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*Y.A.Buketov Karaganda State University (E-mail: alfiya_kurmanova@mail.ru)***The complexation of quercetin with zirconium (IV) in water-ethanol medium**

In this work the interaction between quercetin and zirconium (IV) ions was studied in water-ethanol medium. The optimal conditions of the complex formation were found for the system: quercetin – zirconium – water – ethanol by using spectrophotometric method. The time and solvent dependences were evaluated.

Key words: interaction of quercetin with zirconium ions, optimal, optical density.

Flavonoids are a class of natural compounds with a high range of biological activities [1]. One of the main biological properties of flavonoids is the ability to reduce oxidizing processes; this can fully be used against cancer and cardio-vascular diseases. Despite the useful properties of these compounds only few of them are currently used in a pharmaceutical field. This occurs because of the fact that most of flavonoids are water insoluble. If one wants to introduce a medicine on a market, he should pay attention not only on a biological activity, but also on a water solubility of the product.

Despite the fact that flavonoids have been studying for more than 60 year, only few researches were made on a transfer of flavonoids to water soluble forms [2]. One of the methods of making compound water soluble is a complex formation. Moreover it is suggested that a biological activity can be increased if an organic ligand is coordinated with an appropriate metal-ion [3–5]. A lot of researches proved this hypothesis, although all their experiments were held in methanol solution. That's why the question about can this hypothesis be used for all metals and for all conditions rises. This article gives an answer to this question, considering an example of quercetin-zirconium (IV) complex in water-ethanol medium.

One of easily accessible and biological active flavonoids is quercetin (Fig.1) [6]. It is known that quercetin is an antioxidant.

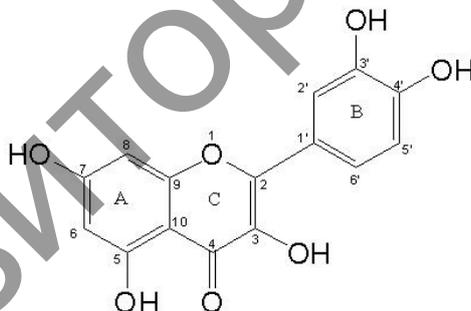


Figure 1. Quercetin

However, it can only be dissolved in ethanol and other organic solvents as methanol and acetylacetone. That is why it has not yet been used as an individual medicine. Several researches reported that quercetin can easily form complexes with metal ions, although all experiments were held in methanol [7–9]. In this work a new approach as introduced — the ability to form complex in water-ethanol medium.

Zirconium (IV) was chosen for this approach, as one of d-metals and good biologically active ions. From the pharmacology point of view zirconium (IV) complexes are noted for their significant biological properties, namely antibacterial and antifungal activities [10].

After studying the complex formation between quercetin and Zr(IV) the conditions of the formation were investigated.

Experimental

All materials and solvent were analytically and chemically pure graded. Quercetin is purchased from ISPH «Phytochemistry». Absorbance of investigated solutions was obtained on «CPhC-3».

Synthesis of the complex: 1 mL $1 \cdot 10^{-3}$ mol/L of quercetin solution was mixed with 0,5 mL $1 \cdot 10^{-3}$ mol/L of zirconium oxychloride, then 4 mL of water-ethanol mixture (1,5 mL H₂O + 1,5 mL 96 % ethanol) was

added to the reaction mixture. The solution became orange. After stirring UV-vis absorption spectra were recorded in the spectral range 300–700 nm using water as a comparison solution. UV-vis (λ , nm, $\lg \epsilon$, H₂O): 370 nm ($\epsilon = 1042.36 \pm 0,03$), 395 nm ($\epsilon = 1420.71 \pm 0,08$) and 485 nm ($\epsilon = 2966.66 \pm 0,01$).

Results and discussion

As the result of the preliminary experiments it was determined that quercetin formed orange complex with zirconium (IV) ions in water-ethanol medium. The UV-vis spectra of initial flavonoid and complex showed 3 absorption bands (Fig. 2), two of which were identical in both samples: 360 nm and 395 nm. However regarding the third band it is shown that a bathochromic shift is occurred.

