Ministry of Health of the Russian Federation

Volgograd State Medical University

Department of Pharmaceutical and Toxicological Chemistry

GENERAL PHARMACEUTICAL CHEMISTRY

Precipitation titration. Mercurimetry. Mercurometry.

Lesson 11

V term

Volgograd, 2022

QUESTIONS FOR THE LESSON

1. General description of the mercurimetric titration.
2. Mercurimetric titrants.
3. Indicators of mercurimetry.
4. Advantages and disadvantages of the mercurimetric method.
5. Application of Mercurimetry in pharmaceutical analysis.
6. Mercurometry.

MERCURIMETRIC TITRATION

GENERAL CHARACTERISTIC OF MERCURIMETRIC TITRATION

Mercurimetry is a titrimetric analysis method based on the formation of stable, weakly dissociating, soluble mercury (II) compounds - $HgCl_2$, $HgBr_2$, HgI_2, $Hg(CN)_2$, $Hg(SCN)_2$, which are present in solutions as complex compounds.

The method is used to determine the anions Cl^-, Br^-, CN^-, SCN^-.

During the reaction, stable complexes are formed, e.g:

$$Hg^{2+} + 2Cl^- = HgCl_2$$

$$Hg^{2+} + 4I^- = [HgI_4]^{2-}$$

$$Hg^{2+} + 2SCN^- = Hg(SCN)_2$$

TITRANTS OF THE MERCURIMETRIC METHOD

Titrants: standard solution of mercury (II) nitrate $Hg(NO_3)_2$ or mercury (II) perchlorate $Hg(ClO_4)_2$. Usually with a molar concentration of 0.05 mol/l.

The titrant solution is first prepared with an approximate concentration, and then standardized with standard solutions of NaCl or NH_4SCN in the presence of an indicator.

MERCURIMETRIC TITRATION INDICATORS

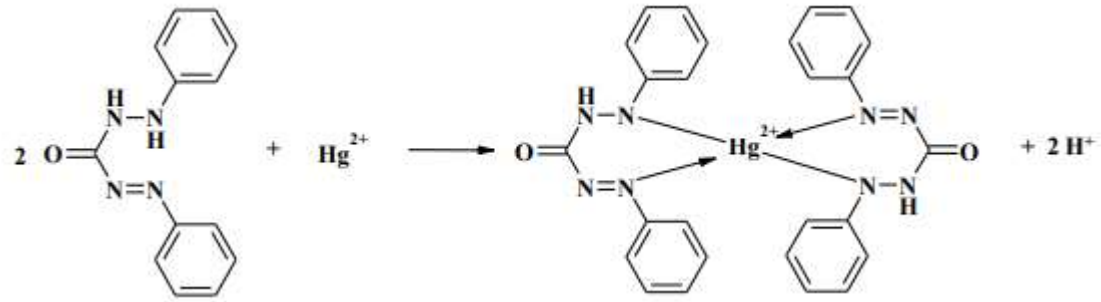
Sodium nitroprusside $Na_2[Fe(CN)_5NO]_*2H_2O$, diphenylcarbazone, diphenylcarbazide and some others are used as indicators in mercurimetry.

- **Sodium nitroprusside** forms a white precipitate with Hg^{2+} cations:

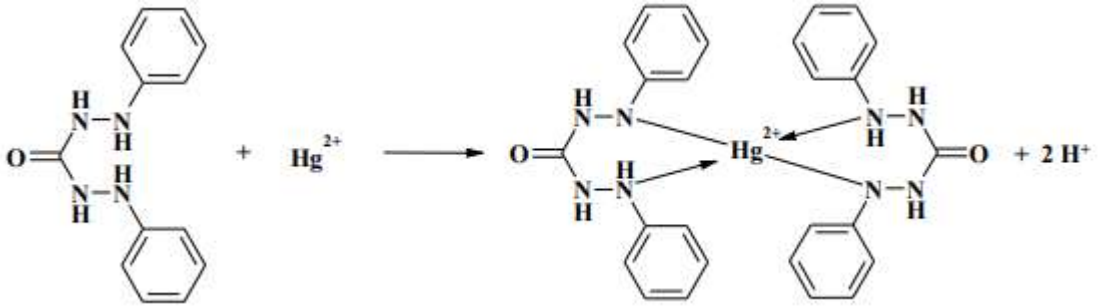
$$Hg^{2+} + [Fe(CN)_5NO]^{2-} + 2\ H_2O = Hg[Fe(CN)_5NO] \cdot 2\ H_2O$$

A white precipitate appears at the point of equivalence (the solution is turbid).

