Ministry of Health of the Russian Federation

Volgograd State Medical University

Department of Pharmaceutical and Toxicological Chemistry

GENERAL PHARMACEUTICAL CHEMISTRY

Redox Titration.

Iodometry.

Lesson 13

V term

Volgograd, 2022

QUESTIONS FOR THE LESSON

1. General characteristics of the iodometric titration method.
2. Standard solutions in iodometry.
   2.1 Preparation, stability and standardization of iodine solution.
   2.2 Preparation, stability and standardization of sodium thiosulphate solutions.
3. Fixing the titration end-point.
4. Conditions for iodometric titration.
5. Advantages and disadvantages of iodometry.
6. Application of iodometry in pharmaceutical analysis.

IODOMETRY

Iodometry is a redox titration method based on reactions involving oxidation of reducing agents by free iodine I2 or reduction of oxidants by potassium iodide KI. Both processes can be expressed by the following scheme:

$$I_2 + 2\bar{e} \leftrightarrow 2I^-$$

$$2I^- - 2\bar{e} \leftrightarrow I_2$$

The following iodometric titration methods are classified as follows.

1. **Direct titration** is used to determine substances which are easily oxidised by elemental iodine. The *titrant* is an *iodine* solution.
2. **Reverse titration** is used to determine substances which are more difficult to oxidize with elemental iodine. In this case the substance to be determined is treated with an excess of iodine and then, after some time, the iodine residue is *titrated* with a *standard solution of sodium thiosulphate* ($Na_2S_2O_3 \cdot 5H_2O$).
3. **Indirect method (substitution method)** is used for the determination of oxidants. In this case the sample is treated with excess potassium iodide and the equivalent amount of elemental iodine is *titrated* with a *standard solution of sodium thiosulphate*.

Preparation, stability and standardisation of iodine solution

Standard solutions of iodine can be prepared as a *primary standard*. Crystalline iodine is slowly dissolved in potassium iodide solution and then diluted to the desired volume.

Usually a solution of iodine of approximately the desired concentration (*secondary standard*) is prepared and then standardised with a suitable primary standard.

Iodine solutions are most commonly standardised with sodium thiosulphate or potassium tartrate. Iodine titration with sodium thiosulphate $Na_2S_2O_3 \cdot 5H_2O$ follows the equation of the reaction:

$$I_2 + 2Na_2S_2O_3 = 2NaI + Na_2S_4O_6$$

The ***stability*** of iodine solutions is low.

Reasons:

- ✓ Volatility of the dissolved substance
- ✓ Interaction with cortical or rubber plugs
- ✓ Oxidation of iodide ions by atmospheric oxygen

This reaction is accelerated in light, when heated and in the presence of acids. Consequently, it is advisable to keep the solution cold, in a dark place.

Preparation, stability and standardisation of sodium thiosulphate solutions

A solution of sodium thiosulphate pentahydrate is usually not prepared according to an exact weighing, as the crystalline hydrate can only be stored without decomposition under special conditions (e.g. over saturated CaCI2 solution).

Working solutions of sodium thiosulphate are prepared with approximate concentration from crystalline $Na_2S_2O_3 \cdot 5H_2O$ followed by setting the exact concentration.

Potassium bichromate $K_2Cr_2O_7$ is used for standardisation. First react potassium dichromate with potassium iodide

$$Cr_2O_7^{2-} + 6I^- + 14H^+ = 2Cr^{3+} + 3I_2 + 7H_2O.$$

The iodine released in an equivalent amount to the dichromate is then titrated with sodium thiosulphate solution:

$$I_2 + 2Na_2S_2O_3 = 2NaI + Na_2S_4O_6$$

Sodium thiosulphate solutions are stored in dark or orange vials in diffuse light or in the dark.

Fixing the titration end point

The indication-free method

In the direct method, in cases where iodine is the only coloured substance in the system, the appearance or disappearance of its own yellow-orange colour is a rather sensitive indication for establishing the titration end-point. In colourless solutions, an iodine concentration of 5 - 10^{-6} mol/l can be visually detected

Indicator

The most widely used indicator in both direct and indirect titration methods is a ***starch solution***.

For example, the end-point of titration with iodine solution is indicated by the blue colouring of the iodine-starch complex, while the disappearance of the blue colouring indicates that the end-point of titration in indirect iodometric methods has been reached.

