«General pharmaceutical chemistry »

ARGENTOMETRY

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PRECIPITATION TITRATION

Precipitation titration is a group of titrimetric methods of analysis based on the formation of low solubility compounds that are released from solution as precipitate.

Requirements:

1. The precipitate must be practically insoluble, i.e. the solubility of the precipitate must not exceed 10^{-5} mol/l;
2. The precipitation shall be sufficiently rapid;
3. The titration results should not be distorted by adsorption (co-precipitation) phenomena;
4. It shall be possible to fix the point of

PRECIPITATION TITRATION

Classification of precipitation titration methods

According to the nature of the active reagent interacting with the substances to be determined:

- ✓ Argentometry ($AgN0_3$),
- ✓ Thiocyanatometry (KNCS or NH_4NCS),
- ✓ Mercurometry ($Hg_2(NO_3)_2$),
- ✓ Hexacyanoferratometry ($K_4[Fe(CN)_6]$)
- ✓ Sulfatometry (H_2S0_4)
- ✓ Barimetry ($BaC1_2$).

In terms of technique,

- ✓ direct,
- ✓ reverse titration.

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Argentometric titration is a titrimetric method of analysis based on the formation of low soluble silver compounds.

The argentometric titrimetric method of analysis is based on the use of a **standard solution of silver nitrate** as precipitant:

$$Ag^{+} + Hal^{-} \leftrightarrow AgHal\downarrow$$

A 0.1 mol/L standard solution of silver nitrate can be prepared:

- as a primary standard solution;
- secondary standard solution.

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Determining the titration endpoint

Indicator-free methods

Chloride ions are determined by the so-called **equal clouding method (Gay-Lussac method)**. In this method the analysed solution is titrated with a standard solution of silver nitrate, the end of the titration is determined by taking two samples of the titrated solution into two tubes near the titration endpoint:

- in one of them a drop of a standard solution of silver nitrate is added,

- in the other one a drop of a standard solution of sodium chloride of the same concentration.

The under-titrated solution shows clouding in the tube with silver nitrate, the over-titrated solution shows clouding in the tube with sodium chloride. At the final titration point, the solution in both tubes has the same turbidity.

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Determining the titration endpoint

Indicator-free methods

Bromide and iodide ions are determined by the method of enlightenment. Its essence lies in the fact that when small portions of a standard silver nitrate solution are added to the analyzed solution from the burette, a colloidal silver bromide solution is formed at the beginning, and at the moment of equivalence, colloidal particles coagulate and precipitate in the form of curd flakes, while the solution is clarified.

Of the modern Indicator-free methods in argentometry, **potentiometric determination** of the equivalence point using silver or halide-selective electrodes is most often used.

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Indicator methods

Depending on the indicator used in argentometry , the following methods are distinguished:

- Mohr method based on the reaction between silver ions and halide ions in the presence of an indicator – a solution of potassium chromate;
- Volhard's method (thiocyanatometry), based on the reaction between silver ions and thiocyanate ions in the presence of iron (III) ions as an indicator;
- Fajans method is based on the use of adsorption indicators.

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Mohr method

Sedimentary indicators are substances released from a solution in the form of a precipitate in a well-marked form at or near the equivalence point.

Direct titration

Titrant solution of 0.1 (or 0.05; 0.02; 0.01) mol/l silver nitrate

Indicator solution 0.01 mol/l of potassium chromate

$$Ag^+ + Hal^- \leftrightarrow AgHal\downarrow$$

$$Cl^- + Ag^+ \leftrightarrow AgCl\downarrow \quad \text{white}$$

$$Br^- + Ag^+ \leftrightarrow AgBr\downarrow \quad \text{yellowish white}$$

$$K_2CrO_4 + 2AgNO_3 = Ag_2CrO_4\downarrow + 2KNO_3$$

brick-red sediment

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Mohr method

Conditions of titration by the Mohr method:

1. Titration should be carried out in a neutral or slightly alkaline medium ($6.5 \leq pH \leq 10$).
2. The solution should be free of:
   a) Pb^{2+}, Ba^{2+}, Hg^{2+} cations and others forming chromate precipitates with indicator anions
   b) PO_4^{3-}, CO_3^{2-}, $C_2O_4^{2-}$, AsO_4^{3-} anions and others forming precipitates with silver ions.
3. Near the end point of titration, the solution must be titrated slowly, with vigorous stirring, in order to reduce the error due to adsorption.
4. It is impossible to titrate colored solutions,

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Mohr method

The Mohr method is applicable for the determination of chlorides and bromides, including pharmaceuticals, which include chloride and bromide ions.