- **Diphenylcarbazone and diphenylcarbazide** form coloured complexes with Hg^{2+} ions. The titration is stopped when the solution turns <u>blue-violet</u>.



Diphenylcarbazone



Diphenylcarbazide

- In the determination of iodide ions a **nonindicator method** is used, the titration is carried out until the appearance of <u>pink turbidity</u>.

$$Hg^{2+} + 4\ I^- \rightleftharpoons [HgI_4]^{2-}$$

An excessive drop of mercury (II) nitrate solution reacts with the complex ion $[HgI_4]^{2-}$, releasing a pink-orange precipitate HgI_2:

$$[HgI_4]^{2-} + Hg^{2+} = 2\ HgI_2 \downarrow$$

When iodides are titrated in the presence of chlorides and bromides of organic compounds, the $K_2[HgJ_4]$ complex formed in titration can give precipitate reactions with many alkaloid and nitrogenous base salts containing tertiary or quaternary nitrogen.

ADVANTAGES AND DISADVANTAGES OF MERCURIMETRY

The method has a number of ***advantages***:

- ✓ allows a large group of anions, alkaloid halide salts and nitrogenous bases to be determined by direct titration in acidic medium;
- ✓ many ions do not interfere with determination;
- ✓ mercury (II) nitrate and perchlorate are less deficient than silver nitrate used for the same anions.

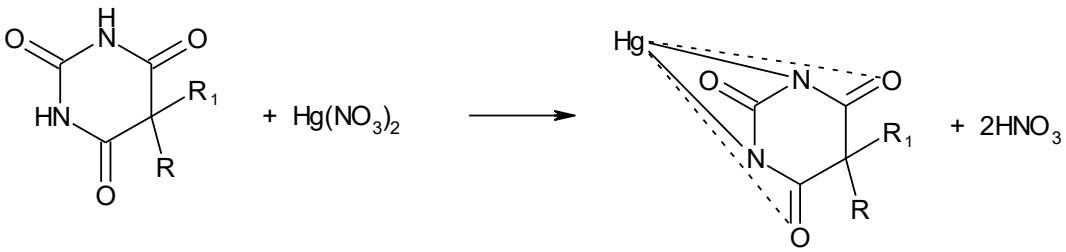
A ***disadvantage*** of the method is the high toxicity of mercury (II) compounds, so great care must be taken when working with them.

APPLICATIONS OF MERCURIMETRY IN PHARMACEUTICAL ANALYSIS

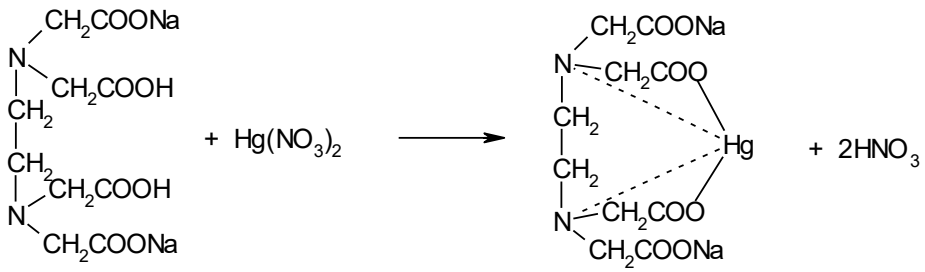
Example. Quantification of barbiburates

The reaction between barbituric acid derivatives and the mercury (II) ion, which produces water-insoluble compounds, is used for mercurimetric determination by combining it with complexometry.

Acidic forms of barbiturates are dissolved in ethanol. 10% sodium acetate solution and an excess of 0.1 M mercury (II) nitrate solution are added.



The precipitate of mercury(II) barbiturate is filtered off. And in the filtrate the excess of mercury (II) nitrate is titrated by the complexometric method (titrant Trilon B solution, xylenol orange indicator) in the presence of hexamethylentetramine.



The point of equivalence is determined by the colour change of the indicator.

FEATURES OF THE MERCURIMETRIC METHOD IN PHARMACEUTICAL ANALYSIS

- The titration of halides proceeds easily, but some nitrogen-containing compounds (antipyrine, dibasol, nicotinic acid) included in the mixtures give a precipitate reaction with mercury (II) ions and interfere with titration. Barbiturates and sulfonamides also form precipitates with mercury (II) salts, but by acidification with nitric acid titration is possible in their presence.
- Mercury (II) salts can be reduced to metallic mercury if strong reducing agents (ascorbic acid, sodium thiosulphate, sodium tetrathionate etc.) are included in the drug mixture. Therefore mercurimetric titration in their presence is not possible by common methods.
- Iodides may not be titrated without an indication in the presence of thiamine bromide, amidopyrine, antipyrine, atropine sulfate, dimedrol, novocaine, pilocarpine hydrochloride, morphine hydrochloride, dicaine, dibazole, theobromine, hexamethylentetramine and organic solvent preparations (ethyl alcohol and glycerol). In the presence of the last, a precipitate of mercury iodide (II) dissolves. Chloroform does not dissolve the precipitate and does not interfere with titration.

