



Spectrophotometric investigation of the uranyl–phenylephrine system

LEPOSAVA PAVUN^{1*#}, DUŠAN MALEŠEV¹ and DRAGAN VESELINOVIĆ^{2#}

¹Faculty of Pharmacy, University of Belgrade, Serbia, Vojvode Stepe 450, Belgrade and ²Faculty of Physical Chemistry, University of Belgrade, Studentski trg 12, Belgrade, Serbia

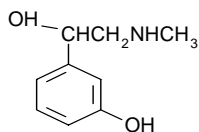
(Received 2 October 2006, revised 9 March 2007)

Abstract: Using spectrophotometric methods and pH-metric measurements, it was found that the uranyl ion and phenylephrine form a 1:2 complex in the pH region 2.50–4.25 with two absorption maxima at 314.2 nm and 340.6 nm. The thermodynamic stability constant at $I = 0$ and $T = 298$ K (room temperature) of the $\text{UO}_2(\text{II})$ –phenylephrine complex, $\text{UO}_2(\text{C}_9\text{H}_{12}\text{O}_2\text{N})_2$, is $\log \beta_2^0 = 14.0$ and $\Delta G_2^\ominus = -79.6$ kJ mol⁻¹. A linear dependence of the absorbance at 340.6 nm on the concentration of phenylephrine was obtained in the range from 0.0025 mol dm⁻³ to 0.0245 mol dm⁻³ using a solution of 0.025 mol dm⁻³ $\text{UO}_2(\text{NO}_3)_2$ at pH = 3.90 and $I = 0.075$ mol dm⁻³. The measurement error was 2.1 %.

Keywords: complex, uranyl ion, phenylephrine, thermodynamic stability constant.

INTRODUCTION

Phenylephrine ((*R*)-1-(3-hydroxyphenyl)-2-(methylamino)ethanol, $\text{C}_9\text{H}_{13}\text{O}_2\text{N}$) is a white crystalline powder, and belongs to the group of medicines called sympathomimetics. It acts by stimulating the alpha-receptors in certain areas of the body. It is used locally, as a decongestant, for non-specific and allergic conjunctivitis, sinusitis and nasopharyngitis.^{1,2}



Phenylephrine

Phenylephrine has been investigated spectrophotometrically using interactions with 1-nitroso-2-naphthol,³ ninhydrin in sulfuric acid⁴ and nitrobenzene derivatives.⁵ On the other hand, due to the presence of an amino group and a phenyl group in the molecule ($pK_a(-\text{OH}) = 8.9$ and $pK_a(-\text{NH}_2^+) = 10.1$),¹ phenyl-

* Corresponding author. E-mail: leposava.pavun@pharmacy.bg.ac.yu

Serbian Chemical Society member.

doi: 10.2298/JSC0709799P

ephine forms a complex with Fe^{3+} ($\text{Fe}^{3+}/\text{phenylephrine} = 2:1$).^{6,7} However, there are no data in the literature about complexes of phenylephrine and the UO_2^{2+} ion or other metal ions. The purpose of the present work was to investigate the UO_2^{2+} -phenylephrine complex and the possibility of the employment of the complex for the spectrophotometric determination of phenylephrine in aqueous media.

EXPERIMENTAL

Reagents and solutions

Uranyl nitrate (Fluka A.G.), HNO_3 , NaOH , NaNO_3 (Merck) and phenylephrine hydrochloride (Zdravlje, Serbia), all *p.a.*, were used without further purification.

Uranyl nitrate solution was standardized gravimetrically, by precipitation with oxine (8-hydroxyquinoline).⁸

A solution of phenylephrine hydrochloride was prepared by dissolving a precisely measured mass of dry phenylephrine hydrochloride in deionized water. The phenylephrine hydrochloride had previously been dried in a desiccator over silica gel. This solution was stored in a refrigerator.