The Mohr method **cannot be used** to determine:

- iodide and rhodanide ions due to their strong adsorption on the sediment surface;
- salts of hydrochloric acids and weak bases, since as a result of hydrolysis, an acidic medium is formed in their solutions;

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Mohr method

Application in pharmaceutical analysis

The Mohr method is mainly used for the quantification of sodium and potassium chlorides and bromides in neutral or weakly alkaline solutions.

The drugs **potassium chloride**, **sodium chloride**, **potassium bromide** and **sodium bromide** are titrated in a neutral medium, potassium chromate is used as an indicator.

$$NaCl + AgNO_3 \rightarrow AgCl\downarrow + NaNO_3$$

$$KCl + AgNO_3 \rightarrow AgCl\downarrow + KNO_3$$

$$NaBr + AgNO_3 \rightarrow AgBr\downarrow + NaNO_3$$

$$KBr + AgNO_3 \rightarrow AgBr\downarrow + KNO_3$$

The excess titrant (the first drop) interacts with the indicator to form an orange-red precipitate, according to which the end point of titration is set:

$$2AgNO_3 + K_2CrO_4 \rightarrow Ag_2CrO_4\downarrow + 2KNO_3$$

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Volhard's method

The Volhard's method is based on titration of a solution containing silver ions with **standard solutions** of NH_4NCS or $KNCS$:

$$Ag^+ + NCS^- \leftrightarrow AgNCS\downarrow$$

The indicator in this method is iron-ammonium alum $NH_4[Fe(SO_4)_2] \cdot 12H_2O$.

$$NH_4[Fe(SO_4)_2] + 3NH_4NCS \leftrightarrow Fe(NCS)_3 + 2(NH_4)_2SO_4$$

As standard solutions are used:

- in the method of direct titration – a solution of **ammonium thiocyanate or potassium thiocyanate**;
- in the reverse titration method – the solutions of **silver nitrate and ammonium or potassium thiocyanate.**

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Volhard's method

Preparation of NH_4NCS solution.

Ammonium thiocyanate is not a standard substance, since the salt is hygroscopic. Therefore, a solution of the required concentration is prepared from it – approximately 0.1 or 0.05 mol / l, and then it is standardized according to the standard substance $AgNO_3$ or according to the standard solution$AgNO_3$.

Conditions of titration by the Volhard'smethod:

1. Titration should be performed in an acidic environment to prevent hydrolysis of the indicator .
2. During titration, the solution must be vigorously mixed to reduce the error due to the adsorption of ions on the surface of the precipitate.
3. The analyzed solution should be free of:
   - mercury salts (I) and (II) reacting with NCS-ions:
   - oxidants $KBrO_3$, $KMnO_4$ and other oxidizing NCS-ions;
   - anions F^-, PO_4^{3-}, $C_2O_4^{2-}$ and others forming strong complexes with the indicator.

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Volhard's method

Determination of Ag+ ions by the Volhard's method (direct titration)

A standard solution of ammonium thiocyanate reacts primarily with silver ions, forming a unsolvable compound:

$$Ag^{+} + NH_4NCS \leftrightarrow AgNCS + NH_4^{+}$$

At the end point of titration, the excess titrant drop reacts with Fe^{3+} ions and turns the solution red:

$$NH_4[Fe(SO_4)_2] + 3NH_4NCS \leftrightarrow Fe(NCS)_3 + 2(NH_4)_2SO_4$$

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Volhard's method

Application of the Volhard's method (direct titration) in pharmaceutical analysis

Determination of silver cations in colloidal solutions (collargol and protargol). At the beginning, colloidal preparations are destroyed by boiling in a mixture of concentrated sulfuric and nitric acids. The resulting silver ions are then titrated with ammonium thiocyanate. Indicator iron-ammonium alum.

$$Ag^{+} + NH_4NCS \leftrightarrow AgNCS + NH_4^{+}$$

$$NH_4[Fe(SO_4)_2] + 3NH_4NCS \leftrightarrow Fe(NCS)_3 + 2(NH_4)_2SO_4$$

Collargol should contain at least 70% silver, and protargol — 7.5-8.5%.

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Volhard's method

Determination of anions by the Volhard's method (reverse titration)

Reverse titration is used to determine anions. To the analyzed solution, double the minimum, precisely measured volume of the **standard silver nitrate solution** (1st working solution) is added, which reacts with the determined anions, for example, chloride ions:

$$\mathbf{AgNO_3 + Cl^- \leftrightarrow AgCl\downarrow + NO_3^-}$$

The unreacted silver nitrate residue is titrated with a **second standard solution of ammonium thiocyanate**:

$$\mathbf{AgNO_3 + NH_4NCS \leftrightarrow AgNCS\downarrow + NH_4NO_3}$$

at the end of titration, an excess drop of NH_4NCS solution reacts with the indicator:

$$\mathbf{NH_4[Fe(SO_4)_2] + 3NH_4NCS \leftrightarrow Fe(NCS)_3 + 2(NH_4)_2SO_4}$$

and the solution turns red.