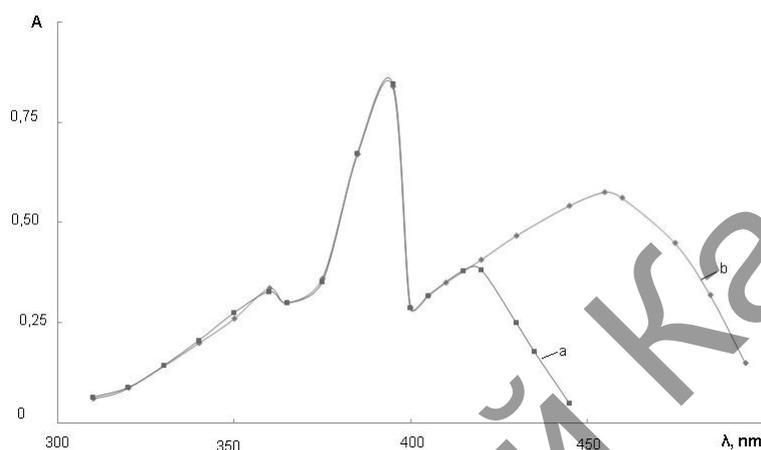


Figure 2. UV-vis spectra of quercetin (a) and its complex with zirconium (IV) (b)

This reason of this shift is the increase of conjugation during complex formation. A new ring can be formed between the 3-hydroxy – metal – the 4-carbonyl group in the C-ring [11]. These sites are the first possible ones to form the complex, because of the acidity of C3-oxo group of quercetin and no steric hindrance to oxygen of carbonyl group (C4) to form a ring between itself – Zr(IV) – 3-OH group. Thus UV-vis spectra proved the formation of a new quercetin – zirconium (IV) complex. The 5-OH group can't be involved because of lesser proton acidity [12].

The investigation of optimal conditions. The optimal conditions of complex formation are essential to understand when and how a complex is formed. Furthermore they can give more information about a structure of the complex.

The time dependence. During the preliminary experiments it was determined that an absorbance of the complex is changing within a time. That is why the time dependence was investigated in the system: zirconium (IV) – quercetin – water – ethanol (Fig. 3).

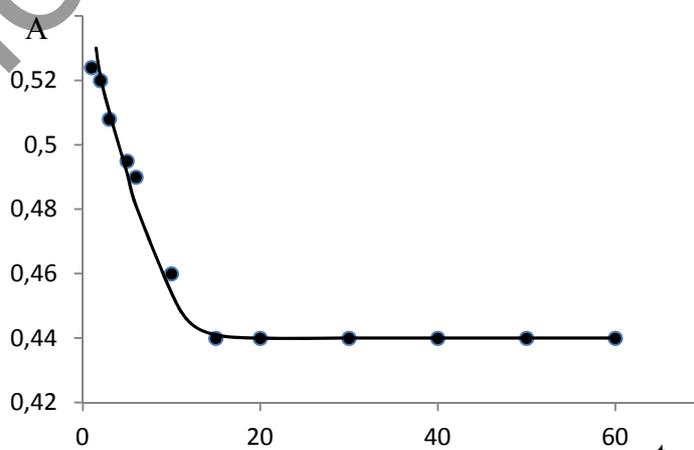


Figure 3. Kinetic curve of Zr (IV) – quercetin complex

As it is seen from figure 3, the absorbance decreases during first 15 minutes, then it remains almost constantly, which contributes to the fact that the complete complex formation occurs after 15 minutes. Thus, further researches were made after 15 minutes from solutions' preparations.

The solvent dependence. As it was said previously the major problem of flavonoids is water insolubility. That's why it is important to make fully or partly water soluble compound to use it as a medicine in future.

It is known, that quercetin dissolves in ethanol and not in water. Considering its complex with zirconium (IV), its solubility in water is also not high, that's why further experiments were studied in water-ethanol medium. It was established, that if the content of ethanol is under 15 %, it falls in precipitation.

Priory it was shown that the ethanol's content influenced on complex absorbance; thus it can be suggested, that ethanol is involved in complex structure.

The dependence of quercetin – zirconium (IV) complex absorbance on solvent's concentration is on fig. 4. As the received results show, that with the increase of ethanol concentration, the absorbance of complex solution increases too. However, the absorbance increases only till 65 % and then it goes down. The filling of water molecules in the inside coordination sphere of zirconium ions on the ethanol molecules is carried out during increase of ethanol, accompanying with the increase of absorbance. It was determined the complete structure of the complex forms at 65 % ethanol in the system. Further experiments were carried out using optimal ethanol's volume — 65 %.

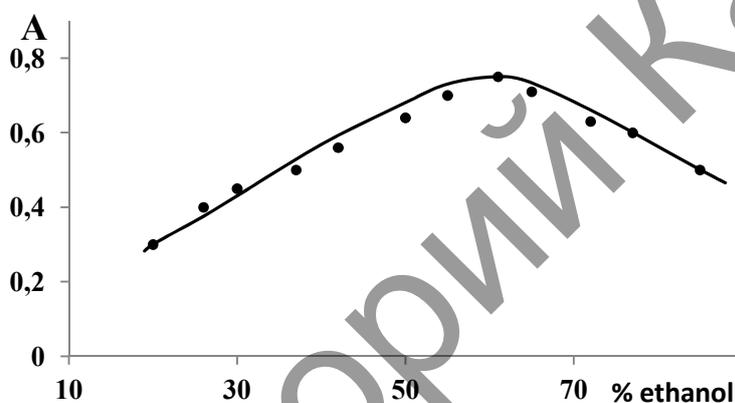


Figure 4. Effect of solvent

The stability constant of complex is $(9.56 \pm 0.01) \cdot 10^9$, this number shows that the complex is averagely stable. Complex forms at the room temperature.