All solutions were prepared by dilution of $0.0100 \text{ mol dm}^{-3}$ solutions of $\text{UO}_2(\text{NO}_3)_2$ and $0.0500 \text{ mol dm}^{-3}$ solutions of phenylephrine hydrochloride.

The pH of all solutions was adjusted using HNO_3 or NaOH solutions, and the ionic strength of the final solutions was kept constant by addition of the required volume of a 1 mol dm^{-3} solution of NaNO_3 .

Apparatus

The spectrophotometric measurements were performed on a Beckman DU-650 spectrophotometer, using 1 cm quartz cells. The pH values were measured using a pH-meter (pHM-28 Radiometer) and a combined electrode (accuracy ± 0.01 pH units). Buffers solutions (Radiometer), pH 4.01 and pH 7.00 at 25 °C, were used for calibrating the pH-meter.

RESULTS AND DISCUSSION

Absorption spectra

Phenylephrine and the uranyl(II) ion formed a complex in the pH interval 2.50 – 4.25. Above pH 4.25, the solution of the complex turns orange and a sediment, *i.e.*, the hydroxide products of the uranyl(II) ions, is formed. Phenylephrine is stable at $\text{pH} \leq 7$.

The absorption spectra (Fig. 1) were recorded using the solutions of $0.002 \text{ mol dm}^{-3}$ $\text{UO}_2(\text{NO}_3)_2$ and $0.040 \text{ mol dm}^{-3}$ phenylephrine and their mixture, where the concentrations of components were the same as in the single solutions, at a constant pH 4.00 and ionic strength (0.03 mol dm^{-3}). Water was used as the blank.

Also, the calculated spectrum of the complex, $\Delta A = f(\lambda)$, (Fig. 1, curve 4), was obtained using the following equation for the calculation of the complex absorbance, ΔA :

$$\Delta A = A_M - A_U - A_P \quad (1)$$

where A_U , A_P and A_M are the absorbance of the solutions of $\text{UO}_2(\text{NO}_3)_2$, phenylephrine and their mixture, respectively, at the corresponding wavelengths (λ).

The absorption spectrum of the complex has two maxima, the more intensive one being at 314.2 nm and the other one at 340.6 nm. All measurements were per-

formed at 340.6 nm since the absorbance of the $\text{UO}_2(\text{NO}_3)_2$ solution increases abruptly at lower wavelengths.

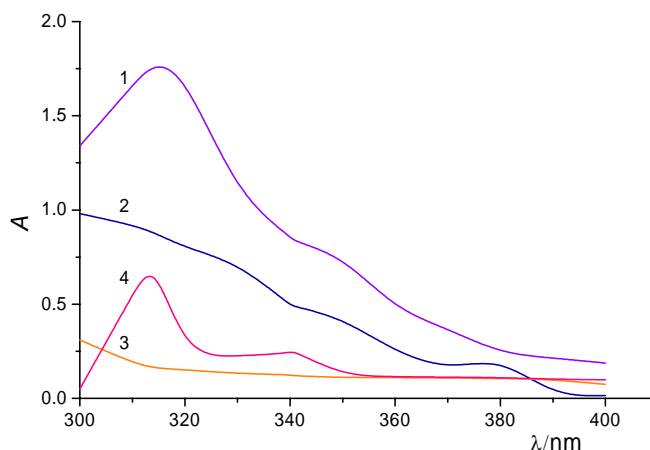


Fig. 1. Absorption spectra. 1: mixture $0.002 \text{ mol dm}^{-3} \text{UO}_2(\text{NO}_3)_2$ and $0.040 \text{ mol dm}^{-3}$ phenylephrine; 2: $0.002 \text{ mol dm}^{-3} \text{UO}_2(\text{NO}_3)_2$; 3: $0.020 \text{ mol dm}^{-3}$ phenylephrine; blank was water; 4: Calculated absorption spectra of the complex (ΔA).

The absorption spectrum of the UO_2^{2+} -phenylephrine complex was recorded in pH range from 2.50 to 4.25 (Fig. 2, curves 1–3), using the previously described procedure. The positions of absorption maxima are independent of pH, indicating the formation of only one type of complex in this pH interval.