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Volhard's method

Advantages of the Volhard's method

In comparison with the Mohr method, the Folgard method has a number of advantages:

- ✓ the determination of Ag^{+}, Cl^{-}, Br^{-}, I^{-}, NCS^{-} is performed in an acidic medium;
- ✓ the cations Ba^{2+}, Pb^{2+} and others that interfere with the determination of anions by the Mohr method do not interfere with

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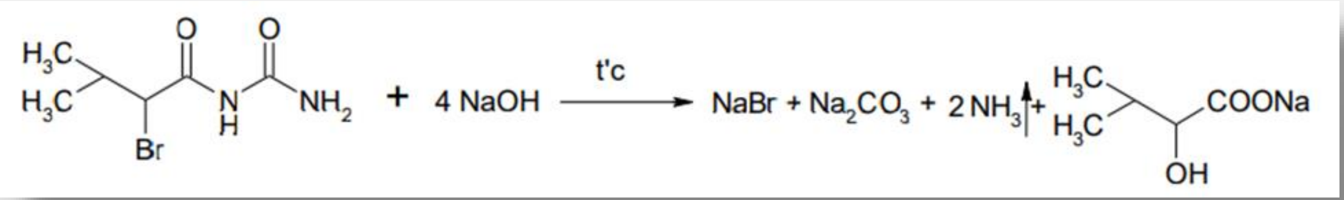
Volhard’s method

Application of the Volhard’s method (reverse titration) in pharmaceutical analysis



$$NaBr + AgNO_3 \rightarrow AgBr\downarrow + NaNO_3$$

$$AgNO_3 + NH_4SCN \rightarrow AgSCN\downarrow + NH_4NO_3$$

$$3NH_4SCN + FeNH_4(SO_4)_2 \rightarrow Fe(SCN)_3 + 2(NH_4)_2SO_4$$

Bromisoval

Titrant NH_4SCN

Indicator $NH_4[Fe(SO_4)_2]$

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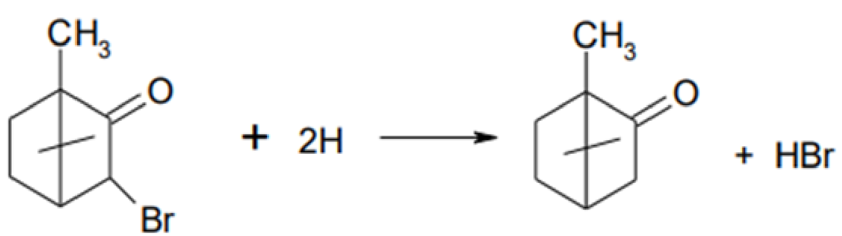
Volhard's method

Application of the Volhard's method (reverse titration) in pharmaceutical analysis

$$Zn + 2KOH + 2HOH \longrightarrow K_2[Zn(OH)_4] + 2H$$



$$HBr + KOH \longrightarrow KBr + HOH$$

$$KBr + AgNO_3 \longrightarrow KNO_3 + AgBr\downarrow$$

$$AgNO_3 + NH_4SCN \rightarrow AgSCN\downarrow + NH_4NO_3$$

$$3NH_4SCN + FeNH_4(SO_4)_2 \rightarrow Fe(SCN)_3 + 2(NH_4)_2SO_4$$

Bromcamphora

Titrant NH_4SCN

Indicator $NH_4[Fe(SO_4)_2]$

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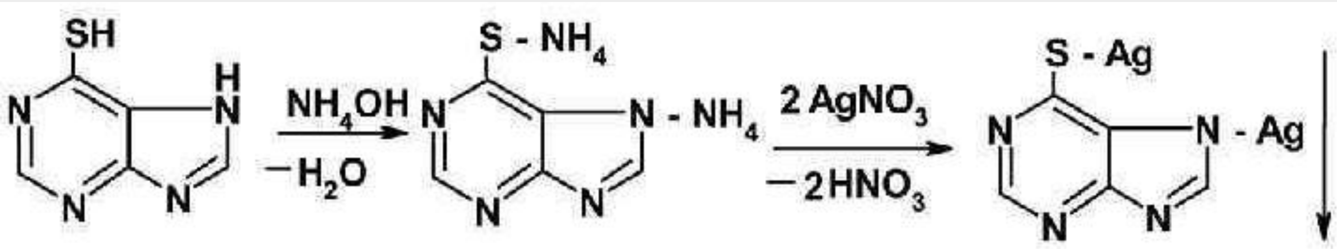
Volhard's method

