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# Photometric determination of Fe (III) with sulfosalicylic acid using the standard addition method in oral drops Ferropol

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**Abstract**

**Background**: Iron deficiency in the human body decreases the hemoglobin level and so iron deficiency anemia occurs. In this case, doctors recommend the use of medical preparations in different forms: solid or liquid.
**Material and methods**: In order to determine the quantity of Iron (III) in different medical preparations that contain Iron (III)-hydroxide polymaltose complex the analysis starts with the breakdown of the complex in acidic media. At the interaction of the mineral acids with Fe (III) hydroxide polymaltose complex during heating the brown color disappears and Fe (III) ions pass into the solution.
**Results**: It was shown that iron forms with sulfosalicylic acid a red-violet compound in acid media that absorbs light at a wavelength of 505 nanometers. The object of the study consists in the photometric method of the analysis of Fe in liquid forms, with the addition of sulfosalicylic acid using the standard addition method. Due to the fact that in a basic medium Fe (II) gently oxidizes to the Fe (III), then by the photometric method with sulfosalicylic acid it is quantitatively determined even Fe (III), as well as the summary content of Fe (II) and Fe (III) in the analyzed solution.
**Conclusions**: A new method of iron analysis was developed. It can be recommended to determine the iron in liquid medical preparations.
**Key words**: iron deficiency, photometric determination of iron, analysis of iron, quality assurance.

## Introduction

Iron is an important element of the human body. The deficiency of iron in the body decreases the hemoglobin level in the blood and causes iron-deficiency anemia. To combat this phenomenon doctors recommend the usage of medicinal preparations as active substance containing Fe (II) or Fe (III) in various forms: solid [1] or liquid [2]. In this case, the development of methods for the quality analysis of dosage forms of Fe remains quite actual.

Ferropol oral drops contain as active substance 50 mg/ml Fe (III) hydroxide with polymaltose, which is equivalent to 50 mg / ml of iron. The macromolecular compound of the Fe (III) is stable, it does not eliminate free iron ion form, by the structure it is similar to natural compounds of Fe. Due to this similarity, Fe (III) passes from the intestine into the blood only by the way of active absorption, which explains the impossibility of poisoning the preparation unlike simple salts of Fe, which absorption depends on concentration.

## Material and methods

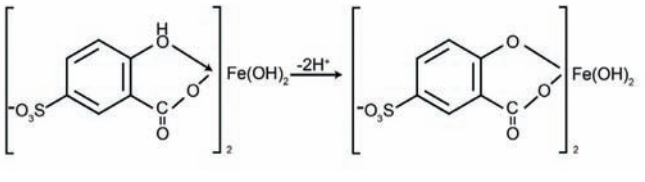
For the quantitative determination of Fe (III) in various liquid formulations (forms) which contain the complex compound of the Fe (III) hydroxide with polymaltose and have a dark brown color, firstly it is necessary to decompose this complex macromolecular compound in the acid medium [2]. At the interaction of the mineral acids with Fe (III) hydroxide polymaltose complex during heating the brown color disappears and Fe (III) ions pass into the solution.

Both, the absorption spectrum of the standard solution of Fe (III), as well as the spectrum of the test solution to Fe (III), obtained from the oral drops of Ferropol, with sulfosalicylic acid in an acid medium have been recorded using the spectrophotometer Agilent 5483. The absorption of test solutions was measured using photoelectric colorimeter KFK-2MP (КФК-2МП) at a wavelength of 490 nm, using the cells with absorption thickness layer of 1 cm. The pHs of the solutions were measured using laboratory ionomer I-160M (И-160М), using as an indicator electrode –the glass electrode.

## Results and discussion

The sulfosalicylic acid is an organic ligand, which is used for the photometric determination of iron in different stages of oxidation [3]. In the acid medium (pH 1.8 - 2.5) the solution forms a Fe (III) complex in ratio to metal: ligand is equal to 1: 1 red - violet absorbing electromagnetic radiation maximum at $\lambda$ = 505 nm [4, 5]. This complex compound is used in practice for the photometric determination of Fe (III) in the presence of Fe (II).

