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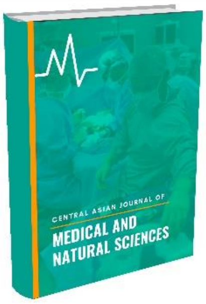

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SYNTHESIS OF COMPLEX COMPOUNDS OF IRON (II) IONS WITH QUERCETIN IN DIFFERENT ENVIRONMENTS AND EVALUATION OF THEIR STABILITY CONSTANTS

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ABSTRACT: In the article, complex compounds of iron (II) ions with quercetin were synthesized in different environments and their stability constants were determined. According to it, the values of the stability constants of the complex formed from Fe(II) cations and quercetin in different environments (pH) were evaluated. According to it, λ=273 nm and λ=402 nm, respectively at pH=2,0 $\beta_K' = 2{,}10 \cdot 10^{-3}$ and $2{,}08 \cdot 10^{-3}$; at pH=4,0 $\beta_K' = 3{,}14 \cdot 10^{-3}$ and $2{,}61 \cdot 10^{-3}$; at pH=6,0 $\beta_K' = 2{,}24 \cdot 10^{-3}$ and $2{,}27 \cdot 10^{-3}$; at pH=7,0 $\beta_K' = 1{,}94 \cdot 10^{-3}$ and $2{,}04 \cdot 10^{-3}$; at pH=9,0 $\beta_K' = 2{,}07 \cdot 10^{-3}$ and $2{,}77 \cdot 10^{-3}$. The obtained results can be used to evaluate the targeted delivery of Fe(II) ions in the case of Fe(II) cations complexes with quercetin.

KEYWORDS: Flavonoid, quercetin, Fe(II) cation, complex, stability constant, solution, pH, molar absorption coefficient, isomolar series.

INTRODUCTION

It is known that flavanoids are among the polyfunctional compounds found in plants, and according to their structure, they act as ligands and tend to form complexes [1]. Iron ions are an essential element for the human body, as they play a crucial role in transporting oxygen through the bloodstream.

Quercetin belongs to the class of flavonoids, found in a variety of fruits and vegetables, and has been widely studied for its health benefits, including antioxidant and anti-inflammatory properties. In particular, complexes of quercetin as a polyfunctional compound with some d-metal ions were synthesized and some of their properties were studied [6,7,8,9,10,11,13,15,16,17,18,19,20,23,24].

Iron (II) ion complexes with quercetin are of great interest to researchers due to their potential applications in various fields, including medicine, food, and cosmetics. The stability of these complexes is affected by various factors, including pH, temperature, and the presence of other molecules [2,3,4,5,12,14,21,22].

One of the factors affecting the stability of complex compounds of iron (II) ions with quercetin is pH. The stability of these complexes is highest around pH=7. At lower pH values, the complex can undergo hydrolysis, resulting in the release of iron (II) ions and quercetin. On the other hand, at high pH values, the complex can be oxidized, resulting in the formation of insoluble compounds. Therefore, it is very important to maintain a neutral pH when using these complexes.

Temperature is another factor affecting the stability of iron (II) ion complexes with quercetin. Generally, these complexes are stable at room temperature. However, at high temperatures, the complex can undergo oxidation, which leads to the formation of insoluble compounds. Therefore, it is important to store these complexes at cool temperatures to maintain their stability.

The presence of other molecules can also affect the stability of Iron(II) ion complexes with quercetin. For example, the presence of ascorbic acid may increase the stability of the complex by preventing quercetin oxidation. In addition, the presence of other metal ions can lead to the formation of insoluble compounds, which leads to the destabilization of the complex. The use of iron (II) ion complexes with quercetin is used in the treatment of iron deficiency anemia. Iron deficiency anemia is a common condition where the body does not have enough iron to produce the hemoglobin needed to carry oxygen in the blood. Iron supplements are commonly used to treat this condition, but they can have adverse effects on the digestive system. Iron (II) complexes with quercetin can be better absorbed by the body, thus providing an alternative treatment method. Iron(II) complexes with quercetin may have the additional benefit of increasing the nutritional value of foods by increasing their iron content. In addition, these complexes can be used in antiaging creams to protect the skin from oxidative stress and inflammation that cause premature aging.