MERCUROMETRY

ESSENCE OF THE METHOD

The mercurometric method of analysis is based on the reaction of Halogenide ion precipitation by mercury (I) salts. The titrant of the method is 0.1M solution of $Hg_2(NO_3)_2$.

$$Hg_2^{2+} + 2Cl^- \longrightarrow Hg_2Cl_2$$

$$Hg_2^{2+} + 2Br^- \longrightarrow Hg_2Br_2$$

$$Hg_2^{2+} + 2I^- \longrightarrow Hg_2I_2$$

TITRANT, ITS PREPARATION AND STANDARDISATION

The titrant of the mercurometric method is a 0.1 mol/l solution of mercury (I) nitrate.

Mercury (I) nitrate is not a standard substance because the salt is hygroscopic, unstable and contains impurities of Hg^{2+}- ions. It is therefore used to prepare a ***secondary standard*** solution.

A calculated sample of $Hg_2(NO_3)_2{*}2H_2O$ is weighed on a technical scale, transferred to a measuring beaker, a solution of 2 mol/l nitric acid is added and heated until the sample is completely dissolved. To the resulting solution, 4-5 drops of metallic mercury are added. The prepared solution is kept over metallic mercury for at least one day, which leads to the reduction of Hg^{2+} -ions:

$$Hg^{2+} + Hg \longrightarrow Hg_2^{2+}$$

The obtained solution is then *standardised* with the standard substances *chemically pure NaCl or KCl* or with their standard solutions.

The concentration of the mercury (1) nitrate solution does not change for several months.

INDICATORS IN MERCUROMETRY

In the mercurometry method, the indicators used are

a) iron (III) thiocyanate solution [$Fe(CNS)_3$];
b) 1 % solution of diphenylcarbazone in 95 % alcohol.

When **iron (III) thiocyanate solution** [$Fe(CNS)_3$] is used, the titration end point is fixed by the *disappearance of the red colour* of the indicator.

The colour change is due to the interaction of one excess drop of titrant with the indicator solution:

$$3Hg_2^{2+} + 2[Fe(SCN)_3] \longrightarrow 3[Hg_2(NCS)_2] + 2Fe^{3+}$$

When titrating with this indicator it is necessary to carry out a control experiment to determine the amount of titrant consumed in the reaction with the indicator. For this purpose all reagents are added to 20-25 ml of purified water in the same quantities as for the sample analysis and titrated with a standard solution of mercury (I) nitrate. The resulting volume of titrant is subtracted from the volume used for the titration of the sample.

Diphenylcarbazone is one of the adsorption indicators. Its use is based on the fact that after complete precipitation of the halide ions the excess drop of titrant reacts with diphenylcarbazone. The result is a blue-violet colour at the titration end-point.

The indicator diphenylcarbazone has several advantages over iron (III) thiocyanate. It can be titrated in

- strongly acidic solutions,
- coloured and turbid solutions (due to the fact that the colour of the sediment or solution in the titration endpoint is very bright),
- the presence of peptising agents.

TITRATION CONDITIONS

1. The medium of the test solution must be acidic. For this purpose the solution is acidified with nitric acid to prevent hydrolysis of the titrant.
2. The titration should be carried out with vigorous stirring of the solution to reduce the error due to adsorption.
3. Determination is interfered with:
    a. sulphate ions - these must be eliminated by precipitating with excess barium nitrate;
    b. iron (III) ions - they are bound into strong complexes by adding excess F^- or PO_4^{3-} ions;
    c. dichromate and permanganate ions - they must be reduced in hydrogen peroxide;
    d. sulphite and sulphide ions should be oxidised with hydrogen peroxide beforehand.
4. Iodide ions cannot be determined by the mercurometric method, as the resulting Hg_2I_2 precipitate decomposes.

ADVANTAGES AND DISADVANTAGES OF MERCUROMETRY

The mercurometric method of analysis has ***advantage*s** over the argentometric method:

- Mercury (I) halides are less soluble than the corresponding silver salts, therefore the end-point of the titration in the mercurometric method is more clearly fixed;

- It excludes the use of expensive silver salts.

The main ***disadvantage*** of the mercury (I) method is that mercury (I) salts are poisonous! When working with them, the rules for working with poisonous substances must be followed.