In *direct* titration the titration end-point is indicated by the *blue colouring* of the iodine-starch complex.

In the *indirect* method the *disappearance of the blue colouring* indicates that the titration end-point has been reached.

Conditions for iodimetric titration

1. Titration with an iodine solution should be carried out in the cold to avoid iodine volatilisation.
2. Iodimetric titration is carried out in slightly acidic, neutral or very slightly alkaline solutions at pH < 8.

Advantages of iodometry

- ✓ Accuracy of determination
- ✓ Can also be carried out without an indicator
- ✓ The ability to titrate a wide range of compounds in non-aqueous media due to the good solubility of iodine in organic solvents.

Disadvantages of iodometry

1. The volatility of the iodine can lead to errors of determination. Therefore in indirect titration an excess of potassium iodide should be added and the titration flasks should be sealed with a stopper;
2. The need for titration in slightly acidic media
3. The titration cannot be carried out in alkaline media, as iodine is oxidised to hypoiodide ions;
4. Many reactions involving iodine or iodide ions are reversible and do not go through to completion, so special conditions must be created in these cases;
5. Adsorption of elemental iodine by the precipitation produced by the reaction;
6. Changes in the concentration of standard solutions during storage and use, requiring additional periodic standardisation of titrant solutions;
7. Strict adherence to the reagent discharge sequence.

Application of iodometry in pharmaceutical analysis

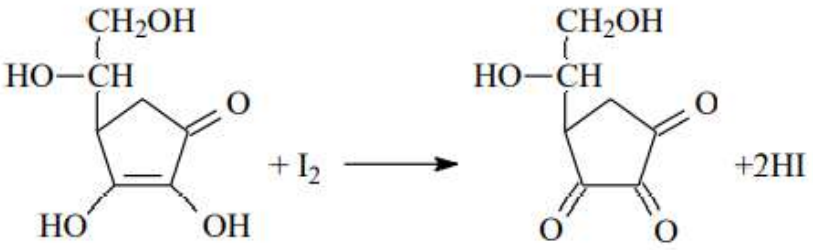
Iodometric titration has found a very wide application in pharmaceutical drug analysis.

Direct iodometry in acidic, neutral and alkaline media allows the determination of inorganic and organic pharmaceutical substances (sodium thiosulphate, ascorbic acid, aldehydes, sulphur-containing amino acids, sodium metamizole, etc.) by their oxidation reactions.

The determination of sodium thiosulphate is based on its direct titration with an iodine solution in a neutral medium in the presence of starch.

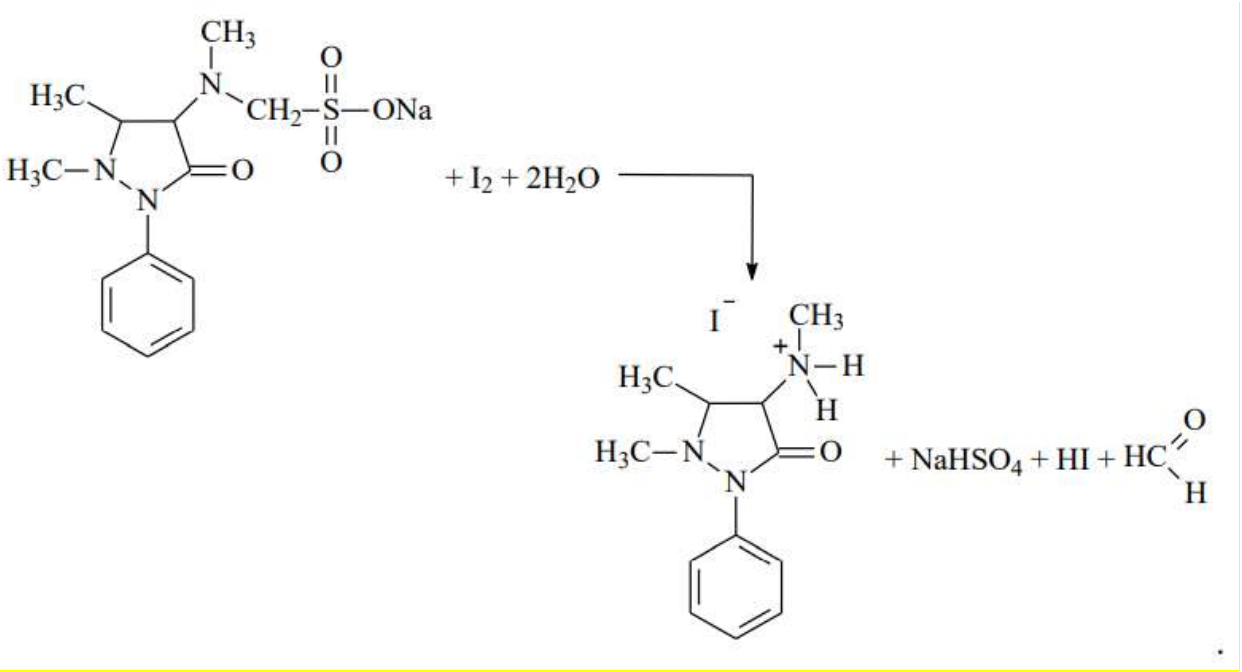
$$I_2 + 2Na_2S_2O_3 = 2NaI + Na_2S_4O_6$$

