

J. Serb. Chem. Soc. 70 (5) 753–763 (2005)
JSCS–3311

UDC 543.4/5:546.32+546.82+547.461.2:615
Original scientific paper

Determination of quercetin in pharmaceutical formations *via* its reaction with potassium titanyloxalate. Determination of the stability constants of the quercetin titanyloxalato complex

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(Received 10 May, revised 9 July 2004)

Abstract: A simple, rapid and accurate procedure for the quantitative determination of quercetin in its pure form and in formulations has been developed. The method is based on the spectrophotometric determination of a complex formed between quercetin and potassium titanyloxalate in 50 % ethanolic solutions. To characterize the quercetin titanyloxalato complex, the stability constants of the complex were determined potentiometrically and spectrophotometrically at different temperatures ($T = 26.0\text{ }^{\circ}\text{C}$, $34\text{ }^{\circ}\text{C}$ and $39.0\text{ }^{\circ}\text{C}$), as well as at different ionic strengths ($I = 5.0 \times 10^{-4}\text{ mol dm}^{-3}$, $3.0 \times 10^{-2}\text{ mol dm}^{-3}$ and $6.0 \times 10^{-2}\text{ mol dm}^{-3}$) and the thermodynamic parameters were calculated. As quercetin is usually conjugated to vitamin C in pharmaceutical formulations, two procedures for the quantitative determination of quercetin by this complexing reaction were tested – both in the absence and presence of ascorbic acid. In both procedures, the Beer law was obeyed over the same concentration range of quercetin, *i.e.*, $0.85\text{ }\mu\text{g mL}^{-1}$ – $16.9\text{ }\mu\text{g mL}^{-1}$. In the first procedure in the absence of ascorbic acid the molar absorptivity coefficient of the quercetin-titanyloxalate complex is $a = 2.49 \times 10^4\text{ mol}^{-1}\text{ dm}^3\text{ cm}^{-1}$, Sandells sensitivity of the method is $S = 1.35 \times 10^{-2}\text{ }\mu\text{g cm}^{-2}$ and the detection limit is $d = 0.67\text{ }\mu\text{g mL}^{-1}$. Whereas, in the presence of ascorbic acid (second procedure) $a = 3.04 \times 10^4\text{ mol}^{-1}\text{ dm}^3\text{ cm}^{-1}$, $S = 1.11 \times 10^{-2}\text{ }\mu\text{g mL}^{-1}$. The proposed method was verified for the determination of quercetin in pharmaceutical dosage forms.

Keywords: quercetin, potassium titanyloxalate, spectrophotometric determination, stability constants, dosage form.

INTRODUCTION

Quercetin ($\text{C}_{15}\text{H}_{10}\text{O}_7$, 2-(3,4-dihydroxyphenyl)-3,5,7-trihydroxy-4H-1-benzopyran-4-one), a plant pigment primary found in onions, tea, apples and berries, is a very important natural compound. It is a building block for several other mem-

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bers of the flavonoid family, the largest and mostly distributed group of secondary plant metabolites. Quercetin, both pure and in its glycosidic forms, exhibits a broad spectrum of biological activities.¹ For example, due to its metal chelation and free radical scavenging capacities, quercetin shows potent antioxidant properties and protects against many different disorders: asthma, heart disease, cancer, *etc.*²⁻⁴

Up to now, HPLC⁵⁻⁹ and CE¹⁰⁻¹² using various detection methods have been the most common and widely spread techniques which have been utilized to purify and measure low levels of quercetin. The majority of these techniques is devoted to the separation, identification and quantification of quercetin from plant extracts, food and plant based beverages, as well as from body fluids. These techniques require expensive instrumentation, as well as lengthy and complicated preparation procedures which are not necessary for routine analysis in pharmaceutical dosage forms. Therefore, the aim of this study was to develop a simple, inexpensive and time saving procedure for the quantitative determination of quercetin in formulations.

Due to its structure (carbonyl group in C₄, hydroxyl group in C₃ position in ring A and *ortho* OH groups in ring B), quercetin easily forms colored complexes with the metal ions from several inorganic reagents, such as NiCl₂¹³, CoCl₂¹⁴, PdCl₂¹⁵ and K₂[TiO(C₂O₄)₂].¹⁶ This feature of quercetin can be utilized for its spectrophotometric determination. In a previous work,¹⁶ it was found that the complexing reaction with potassium titanyl oxalate is particularly suitable for analytical purpose because solutions of quercetin titanyl oxalate complex (Q-TiOx) exhibit excellent characteristics for detection by spectrophotometric techniques (intense color, clear, translucent and stable in time).