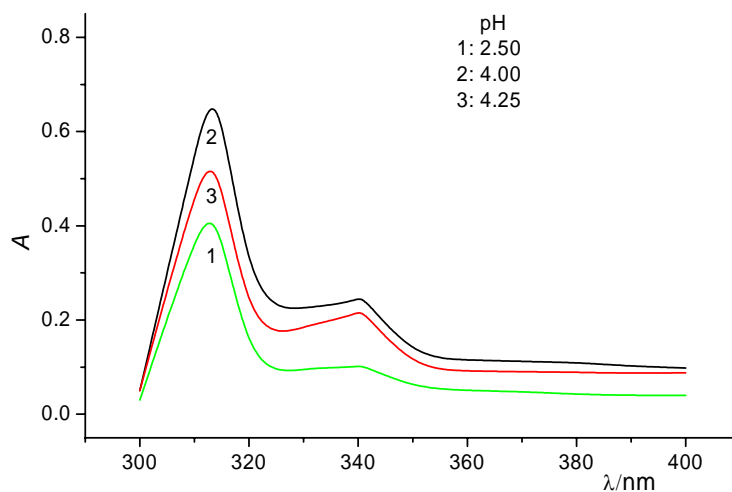


Fig. 2. Absorption spectra of the complex at different pH values; $0.002 \text{ mol dm}^{-3} \text{UO}_2(\text{NO}_3)_2$ and $0.040 \text{ mol dm}^{-3}$ phenylephrine.

The dependence of the absorbance of the complex and the components on pH was investigated at three different values of ionic strength, *i.e.*, at 0.025, 0.050

and $0.075 \text{ mol dm}^{-3}$. The absorbances of solutions of $0.002 \text{ mol dm}^{-3} \text{ UO}_2(\text{NO}_3)_2$, $0.040 \text{ mol dm}^{-3}$ phenylephrine and the mixture (containing the components at concentrations the same as in the individual solutions) were measured at 340.6 nm .

For each ionic strength, three curves $A = f(\text{pH})$ were obtained for solutions $\text{UO}_2(\text{NO}_3)_2$, phenylephrine and their mixture. By subtracting the relevant absorbances of the solution $\text{UO}_2(\text{NO}_3)_2$ and phenylephrine from their mixture, fourth curve $\Delta A = f(\text{pH})$ was obtained (Fig. 3). This curve represents the change of the complex absorbance on pH. The pH region $4.00\text{--}4.20$ was used for this investigation of the complex.

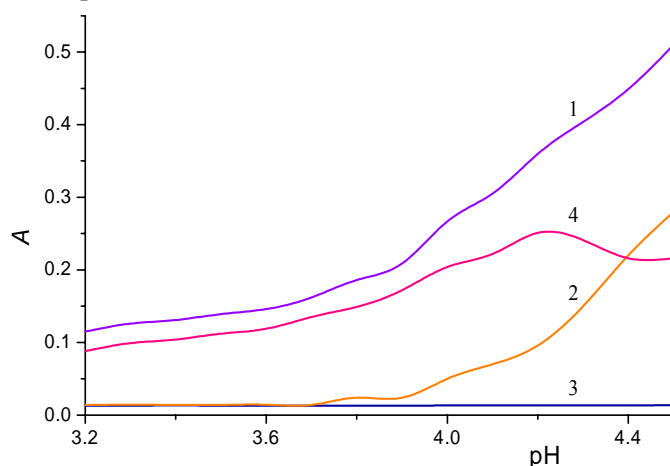


Fig. 3. Dependence of the absorbance on pH: Curve 1: mixture $0.002 \text{ mol dm}^{-3} \text{ UO}_2(\text{NO}_3)_2$ and $0.040 \text{ mol dm}^{-3}$ phenylephrine; Curve 2: $0.002 \text{ mol dm}^{-3} \text{ UO}_2(\text{NO}_3)_2$; Curve 3: $0.040 \text{ mol dm}^{-3}$ phenylephrine; the blank was water; Curve 4: $\Delta A = f(\text{pH})$; $\lambda = 340.6 \text{ nm}$, $I = 0.025 \text{ mol dm}^{-3}$.