For the determination of ascorbic acid a direct titration in an acidic medium is used. This oxidises ascorbic acid to dehydroascorbic acid.



The titration end-point can be recorded both by the appearance of a light yellow colour from an excess drop of iodine solution and by the appearance of a blue colour in the presence of the starch indicator.

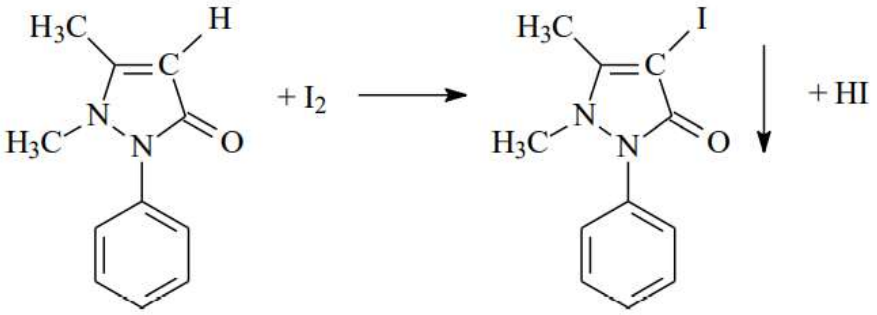
The quantification of sodium metamizole is based on its oxidation with iodine in a weakly acidic aqueous-alcoholic medium according to the scheme



The titration end-point is determined by the appearance of a yellow colour when an excessive drop of titrant is added.

Reverse titration

It should be noted that in some cases in ***the determination of organic substances*** by ***reverse titration*** other processes than the usual iodine oxidation take place. For example, the ***iodometric determination of antipyrine*** is based on the electrophilic replacement of the hydrogen atom in the cycle by an iodine atom.

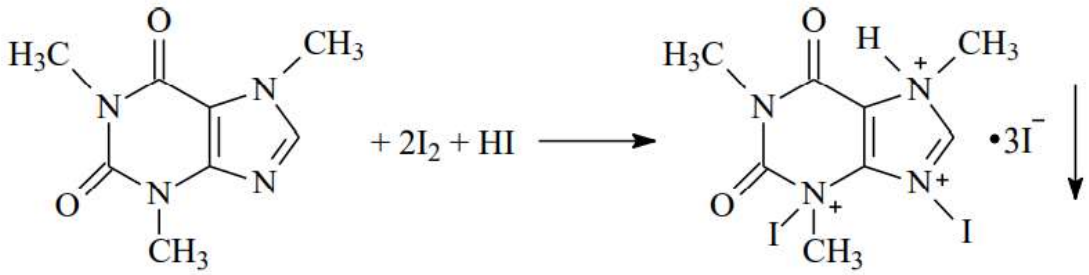


After performing this reaction, the residue I_2 that has not reacted is titrated with a sodium thiosulphate solution.

$$I_2 + 2Na_2S_2O_3 = 2NaI + Na_2S_4O_6$$

Resorcinol, salicylic acid, streptocid, etc. also interact by the electrophilic substitution mechanism. The number of hydrogen atoms substituted depends on the nature of the compound to be determined.