In a basic medium (9 <pH <11.5) Fe (III) with sulfosalicylic acid forms a complex compound of yellow color, which maximally absorbs electromagnetic radiation at $\lambda$ = 424 nm. Ratio metal: ligand complex is 1: 2 and actually it is supposed that in the basic medium occurs only the complex deprotonation [6]:




Due to the fact that in a basic medium Fe (II) gently oxidizes to the Fe (III), then by the photometric method with sulfosalicylic acid it is quantitatively determined even Fe (III), as well as the summary content of Fe (II) and Fe (III) in the analyzed solution [5, 7].

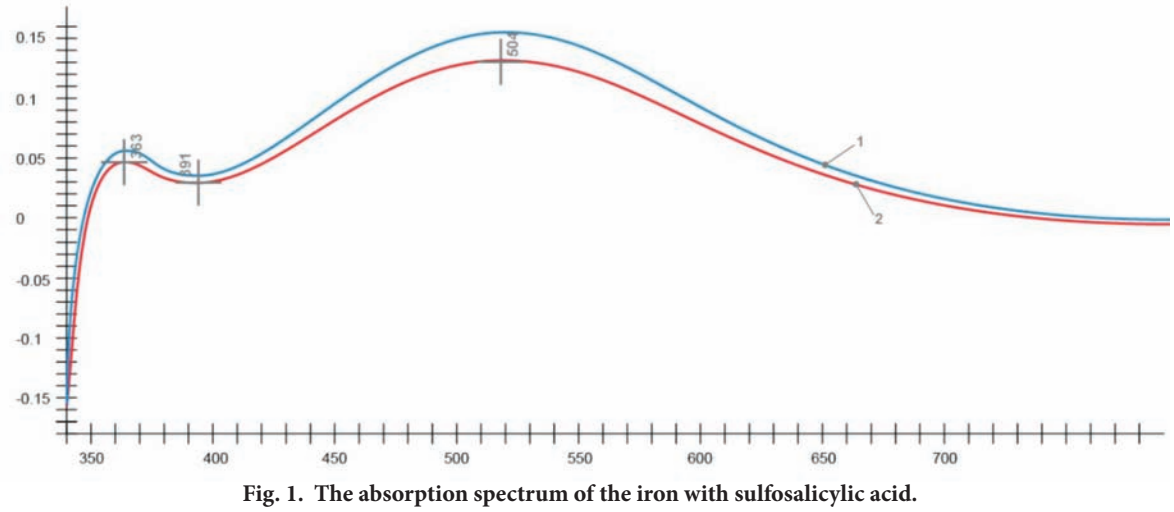



**Fig. 1. The absorption spectrum of the iron with sulfosalicylic acid.**

In this work, we have studied the possibility of photometric determination of Fe (III) in the oral drops Ferropol by standard addition method.

**Preparation of standard solution of Fe (III)**. In this study is used the double salt $(NH_4)2SO_4 \cdot 6H_2O \cdot FeSO_4$ – commonly named as „Mohr salt", which was recrystallized from distilled water. A sample of this salt with a weight of 0.17553g was passed quantitatively into a volumetric flask with the capacity of 500 ml, it was dissolved in distilled water, acidified by 0.5 ml of concentrated $HNO_3$ and the solution was heated on the electric hob until boiling. After cooling the solution was acidified by 3 ml of 1M $H_2SO_4$, diluted with distilled water till mark and was homogenized. The molar concentration of the standard solution was equal to $4.4762 \cdot 10^{-4}$ mol / l and the content of Fe (III) in it was equal to 0.05 mg / ml.

The solution with sulfosalicylic acid of 10% was prepared from the reagent $C_6H_6O_6S \cdot 2H_2O$ and it was filtered after the preparation.

**Preparation of sample for analysis**. Firstly, was established the exact mass of vial with cap. Then with automatic dosing pipette brand DACpette were measured and passed 200 µl of Ferropol oral drops into vial and it was exactly weighed. Then the content of the vial has been quantitatively moved into a volumetric flask with the capacity of 200 ml. Then were added 5 ml of 1M $H_2SO_4$ . It was placed in a water bath at 100°C, where hydrolyzation of Fe (III) polymaltose complex took place and 2 minutes after the brown color of the solution completely disappeared. After cooling the solution was diluted till mark with distilled water and homogenized.