Composition of the complex

The stoichiometric ratio of uranyl ion and phenylephrine in complex was determined by the method of molar ratios.⁹ The absorbances of solutions containing a constant concentration of $\text{UO}_2(\text{NO}_3)_2$ ($0.005 \text{ mol dm}^{-3}$) and different concentrations of phenylephrine ($0.0025\text{--}0.0200 \text{ mol dm}^{-3}$) were measured at 340.6 nm at a constant value of pH 4.00 and of ionic strength (0.05 mol dm^{-3}). The blank was the value of a $0.005 \text{ mol dm}^{-3}$ solution of $\text{UO}_2(\text{NO}_3)_2$. A straight line, $A = f(c(\text{phen})/c(\text{UO}_2^{2+}))$, with an intercept at $c(\text{phen})/c(\text{UO}_2^{2+}) = 2$ was obtained, which showed that the stoichiometric ratio of uranyl ion : phenylephrine in the complex was $1:2$ (Fig. 4).

The composition of the complex was also determined by the method of variation of equimolar solutions.¹⁰ The absorbances of the series of solutions formed by mixing equimolar solutions $\text{UO}_2(\text{NO}_3)_2$ and phenylephrine ($0.025 \text{ mol dm}^{-3}$) at a constant value of pH 3.75 and of ionic strength (0.05 mol dm^{-3}) were measured at 340.6 nm , *i.e.*, the Job's method¹⁰ was employed. The blank was a solution of $\text{UO}_2(\text{NO}_3)_2$ with the same concentration and pH as in the employed mix-

ture. On the curve of the dependence of the absorbencies of these solutions on the molar fractions of the UO_2^{2+} ion, there was a maximum at the molar fraction of $\text{UO}_2^{2+} = 0.33$ (Fig. 5), which confirms that the composition of the complex was $\text{UO}_2^{2+}/\text{phenylephrine} = 1:2$.

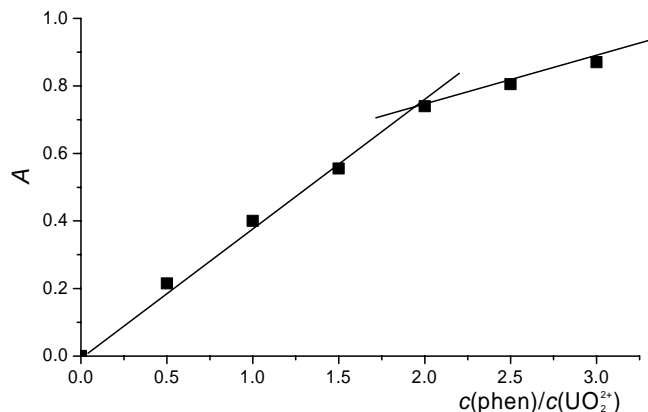


Fig. 4. Method of molar ratios. Dependence of absorbance on molar ratio $c(\text{phen})/c(\text{UO}_2^{2+})$; pH 4.00, $0.005 \text{ mol dm}^{-3} \text{UO}_2(\text{NO}_3)_2$; $0.0025\text{--}0.020 \text{ mol dm}^{-3}$ phenylephrine; Blank: $0.005 \text{ mol dm}^{-3} \text{UO}_2(\text{NO}_3)_2$; $\lambda = 340.6 \text{ nm}$; pH 4.02 ± 0.01 ; $I = 0.03 \text{ mol dm}^{-3}$.