Caffeine and some other alkaloids as well as organic substances of cationic nature react with I_2 in the presence of iodide ions to form poorly soluble polyiodides. Determination is carried out in an acidic medium (most commonly in HCl or H_2SO_4).



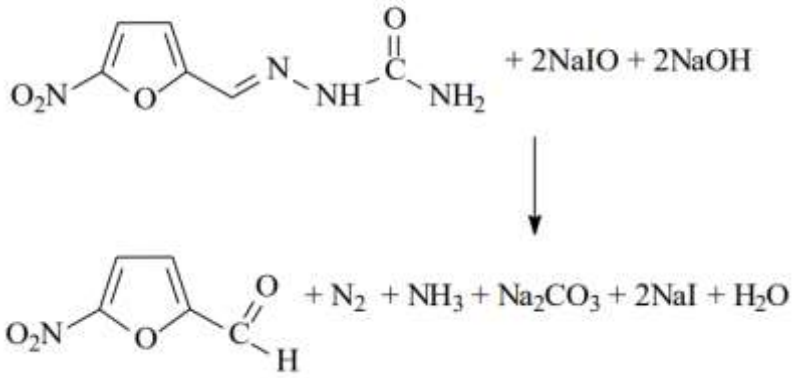
The precipitate formed is separated from the solution and the unreacted I2 is titrated in the filtrate.

$$I_2 + 2Na_2S_2O_3 = 2NaI + Na_2S_4O_6$$

This approach is used for the determination of dibasol, dimedrol, platyphylline hydrotartrate, scopolamine hydrobromide, hexamethylentetramine etc.

Indirect titration

When ***determining furacilin***, a sample of the drug is dissolved in purified water by heating the solution in a water bath at 70-80 °C until the drug is completely dissolved. The resulting solution is cooled, the volume brought to the mark with water and mixed thoroughly. The titration is then carried out by pipetting. Hypoiodide oxidises furacilin to 5-nitrofurfural.



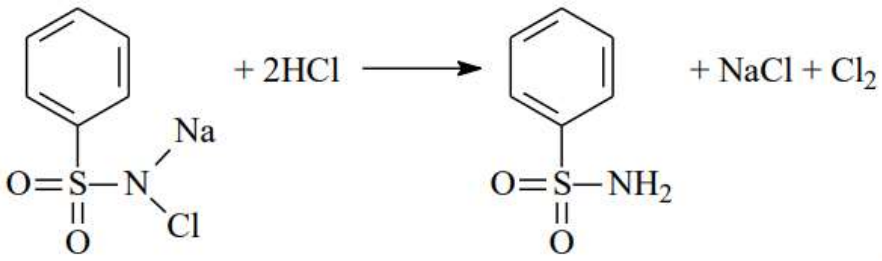
At the end of the oxidation process the solution is acidified with H_2SO_4 (1:5) and the released excess iodine is titrated with sodium thiosulphate in the presence of starch as indicator until the blue colour disappears.

$$NaI + NaIO + H_2SO_4 = I_2 + Na_2SO_4 + H_2O$$

$$I_2 + 2Na_2S_2O_3 = 2NaI + Na_2S_4O_6$$

Parallel control experiment with the same amounts of reagents in the absence of the drug substance is conducted. The concentration of furacilin is calculated from the difference of the titrant volume spent on the titration in the control experiment and in the presence of furacilin.

The determination of chloramine B is based on an iodometric titration of the chlorine released during its decomposition. The reaction is carried out in hydrochloric acid and chlorine is released.

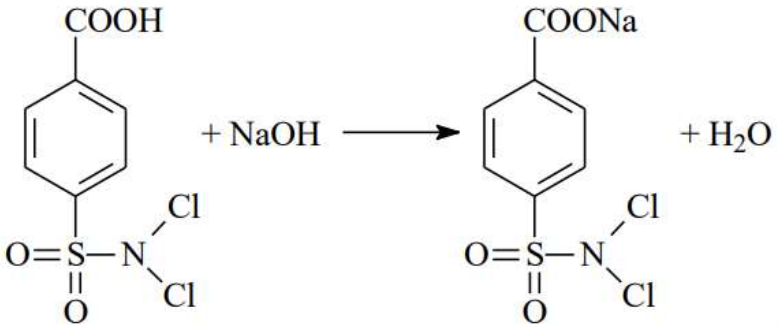


to which an excess of potassium iodide solution is added and the released iodine is titrated with sodium thiosulphate in the presence of starch.