Recent studies in the literature have shown that iron metabolism is disturbed in cancer, neurodegenerative and inflammatory diseases. Iron overload is associated with oxidative stress, inflammation, and tissue damage, while iron deficiency leads to immunosuppression and poor wound healing [1,2,3,4]. Therefore, it is desirable to conduct research on iron metabolism in the body using complex compounds of iron (II) with quercetin. Therefore, it is important to evaluate the stability of complex compounds of iron (II) ions with quercetin.

THE PURPOSE OF THE WORK

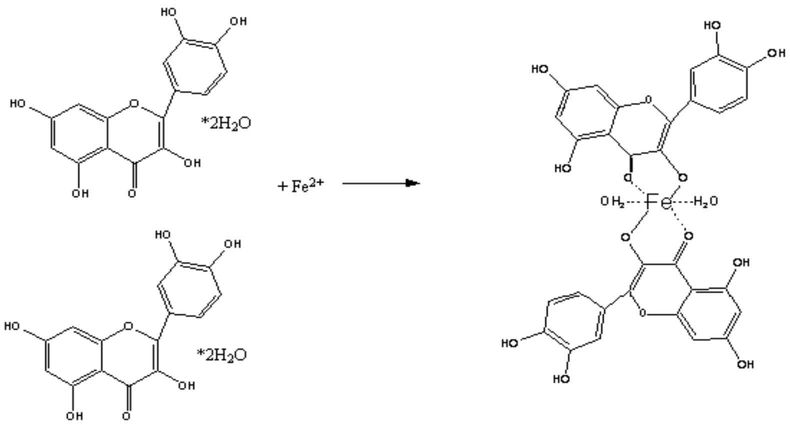
Synthesis of complex compounds of iron (II) ions with quercetin in different environments and evaluation of their stability constants.

Inspection objects and methods

Reagents: Quercetin (Chemically pure), $FeSO_4 \cdot 7H_2O$ (Clean for analysis), methanol (for HPLC), phosphoric acid (Clean for analysis), distilled water,

Measurements. UV spectrophotometer (T80+ UV/VIS), analytical balance (AUY120).

Synthesis of Complex: The reaction of quercetin with iron ions is based on the following equation [8]:



Evaluation of the stability of quercetin complex with Fe (II) ion. In order to study the composition and stability of complex compounds formed by the action of complexing metal (M) and ligand (R) in solution, a series of isomolar solutions with different ratios of initial concentrations of reactants are usually prepared, and then the optical density of these solutions measured in an Ultraviolet (UV) spectrophotometer at certain wavelengths (λ). The stability constant (β) of complex compounds formed in solution is calculated using the isomolar series method. Usually, the molar absorption coefficients of these complexes are found along with the stability constants. Classical calculation algorithms are not always used, in particular, the stability constants of very strong complexes are incorrectly determined. In our opinion, the accuracy of the estimation of stability constants should depend not only on the strength of the formed complexes, but also on the ratio of the initial concentration of the metal (M) and the ligand (R) in the model solutions. Incorrectly selected composition can cause large errors or do not allow to calculate the values of stability constant (β'_K) and absorption coefficient (ε) at all [8,9].

Algorithm for calculating molar coefficient and stability constant. Suppose that the conditional stability constant of the FeR complex is unknown and it is calculated in the traditional way, as shown in the manuals: first, two isomolar series of the isomolar series are selected, and then the molar absorption coefficient is calculated. The molar absorption coefficient of the complex is calculated according to the following formula [1]:

$$\varepsilon_{ij} = \sqrt{\frac{A_i \cdot (A_j)^2 - A_j \cdot (A_i)^2}{A_j \cdot C_{Mi} \cdot C_{Ri} - A_i \cdot C_{Mj} \cdot C_{Rj}}}, \quad (1)$$

where ε_{ij} - is the molar absorption coefficient of the complex; C_{Mi}, C_{Mj}, C_{Ri}, C_{Rj} are initial concentrations of metal (M) ions and ligand (R) in solutions i and j, respectively; A_i and A_j are different optical densities of the same solution at 273 nm and 402 nm. Then similar calculations are performed for other pairs of solutions. The ε_{ij} values obtained for different pairs of solutions vary slightly due to random errors in solution preparation and photometry. Based on the average value of the molar absorption coefficient, the conditional stability constant (β'_K) of the studied complex is calculated [2]:

$$\beta'_K = \frac{A/\varepsilon_K}{\left(C_R - \frac{A}{\varepsilon_K}\right) \cdot \left(C_M - \frac{A}{\varepsilon_K}\right)}, \quad (2)$$

and then according to the algorithm, the stability constant of the same complex is found.