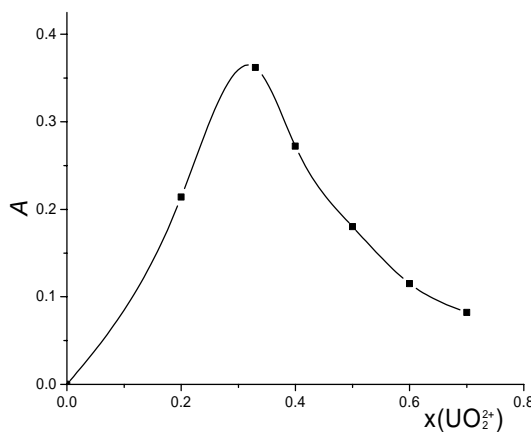


Fig. 5. Method of variations of equimolar solutions (Job's method). Change of absorbance with mol fraction of $x(\text{UO}_2^{2+})$. $c^0(\text{UO}_2^{2+}) = c^0(\text{phen}) = 0.025 \text{ mol dm}^{-3}$; blank is solution of $\text{UO}_2(\text{NO}_3)_2$ with the same concentrations and pH as in mixtures. $\lambda = 340.6 \text{ nm}$; pH 3.75 ± 0.01 ; $I = 0.05 \text{ mol dm}^{-3}$.

Infrared spectra of phenylephrine and of the complex

To find the position where the uranyl ion is linked to phenylephrine, the IR spectra of phenylephrine and of the isolated complex were recorded, using the KBr pellet method, in wave number region from 4000 to 800 cm^{-1} (Fig. 6). The complex was prepared by mixing solutions of $\text{UO}_2(\text{NO}_3)_2$ and phenylephrine in the molar ratio 1:2 and heating on a water bath ($80 \text{ }^\circ\text{C}$) with stirring for 0.5 h. After standing overnight at room temperature, the orange sediment was dried in desiccator over silica gel.

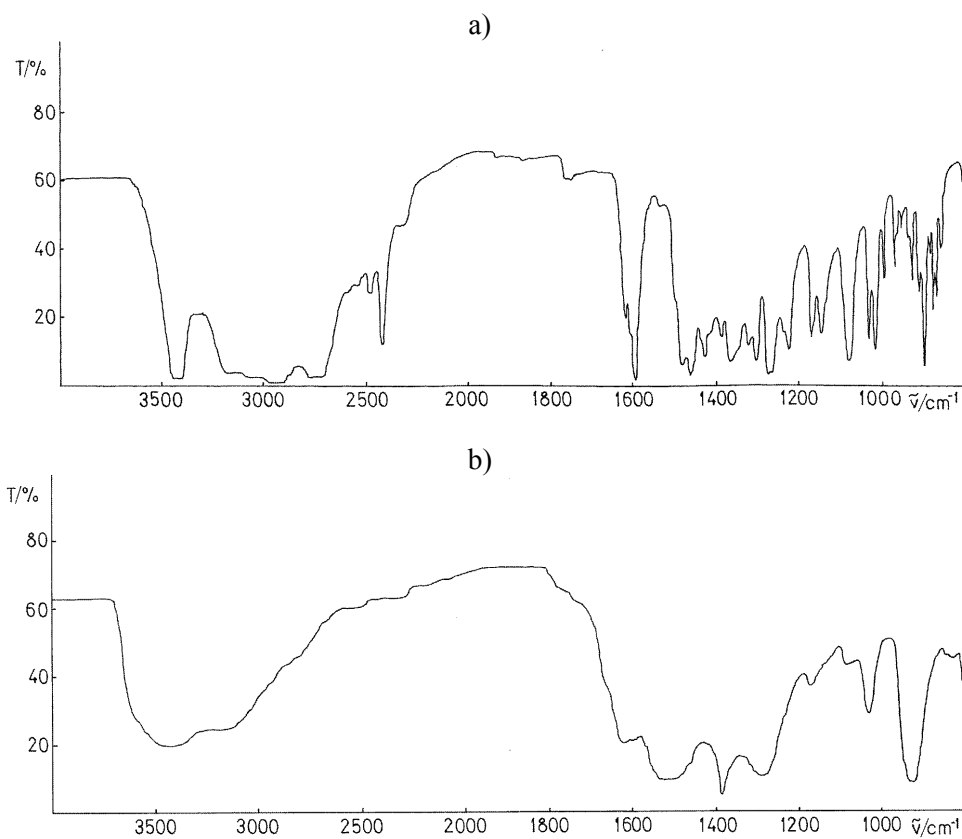
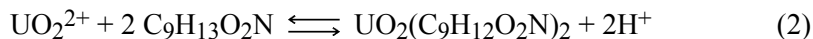