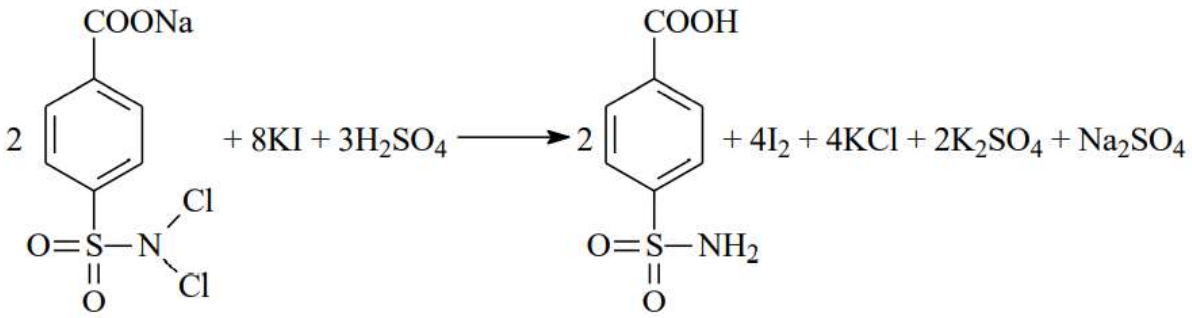
$$Cl_2 + 2KI \longrightarrow I_2 + 2KCl$$

$$I_2 + 2Na_2S_2O_3 \longrightarrow 2NaI + Na_2S_4O_6$$

For the determination of pantocide, it is dissolved in alkali



and then add potassium iodide in sulphuric acid medium



and titrate the released iodine with sodium thiosulphate solution in the presence of starch.

$$I_2 + 2Na_2S_2O_3 \longrightarrow 2NaI + Na_2S_4O_6$$

Iodometric titration is used to ***determine inorganic oxidants*** such as hydrogen peroxide, magnesium peroxide, copper sulphate.

Peroxide determination is carried out by adding potassium iodide to the test solution in acidic medium

$$H_2O_2 + 2KI + H_2SO_4 = I_2 + K_2SO_4 + 2H_2O$$

and titrating the released iodine with sodium thiosulphate solution in the presence of starch until the blue colour disappears.

$$I_2 + 2Na_2S_2O_3 = 2NaI + Na_2S_4O_6$$

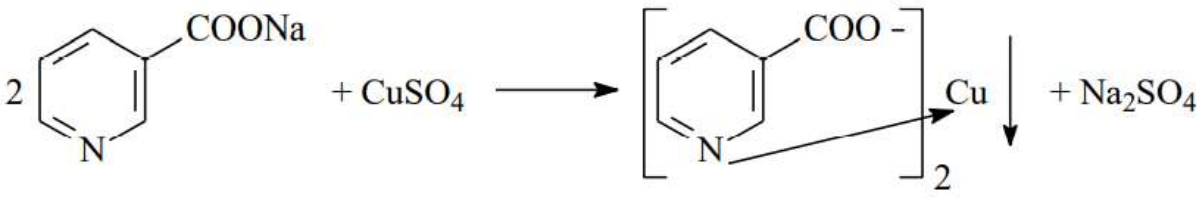
The determination of copper sulphate is based on the interaction of copper ions with potassium iodide.

$$2Cu^{2+} + 4I^- = 2CuI\downarrow + I_2$$

The released iodine is titrated with standard sodium thiosulphate solution in the presence of starch.

$$I_2 + 2Na_2S_2O_3 = 2NaI + Na_2S_4O_6$$

In some cases, organic substances that can interact with Cu^{2+} ions can be determined iodometrically. For example, ***nicotinic acid*** is converted to a sodium salt, which forms a poorly soluble complex compound with Cu^{2+} ions.



The excess Cu^{2+} is determined iodometrically. The indicator is starch.

$$2Cu^{2+} + 4I^- = 2CuI\downarrow + I_2$$

$$I_2 + 2Na_2S_2O_3 = 2NaI + Na_2S_4O_6$$