Application of the Volhard's method (reverse titration) in pharmaceutical analysis



$$AgNO_3 + NH_4CNS \longrightarrow AgCNS + NH_4NO_3$$

$$3NH_4CNS + FeNH_4(SO_4)_2 \longrightarrow Fe(CNS)_3 + 2(NH_4)_2SO_4$$

Mercaptopurine

Titrant NH_4SCN

Indicator $NH_4[Fe(SO_4)_2]$

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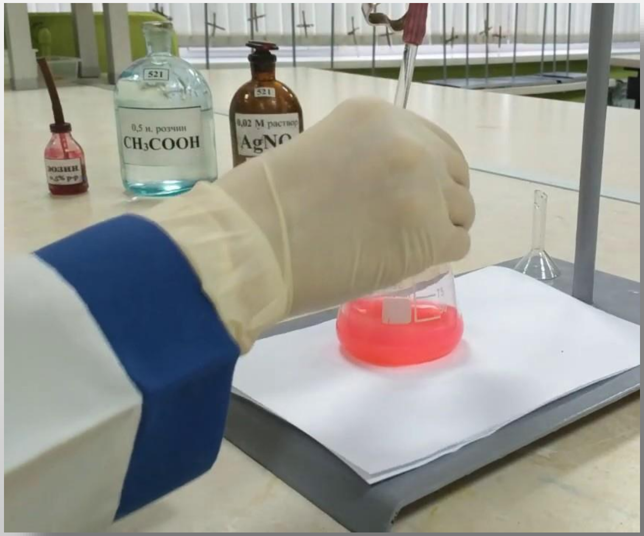
Fajans method

The Fajans method is based on **direct titration** of anions (halides, cyanides, thiocyanates) with a **standard silver nitrate solution** in the presence of **adsorption indicators.**



Silver halides are prone to the formation of colloidal solutions. In the presence of an excess of Hal ions due to the adsorption of AgHal particles acquire a negative charge:

$$nAgHal + Hal^- \rightarrow (AgHal)_n \cdot Hal^-$$

In the presence of an excess of Ag^+ ions, they acquire a positive charge:

$$nAgHal + Ag^+ \rightarrow (AgHal)_n \cdot Ag^+$$

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Fajans method

Adsorption indicators are substances whose adsorption or desorption by sediment is accompanied by a change in color at or near the equivalence point.

As adsorption indicators are used:

Bromophenol Blue

Sodium Eosinate

Fluorescein

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Fajans method

Conditions of titration by the Fajans method

1. **Titration should be performed at a certain pH value,** as this significantly affects the ionization of the indicator.
2. **Titration with an adsorption indicator should be carried out with a large sediment surface.** This is achieved when the precipitate is present in the form of colloidal particles. For this purpose, protective colloids are added to the titrated solution – dextrin, starch, etc.
3. **It is necessary that the indicator ions are adsorbed by the sediment much weaker than the ions being determined**, otherwise the indicator ions will be adsorbed much earlier than the moment of equivalence, which will lead to underestimated analysis results.
4. **Fluorescein** can be used in the determination of chlorides, bromides, iodides and rhodanides, **eosin** – only in the titration of bromides, iodides and rhodanides. Titration of chlorides in the presence of eosin does not give accurate results, since in this case the staining of the precipitate occurs before the end of the reaction.
5. **Titration cannot be carried out in direct sunlight**, since adsorbed indicators greatly increase the sensitivity of salts to light.

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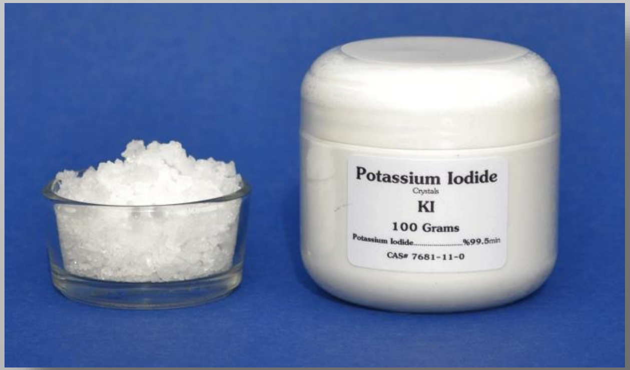
Fajans method