Fig. 6. IR Spectra of a) phenylephrine and b) complex (KBr pellets).

Bands ascribed to bending vibrations of phenolic OH groups in the wave number region $1280 - 930 \text{ cm}^{-1}$ were not present in the spectrum of the complex. This fact indicates that complex formation of UO_2^{2+} with phenylephrine occurs through the phenolic OH group.

Stability constant of the complex

It was found by measuring the pH of a $0.005 \text{ mol dm}^{-3}$ $\text{UO}_2(\text{NO}_3)_2$ solution and of a $0.010 \text{ mol dm}^{-3}$ phenylephrine solution, as well as their mixture containing the same concentrations as in single solutions that $c(\text{H}^+)_{\text{mixture}} > c(\text{H}^+)_{\text{uranyl}} + c(\text{H}^+)_{\text{phen}}$. This means that phenylephrine participated in the formation of the complex according to the reaction:



whereby an H^+ ion is released from the phenyl group.¹¹

The stability constant of the complex $\text{UO}_2(\text{C}_9\text{H}_{12}\text{O}_2\text{N})_2$ was determined at pH 3.90, combining the Bjerrum method (Eqs. (2) and (3)),¹² with Eqs. (4)–(6).^{13–15}

The highest complex concentration which matches the values A_{\max} and $\text{pH} \approx 4.20$ is on the maximum of the curve $\Delta A = f(\text{pH})$ (Fig. 2). It was not possible to calculate concentration of the complex, $c(\text{Complex})$, from A_{\max} using the Bjerrum method. Since the overall concentration of phenylephrine, $c_0(\text{HC}_9\text{H}_{12}\text{O}_2\text{N})$, *i.e.*, $c_0(\text{HL}^+)$, in the mixture was 20 times higher than the concentration of UO_2^{2+} ions, it can be considered that most of the UO_2^{2+} ions were bound in the complex, *i.e.*, the overall concentration of uranyl ions, $c_0(\text{UO}_2^{2+})$ equaled the concentration of the complex ($c(\text{Complex}) \approx c_0(\text{UO}_2^{2+})$). Therefore, the molar absorptivity, a , was calculated from the equation:

$$a = \frac{A_{\max}}{c_0(\text{UO}_2^{2+})} \quad (3)$$

The concentrations of the complex, UO_2^{2+} , and $\text{C}_9\text{H}_{13}\text{O}_2\text{N}$ (c_L) were calculated at $\text{pH} 3.90$ from the following equations:

$$c(\text{Complex}) = \frac{A}{a} \quad (4)$$

$$c_0(\text{UO}_2^{2+}) = c(\text{UO}_2^{2+}) + c(\text{Complex}) \quad (5)$$

$$c_0(\text{HL}^+) = c(\text{HL}^+) + c_L + 2c(\text{Complex}) \quad (6)$$

$$k_{d_1} = \frac{c(\text{H}^+)c_L}{c(\text{HL}^+)} \quad (7)$$

where k_{d_1} is the first dissociation constant of the phenolic hydroxylic groups of phenylephrine in aqueous solution.¹

According to Eq. (2), the stability constant of the complex, β_2 , is:

$$\beta_2 = \frac{c(\text{Complex})}{c(\text{UO}_2^{2+})c_{L^-}^2} \quad (8)$$

The stability constant β_2 was calculated for three different ionic strengths (Table I).