Synthesis of complexes was carried out using methanol and solvents of different media (pH) (1:1 ratio). Solutions of 0.0001 mol/l of quercetin ($C_{15}H_{10}O_7$) and $FeSO_4 \cdot 7H_2O$ were prepared and mixed in the proportions shown in Table 1 using the isomalar series method.

Table 1. Isomolar series

Mixture	C_{Me} mol/l	C_R mol/l
1	0,00010	0, 00090
2	0, 00020	0, 00080
3	0, 00030	0, 00070
4	0, 00040	0, 00060
5	0, 00050	0, 00050
6	0, 00060	0, 00040
7	0, 00070	0, 00030
8	0, 00080	0, 00020
9	0, 00090	0, 00010

THE OBTAINED RESULTS AND THEIR DISCUSSION

Reagent solutions were prepared using accurately weighed portions of chemically pure or analytically pure reagents.

Tables 2, 3, 4, 5, 6 show the optical densities measured simultaneously in different molar ratios (from 1:9 to 9:1) in a spectrophotometer with a quartz cuvette thickness of l=1 cm.

Table 2. Isomolar series at pH=2,0

Mixture	C_M mol/l	C_R mol/l	C_M/C_R	A 273 nm	A 402 nm
1	0,00010	0, 00090	0,11	0,037	0,018
2	0, 00020	0, 00080	0,25	0,035	0,022
3	0, 00030	0, 00070	0,43	0,026	0,013
4	0, 00040	0, 00060	0,67	0,031	0,014
5	0, 00050	0, 00050	1,00	0,037	0,009
6	0, 00060	0, 00040	1,50	0,028	0,009
7	0, 00070	0, 00030	2,33	0,038	0,010
8	0, 00080	0, 00020	4,00	0,038	0,007
9	0, 00090	0, 00010	9,00	0,034	0,008

Table 3. Isomolar series at pH=4,0

Mixture	C_M mol/l	C_R mol/l	C_M/C_R	A 273 nm	A 402 nm
1	0,00010	0, 00090	0,11	0,033	0,044
2	0, 00020	0, 00080	0,25	0,018	0,021
3	0, 00030	0, 00070	0,43	0,006	0,007
4	0, 00040	0, 00060	0,67	0,024	0,015

5	0, 00050	0, 00050	1,00	0,005	0,010
6	0, 00060	0, 00040	1,50	0,012	0,010
7	0, 00070	0, 00030	2,33	0,010	0,005
8	0, 00080	0, 00020	4,00	0,003	0,012
9	0, 00090	0, 00010	9,00	0,006	0,005

Table 4. Isomolar series at pH=6,0

Mixture	C_M mol/l	C_R mol/l	C_M/C_R	A 273 nm	A 402 nm
1	0,00010	0, 00090	0,11	0,050	0,029
2	0, 00020	0, 00080	0,25	0,064	0,037
3	0, 00030	0, 00070	0,43	0,038	0,028
4	0, 00040	0, 00060	0,67	0,029	0,029
5	0, 00050	0, 00050	1,00	0,033	0,027
6	0, 00060	0, 00040	1,50	0,030	0,038
7	0, 00070	0, 00030	2,33	0,041	0,039
8	0, 00080	0, 00020	4,00	0,017	0,021
9	0, 00090	0, 00010	9,00	0,032	0,021

Table 5. Isomolar series at pH=7,0

Aralashma	C_M mol/l	C_R mol/l	C_M/C_R	A 273 nm	A 402 nm
1	0,00010	0, 00090	0,11	0,059	0,037
2	0, 00020	0, 00080	0,25	0,097	0,072
3	0, 00030	0, 00070	0,43	0,079	0,064
4	0, 00040	0, 00060	0,67	0,083	0,067
5	0, 00050	0, 00050	1,00	0,068	0,054
6	0, 00060	0, 00040	1,50	0,071	0,059
7	0, 00070	0, 00030	2,33	0,056	0,050
8	0, 00080	0, 00020	4,00	0,056	0,052
9	0, 00090	0, 00010	9,00	0,064	0,055