Application of the Fajans method in pharmaceutical analysis

$$KI + AgNO_3 \longrightarrow AgI\downarrow + KNO_3$$

$$NaI + AgNO_3 \longrightarrow AgI\downarrow + NaNO_3$$

$$[AgI \cdot I^-] \xrightarrow{Ag^+} [AgI \cdot Ag^+]$$



Potassium iodide
Sodium iodide
Titrant $AgNO_3$
Indicator Sodium Eosinate
Color transition **from yellow to pink**

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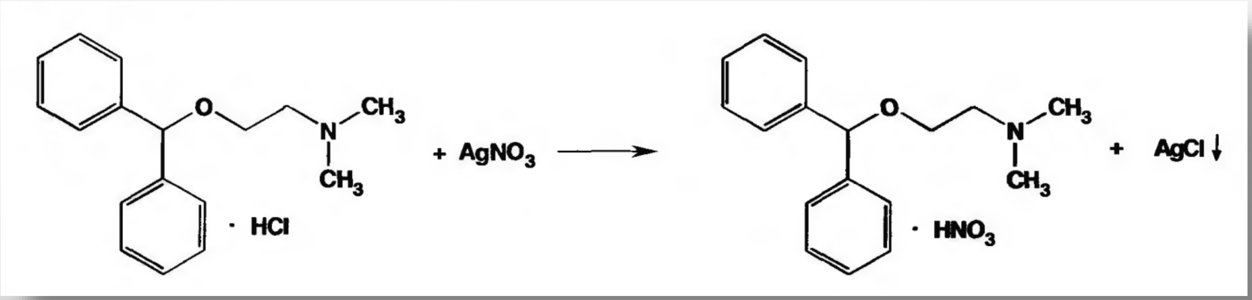
Fajans method

Application of the Fajans method in pharmaceutical analysis



Diphenhydramine
Titrant $AgNO_3$
Indicator Bromophenol Blue
Color transition **from greenish-yellow to purple**

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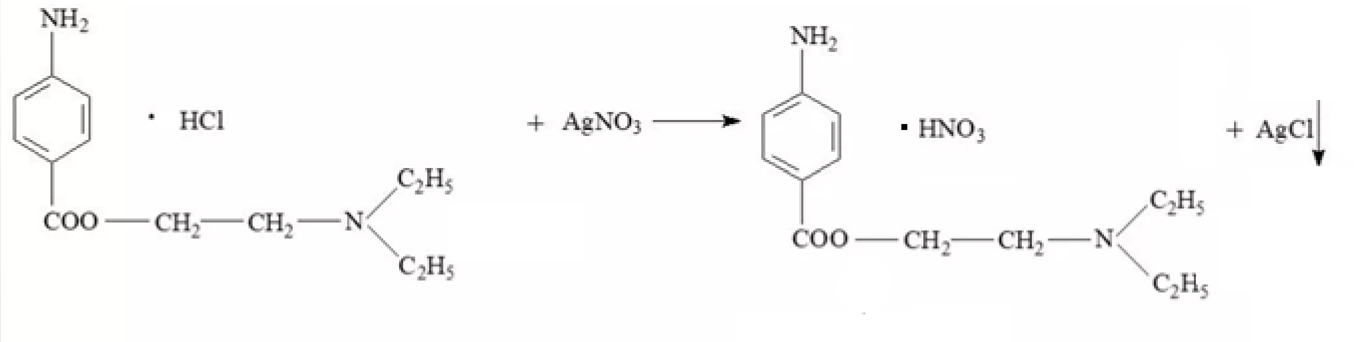
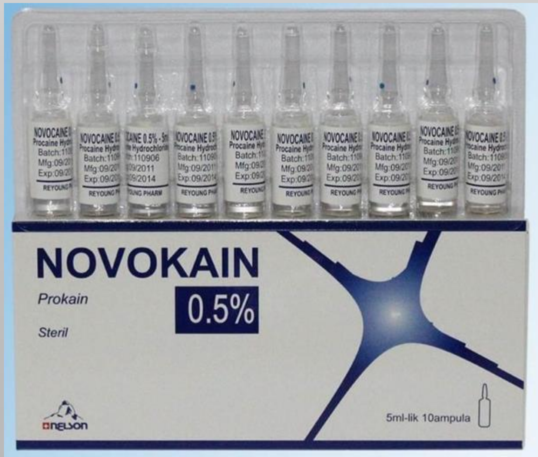
Fajans method

Application of the Fajans method in pharmaceutical analysis



Novocaine
Titrant $AgNO_3$
Indicator Bromophenol Blue
Color transition **from greenish-yellow to purple**



Thank you for attention!