TABLE I. The concentration stability constants, β_2 , of the UO_2^{2+} -phenylephrine complex $\text{UO}_2(\text{C}_9\text{H}_{12}\text{O}_2\text{N})_2$ at different values of ionic strength I , $\text{pH} 3.90$, $T = 298 \text{ K}$

$I / \text{mol dm}^{-3}$	$\beta_2 \times 10^{-13}$	$\log \beta_2$
0.025	1.89	13.28
0.050	1.67	13.22
0.075	1.55	13.19

The thermodynamic stability constant of the complex, β_2^0 , was determined by extrapolation of the curve $\log \beta_2 = f(I^{0.5})$ (Fig. 7) and its value was 1.0×10^{14} . The thermodynamic parameter, the chemical potential, ΔG_2^\ominus , for the formation of the complex at room temperature (25°C) was calculated using the equation:

$$\Delta G_2^\ominus = -RT \ln \beta_2^0 = -79.6 \text{ kJ mol}^{-1} \quad (9)$$

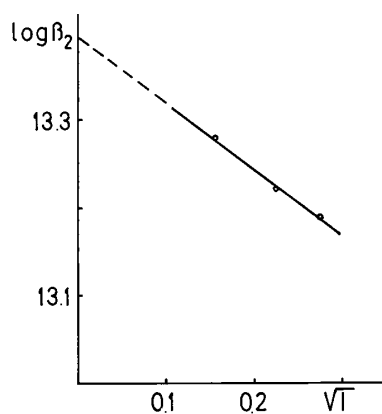


Fig. 7. Dependence of the stability constant, β_2 , of the $\text{UO}_2(\text{II})$ –phenylephrine complex on ionic strength I , $T = 298 \text{ K}$.

Possibility for quantitative determination of phenylephrine

The relatively high value of the stability constant of the uranyl(II)–phenylephrine complex enables the quantitative determination of phenylephrine from the absorbance of the complex at 340.6 nm. A curve of the dependence of the absorbance of the complex on the concentration of phenylephrine was constructed using solutions containing a constant concentration of $\text{UO}_2(\text{NO}_3)_2$ ($0.025 \text{ mol dm}^{-3}$) and different concentrations of phenylephrine at pH 3.90 and a constant ionic strength of $0.075 \text{ mol dm}^{-3}$. Water was used as the blank. A linear dependence of the absorbance of the complex on the concentration of phenylephrine was obtained in the interval 0.0025 – $0.0245 \text{ mol dm}^{-3}$. The regression equation $y = 7.88x - 0.0095$ was calculated with a high correlation coefficient of $r = 0.9997$. The accuracy of the method was determined for three different phenylephrine concentrations (Table II).

TABLE II. The spectrophotometric determination of phenylephrine

$c_{\text{phen}} / \text{mol dm}^{-3}$		$SD \times 10^4$	$CV / \%$
Taken	Found		
0.0050	0.0048	3.30	2.1
0.0125	0.0125	2.33	1.9
0.0225	0.0226	2.74	1.9

Due to the fact that the UO_2^{2+} ion forms complexes with other compounds (such as rutin,¹⁶ 3-hydroxyflavone¹¹ and hesperidin¹⁵) and these complexes have high absorbances in the spectral domain of the investigated UO_2^{2+} –phenylephrine complex, it is necessary to exclude these compounds from the investigated solutions.

CONCLUSION

The thermodynamic stability constant at $25 \text{ }^\circ\text{C}$ of the $\text{UO}_2(\text{II})$ –phenylephrine complex $\log \beta_2^0 = 14.0$ and $\Delta G_2^0 = -79.6 \text{ kJ mol}^{-1}$ indicate the formation of a stable complex. Since the absorbance of the complex at 340.6 nm is linear function of

the phenylephrine concentration without a large excess of UO_2^{2+} ions, spectrophotometric measurements can be used for the quantitative determination of phenylephrine in aqueous solutions without interfering compounds. Also, the high stability constant of the complex indicates that the complex could be used for other purposes, such as the extraction or desorption of uranyl ions.