Table 6. Isomolar series at pH=9,0

Mixture	C_M mol/l	C_R mol/l	C_M/C_R	A 273 nm	A 402 nm
1	0,00010	0, 00090	0,11	0,066	0,055
2	0, 00020	0, 00080	0,25	0,064	0,069
3	0, 00030	0, 00070	0,43	0,064	0,082
4	0, 00040	0, 00060	0,67	0,057	0,085
5	0, 00050	0, 00050	1,00	0,074	0,100
6	0, 00060	0, 00040	1,50	0,053	0,094

7	0, 00070	0, 00030	2,33	0,066	0,126
8	0, 00080	0, 00020	4,00	0,061	0,122
9	0, 00090	0, 00010	9,00	0,065	0,124

The averaged ε_{ij} value is consistent with literature data. Thus, the choice of isomolar series used to evaluate the stability of complex compounds by the method of isomolar series affects the accuracy of this evaluation. In order to achieve sufficiently accurate results, the combined use of data obtained for solutions belonging to the same series required (both mixtures must have an excess of metal or reagent). Thus, the ε-molar absorption coefficients of complexes formed by quercetin with iron (II) ions in different pH media are presented in Table 7.

Table 7. ε-Molar absorption coefficients of the complex in different environments

№	Environments	273 nm	402 nm
1	pH=2,0	ε = 6,95 ·10^-5^ → $\varepsilon = 6{,}95 \cdot 10^{-5}$	$\varepsilon = 2{,}23 \cdot 10^{-5}$
2	pH=4,0	$\varepsilon = 2{,}39 \cdot 10^{-5}$	$\varepsilon = 2{,}43 \cdot 10^{-5}$
3	pH=6,0	$\varepsilon = 7{,}33 \cdot 10^{-5}$	$\varepsilon = 6{,}44 \cdot 10^{-5}$
4	pH=7,0	$\varepsilon = 1{,}32 \cdot 10^{-4}$	$\varepsilon = 1{,}11 \cdot 10^{-4}$
5	pH=9,0	$\varepsilon = 1{,}30 \cdot 10^{-4}$	$\varepsilon = 2{,}45 \cdot 10^{-4}$

β'_K-stability constants of these complex compounds were calculated based on ε-molar absorption coefficients Table 8.

Table 8. β'_K-stability constants of the complex in different environments

№	Environments	273 nm	402 nm
1	pH=2,0	$\beta'_K = 2{,}10 \cdot 10^{-3}$	$\beta'_K = 2{,}08 \cdot 10^{-3}$
2	pH=4,0	$\beta'_K = 3{,}14 \cdot 10^{-3}$	$\beta'_K = 2{,}61 \cdot 10^{-3}$
3	pH=6,0	$\beta'_K = 2{,}24 \cdot 10^{-3}$	$\beta'_K = 2{,}27 \cdot 10^{-3}$
4	pH=7,0	$\beta'_K = 1{,}94 \cdot 10^{-3}$	$\beta'_K = 2{,}04 \cdot 10^{-3}$
5	pH=9,0	$\beta'_K = 2{,}07 \cdot 10^{-3}$	$\beta'_K = 2{,}77 \cdot 10^{-3}$

Therefore, evaluating the safety and effectiveness of complex compounds of iron (II) ions with quercetin on the human body, optimizing their targeted delivery to the body is one of the urgent problems that must be fulfilled in the future.

CONCLUSIONS

1. Complex compounds of iron (II) ions with quercetin were synthesized in different environments and their stability constants were determined.
2. The stability constants of the complex formed from Fe(II) cations and quercetin in different environments (pH) at λ=273 nm and λ=402 nm, respectively: at pH=2,0 $\beta'_K = 2{,}10 \cdot 10^{-3}$ and 2,08·

10^{-3}; at pH=4,0 $\beta'_K = 3{,}14 \cdot 10^{-3}$ and $2{,}61 \cdot 10^{-3}$; at pH=6,0 bo‘lganda $\beta'_K = 2{,}24 \cdot 10^{-3}$ and $2{,}27 \cdot 10^{-3}$; at pH=7,0 $\beta'_K = 1{,}94 \cdot 10^{-3}$ and $2{,}04 \cdot 10^{-3}$; pH=9,0 $\beta'_K = 2{,}07 \cdot 10^{-3}$ va $2{,}77 \cdot 10^{-3}$.

3. The obtained results can be used to evaluate the targeted delivery of Fe(II) ions in the case of Fe(II) cation complexes with quercetin.

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