Conclusion

This work describes the investigations of the interaction in the system: quercetin – zirconium (IV) – water – ethanol. Furthermore the optimal conditions of complex formation in the system were investigated. It was shown that the complex formation depended on time and ethanol volume in the system. It was also established that ethanol molecules can be included in the structure of the complex.

References

- 1 Vasil'eva I.S., Paseshnichenko V.A. Review of natural compounds distribution // The achievements of biological chemistry. — 2000. — Vol. 3. — P. 153–156.
- 2 Hauser C.R., Lindsay J.K. Certain Acylations of Ferrocene and Some Condensations Involving the α -Hydrogen of Acetylferrocene // J. Org. Chem. — 1957. — Vol. 22. — P. 482–485.
- 3 Thompson M., Williams C.R. Heterogeneous effect of flavonoids on K⁺ loss and lipid peroxidation induced by oxygen-free radicals in human red cells // Anal. Chim. Acta. — 1976. — Vol. 85. — P. 375–380.
- 4 Fernandez M.T., Mira M.L. et al. Iron and copper chelation by flavonoids: an electrospray mass spectrometry study // Inorg. Biochem. — 2002. — Vol. 92. — P. 5–10.
- 5 Boudet A.C., Cornard J.P., Merlin J.C. The analysis of flavonoid via complex reactions // Spectrochim. Acta A. — 2000. — Vol. 56. — P. 29–33.
- 6 Mukhametzhonov M.N., Kagarlickij A.D. et al. Information of quercetin's new derivatives // The Problems of Efficient Medical and Technical Plants of Kazakhstan Usage. — Almaty: Gylym, 1986. — P. 230–232.

- 7 *Tan Jun, Wang Bochu, Zhu Liangcia.* Hydrolytic cleavage of DNA by quercetin manganese (II) complexes // *Colloids and Surfaces B. Biointerfaces.* — 2007. — Vol. 55. — P. 152–157.
- 8 *Birjees Bukhari S., Memon S. et al.* Synthesis, characterization and antioxidant activity copper-quercetin complex // *Spectrochim. Acta Part A.* — 2009. — Vol. 71. — P. 1906–1911.
- 9 *Birjees Bukhari S., Memon S. et al.* Synthesis, characterization and investigation of antioxidant activity of cobalt – quercetin complex // *Journal of Molecular Structure.* — 2008. — Vol. 892. — P. 46–51.
- 10 *Evelina G. Ferrer, María V. Salinas et al.* Synthesis, characterization, antitumoral and osteogenic activities of quercetin vanadyl (IV) complexes // *Journal of Biol. Inorg. Chem.* — 2006. — Vol. 11. — № 6. — P. 791–801.
- 11 *Aswatha Ram H.N. et al.* In vitro free radical scavenging potential of methanol extract of entire plant of *Phyllanthus Reticulatus* Poir. // *Pharmacology online.* — 2008. — Vol. 2. — P. 440–451.
- 12 *Brand-Williams W., Cuvelier M.E., Berset C.* Use of a free radical method to evaluate antioxidant activity // *Lebensm. Wiss. Technol.* — 1997. — Vol. 28. — P. 25–30.

О.П.Лойко, А.И.Халитова, А.Ф.Курманова

Этанол-сулы ортада кверцетин мен цирконийдің (IV) комплекс түзу қабілеті

Сулы-этанолды ортада кверцетин мен цирконий (IV) арасындағы әрекеттесулер зерттелді. Спектрофотометриялық әдісті қолдану арқылы кверцетин–цирконий (IV)–су–этанол жүйесінде комплекс түзілудің оңтайлы жағдайлары табылды. Комплекс ерітінділерінің оптикалық тығыздығының уақыт пен еріткіш құрамына тәуелділігі белгіленді.

О.П.Лойко, А.И.Халитова, А.Ф.Курманова

Комплексообразование кверцетина с цирконием (IV) в водно-этанольной среде

В статье изучено взаимодействие между кверцетином и ионами циркония (IV) в водно-этанольной среде. Найдены оптимальные условия образования комплекса в системе кверцетин–цирконий (IV)–вода–этанол с использованием спектрофотометрического метода. Исследованы зависимости оптической плотности комплексного соединения от времени и содержания растворителя.