In some flasks with the capacity of 50 ml was added the same volume of the initial test solution of Ferropol oral drops (2.0 ml). Starting from the second flask in each flask were added various volumes of the standard solution of Fe (III) as shown in table 1. Then in all flasks were added 5 ml of sulfosalicylic acid, the solutions were diluted up to the mark with distilled water, then homogenized and left to stand for 10 minutes.

In parallel in a volumetric flask with the capacity of 50 ml there were added 5 ml of sulfosalicylic acid and the volume was made up to the mark with distilled water (Solution for comparison).

The preventive experiments showed that the absorption spectrum of the solution to be analyzed of Fe (III), obtained from the oral drops of Ferropol, with sulfosalicylic acid is similar to the absorption spectrum of a standard solution of Fe (III) with this ligand in the acid medium and maximally absorbs the electromagnetic radiation in the visible region of the electromagnetic spectrum at a wavelength of 504 nm (fig. 1).

The spectrophotometric standard addition method is a modification of the method of the comparison and in practice it is used to determine the unknown concentration or the mass of the substance by the calculation method or graphics.

By the method of calculating the two absorbances are compared between the two of them: the first $A_x$ – absorbance of a solution which only contains the analyte with the unknown mass mx, and the second $A_{x+a}$ – absorbance of the solution which contains the same known mass mx of the substance to be analyzed, and further addition of the standard solution with ma mass.

If these two solutions are prepared in two flasks of equal capacity, then comparing the absorbances easily results the relation to calculate the unknown mass m x Fe (III) in the solution to be analyzed of Ferropol oral drops, to which are measured the absorbances $A_x$ and $A_{x+a}$

$$m_x = \frac{A_x}{A_{x+a} - A_x} \cdot m_a \quad (1)$$

The addition mass ($m_a$, mg) in the solution where the absorbance $A_{x+a}$ was measured was calculated according to the relation:

$$m_a = m_i \cdot V_i, \quad (2)$$

where:

$m_i$ – the content of iron in a ml of the initial standard solution of the Fe (III), mg / ml;

$V_i$ – the volume of the initial standard solution of Fe (III) which was added, ml.

The mass of Fe (III) ($m_{Fe}$, mg) in the initial solution of oral drops Ferropol was calculated by the equation:

$$m_{Fe} = m_x \cdot \frac{V_0}{V_1}, \quad (3)$$

in which:

$V_0$ – the capacity of the flask with initial solution of Ferropol oral drops, ml;

$V_1$ – fraction of the initial solution of Ferropol oral drops, which has been taken for the preparation of the two solutions, with the absorbances of $A_x$ and $A_{x+a}$, ml.

By combining the equations (1), (2) and (3), we obtain the relation to calculate the mass of Fe (III) ($m_{Fe}$, Mg) in the initial solution of oral drops of Ferropol:

$$m_{Fe} = \frac{A_x \cdot m_i \cdot V_i \cdot V_0}{(A_{x+a} - A_x) \cdot V_1}, \quad (4)$$

all the notes see above.

In the pharmaceutical liquid forms content of the active substance is usually expressed in mg/ml. In its turn the volume (V) of the liquid of the pharmaceutical form is connected to the mass and its density by the equation:

$$V = \frac{m_p}{\rho} \quad (5)$$

where:

$m_p$ – The mass of the liquid pharmaceutical sample, g;

ρ – density of liquid form, g/ml.

Introducing the equation (5) in the relation (4) we obtain the final formula to calculate the mass of Fe (III) in the oral drops of Ferropol (m Fe, mg/ml):

$$m_{Fe} = \frac{A_x \cdot m_i \cdot V_i \cdot V_0 \cdot \rho}{(A_{x+a} - A_x) \cdot V_1 \cdot m_p}, \quad (6)$$

all the notes see above.

**Table 1**

**Data for the determination of Fe (III) with sulfosalicylic acid in the acid media of the oral drops Ferropol by the photometric method of standard addition**

| No | V1, ml | Vi, ml | ma, mg | pH | Ax și Ax+a | mFe , mg/ml |
|---|---|---|---|---|---|---|
| 1 | 2,0 | - | - | 2,07 | 0,067 | - |
| 2 | 2,0 | 1,0 | 0,050 | 2,04 | 0,101 | 49,26 |
| 3 | 2,0 | 1,5 | 0,075 | 2,03 | 0,118 | 49,26 |
| 4 | 2,0 | 2,0 | 0,100 | 2,01 | 0,134 | 50,00 |
| 5 | 2,0 | 2,5 | 0,125 | 2,00 | 0,149 | 51,07 |
| 6 | 2,0 | 3,0 | 0,150 | 1,99 | 0,167 | 50,25 |

