + NO + H_2O$$

The titration is carried out in the presence of EDTA complexon, which binds the produced iron (III) into a stable complexonate, shifting the balance to the right and thereby increases the completeness of the reaction.

Determination of sulphonamide

The assay of sulphonamideis based upon the reaction:



The *titrant is sodium nitrite* (0.1 M solution). The sulphonylamide is titrated in the presence of KBr at 18-20°C or at 0-10°C. KBr catalyses the diazotization process and cooling of the reaction mixture avoids loss of nitric acid and prevents decomposition of the diazonium salt.

The point of equivalence can be established using

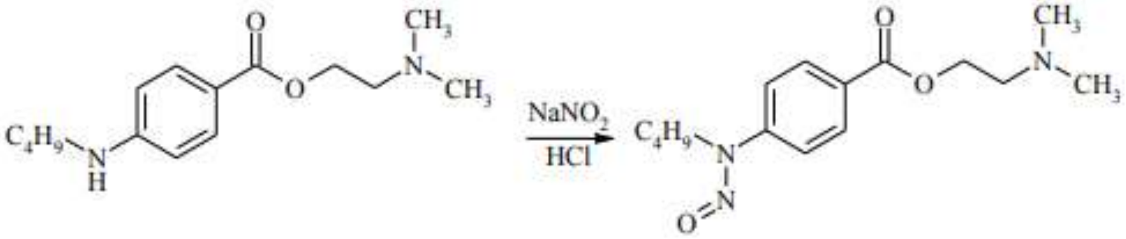
- an internal indicator (tropeolin 00);
- an external indicator (iodine starch paper)
- or potentiometrically.

Determination of Tetracaine

Titrant - 0.1 M sodium nitrite solution.

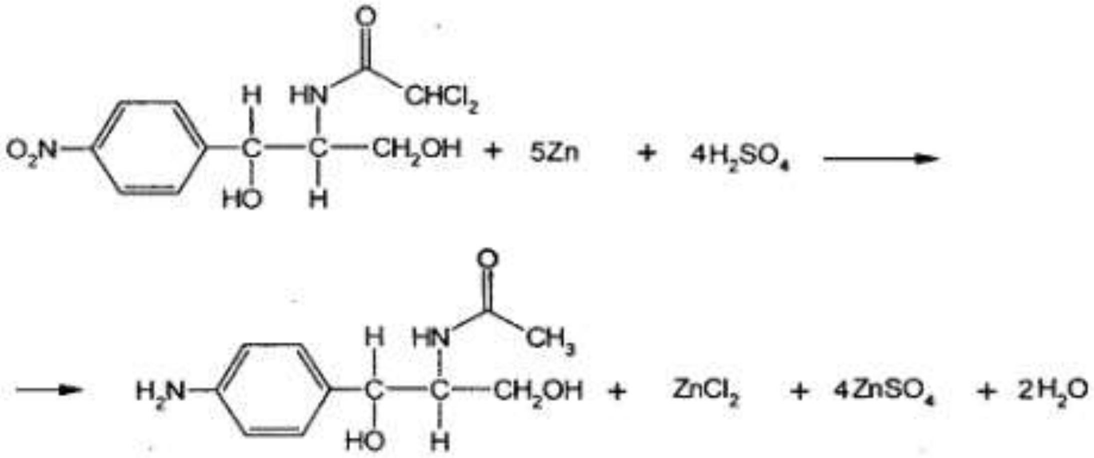
Equivalence point is determined by

- the indicator tropeolin 00
- or potentiometrically:



Determination of Chloramphenicol

For the nitritometric quantification of Chloramphenicol, the aromatic nitro group is hydrogenated prior to the process:



In the second step, *titrate with sodium nitrite*.

The end point of the titration is fixed with iodide-starch paper.