ИЗВОД

СПЕКТРОФОТОМЕТРИЈСКО ИСПИТИВАЊЕ УРАНИЛ-ФЕНИЛЕФРИН СИСТЕМА

ЛЕПОСАВА ПАВУН¹, ДУШАН МАЛЕШЕВ¹ и ДРАГАН ВЕСЕЛИНОВИЋ²

¹Институт за физичку хемију, Фармацеутички факултет, Универзитет у Београду, Војводе Степе 450, Београд и ²Факултет за физичку хемију, Универзитет у Београду, Студентски брз 12, Београд

Применом спектрофотометријских метода и рН-метријских мерења утврђено је да $\text{UO}_2(\text{II})$ -јон и фенилефрин граде 1:2 комплекс у области рН 2,50 – 4,25 са два апсорпциона максимума на 314,2 nm и 340,6 nm. Термодинамичка константа стабилности комплекса $\text{UO}_2(\text{II})$ -фенилефрин, $\text{UO}_2(\text{C}_9\text{H}_{12}\text{O}_2\text{N})_2$, на $I = 0$ и на собној температури (25 °C) износи $\log \beta_2^0 = 14,0$, а $\Delta G_2^{\ominus} = -79,6 \text{ kJ mol}^{-1}$. Линеарна зависност апсорбације од концентрације фенилефрина у воденом раствору $\text{UO}_2(\text{NO}_3)_2$ концентрације $0,025 \text{ mol dm}^{-3}$ на 340,6 nm добијена је у интервалу $0,0025\text{--}0,0245 \text{ mol dm}^{-3}$ на рН 3,90 и $I = 0,075 \text{ mol dm}^{-3}$. Грешка мерења износи 2.1 %.

(Примљено 2. октобра 2006, ревидирано 9. марта 2007)

REFERENCES

1. A. C. Moffat, J. V. Jackson, M. S. Moss, *Clarke's Isolation and Identification of Drugs*, The Pharmaceutical Press, London, 1986, p. 893
2. E. Mutschler, H. Dernardorf, *Drug Actions*, Medipharm Scientific Publishers, Stuttgart, 1995, pp. 222 and 226
3. K. G. Bhansali, *Indian J. Pharm. Sci.* **41** (1979) 153
4. I. Muszalska, M. Zajac, G. Wrobel, M. Nogowska, *Acta Pol. Pharm.* **57** (2000) 247
5. E. H. El-Mossalamy, *Spectrochim. Acta A* **60** (2004) 1161
6. D. Malešev, D. Veselinović, Z. Radović, L. Pavun, *Arh. Farm.* **1–2** (1995) 9
7. L. Pavun, D. Malešev, D. Veselinović, *Arh. Farm.* **53** (2003) 27
8. I. Vogel, *Quantitative Inorganic Analysis*, Longmans, Green and Co, London, 1951, p. 471
9. J. Yoe, A. Jones, *Ind. Eng. Chem. Anal. Ed.* **16** (1944) 111
10. H. Irving, T. Pierce, *J. Chem. Soc.* (1959) 2565
11. D. Malešev, Z. Radović, M. Jelikić Stankov, *Monatsh. Chem.* **121** (1990) 455
12. J. Inczédy, *Analytical Applications of Complex Equilibria*, Horwood and Willy, New York, 1976, p. 137
13. D. Malešev, Z. Radović, M. Jelikić Stankov, *Monatsh. Chem.* **122** (1991) 429
14. D. Malešev, Z. Radović, M. Jelikić Stankov, *Spectrosc. Letters* **26** (1993) 1985
15. V. Kuntić, M. Kosanić, D. Malešev, Z. Radović, U. Mioč, *J. Serb. Chem. Soc.* **63** (1998) 565
16. V. Kuntić, D. Malešev, Z. Radović, M. Kosanić, *J. Agric. Food Chem.* **46** (1998) 5139.