($V_0$= 200 ml; $m_i$=0,05 mg/ml; $m_p$=0,2272 g; ρ=1,136 g/ml)

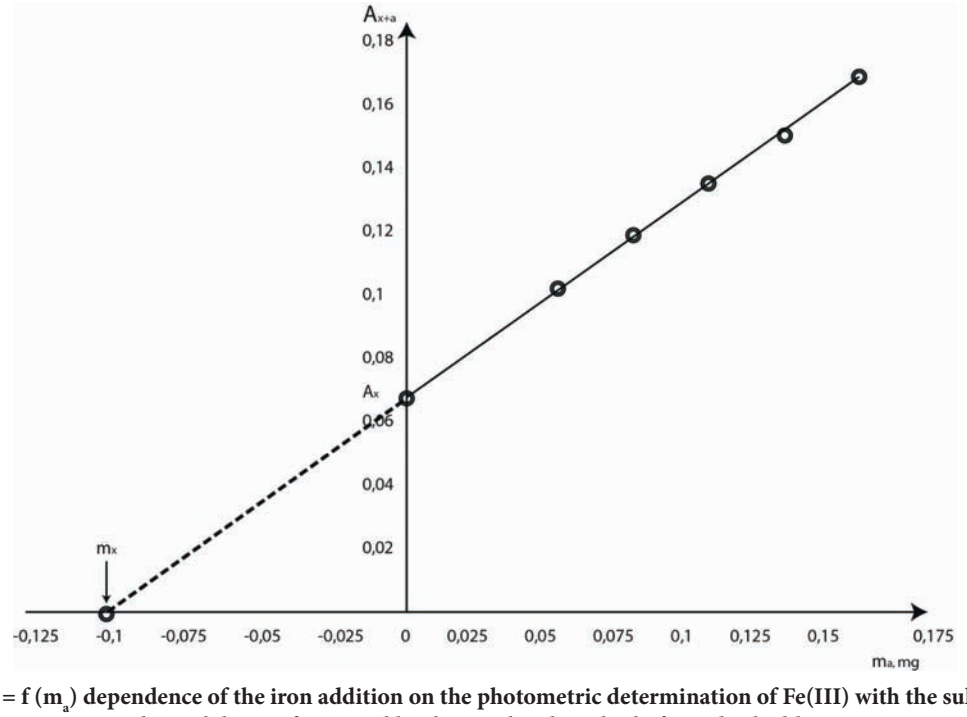



**Fig. 2. The $A_{x+a} = f(m_a)$ dependence of the iron addition on the photometric determination of Fe(III) with the sulfosalicylic acid in the oral drops of Ferropol by the graphical method of standard addition.**

The obtained experimental data and the results of calculating the mass of Fe (III) in the oral drops of Ferropol by the relation (6), as well as the value of pH in the studied solutions are presented in table 1.

The data in table 1 were statistically processed to obtain the average content of Fe (III) Ferropol oral drops equal to 49.97 ± 0.94 mg/ml, having a 0.95% confidence interval.

In the graphical method of standard addition the solution absorbance $A_{x+a} = f(m_a)$ is a straight line that intersects on the ordinate axis the absorbance value Ax (see Fig. 2). At the extrapolation of this line to the intersection with the x-axis was obtained the mean value of Fe (III) mass in the solutions where the absorbances $A_{x+a}$: - $m_a = m_x$ were measured. In the Fig. 2 we find that mx = 0.10mg Fe (III).

The content of Fe (III) ($m_{Fe}$, mg/ml) in the oral drops of Ferropol, using the data from Table I has been calculated according to the relation:

$$m_{Fe} = \frac{\overline{m}_x \cdot V_0 \cdot \rho}{V_1 \cdot m_p}, \quad (7)$$

(all of the notes see above) and we obtained $m_{Fe}$ = 50 0 mg/ml.

## Conclusions

It was elaborated a new method of photometric analysis of iron in the oral drops of Ferropol using the sulfosalicylic acid by the method of standard addition. The elaborated method can be recommended to analyze the iron in the liquid pharmaceutical forms.

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