For this reason, in this work the conditions of the reaction between quercetin and K₂[TiO(C₂O₄)₂] were optimized to provide a simple and sensitive procedure for the determination of quercetin in pharmaceutical dosage forms. In this way, expensive instrumental techniques and complicated procedures, generally used for quercetin determination, can be avoided. The stability constants and thermodynamic parameters for the formation of this complex were also determined in two different manners.

EXPERIMENTAL

Chemicals

Potassium titanyl oxalate and potassium hydrogen phthalate (Anala R) were obtained from BDH (Poole, England), quercetin, absolute ethanol, ascorbic acid, sodium nitrate and carbonate free sodium hydroxide were from Merck (Darmstadt, Germany). *Quercetin + C* capsules were obtained from Twin Laboratories Inc. (Ronkonkoma, New York, USA). All reagents were of p.a. grade and were used without further purification.

The sodium hydroxide was standardized by potentiometric titration against potassium hydrogen phthalate (dried 1 h at 120 °C). The stock solution of potassium titanyl oxalate was prepared in deionized water that had been boiling 30 min under a nitrogen atmosphere. Stock solutions of quercetin and sample solutions of pharmaceutical dosage forms were stored in a refrigerator and protected from sunlight.

Instrumentation

An ordinary saturated combined electrode (CW. 733, Russel, Auchtermuchy, Fife, U.K.) and a pH-meter (Radiometer, Copenhagen, Denmark) were used for pH measurements. Buffers for ethanol–water mixture (0.01 mol dm⁻³ oxalic acid and 0.01 mol dm⁻³ lithium hydrogen oxalate, as well as 0.01 mol dm⁻³ succinate and 0.01 mol dm⁻³ lithium succinate)¹⁷, pH 2.5 and pH 5.1 were used for the calibration of the pH-meter. The concentration of hydrogen ions were calculated from the activity of hydrogen ions and from the activity coefficient which was corrected according to the temperature, the ionic strength as well as the dielectric constant for a 50 % ethanol-water mixture. The temperature was controlled within: ± 0.2 °C with a circulating water thermostat (Serie U, MLW, Freital, Germany). Spectrophotometric measurements were performed on a Beckman DU-650 spectrophotometer (Fullerton, USA) using a 1 cm quartz cell.

2.3. Potentiometric measurements

The potentiometric titrations were carried out in a 51 mL glass vessel, surrounded by a thermostating jacket, and tightly closed by a cover with five openings. A thermometer, the combined electrode, nitrogen inlet tubes and a titration burette were introduced through four of the openings, whereas the remaining opening was closed with a glass stopper. To commence the experiment, 20.0 mL of the quercetin solution in absolute ethanol $[Q] = 5.0 \times 10^{-3}$ mol dm⁻³, 5.0 mL of an aqueous solution of potassium tityloxalate $K_2[TiO(C_2O_4)_2] = 5.0 \times 10^{-3}$ mol dm⁻³ and the required volume (either 0.1 mL, 0.6 mL or 1.2 mL) of an aqueous solution of sodium nitrate $NaNO_3 = 2.0$ mol dm⁻³ were transferred into the reaction vessel and diluted with deionized water to a final volume $V = 40.0$ mL. In this way, the concentrations of quercetin and potassium tityloxalate in the 50% ethanolic solution were $[Q] = 2.5 \times 10^{-3}$ mol dm⁻³ and $K_2[TiO(C_2O_4)_2] = 6.3 \times 10^{-4}$ mol dm⁻³, 3.0×10^{-2} mol dm⁻³. The reaction mixture was thermostated at the required temperature ($T = 26.0$ °C, 34.0 °C or 39.0 °C), stirred at 900 rpm, and deoxygenated by bubbling a stream of nitrogen through the liquid phase for 20 min. The inert atmosphere was maintained during titration by continuously passing nitrogen above the solution. The titration was performed with a carbonate free 50 % ethanolic solutions of sodium hydroxide, $[NaOH] = 4.8 \times 10^{-2}$ mol dm⁻³. All potentiometric titrations, with about 180 experimental points each, were done in triplicate.

Spectrophotometric measurements

Spectrophotometric determination of the stability constants. To determine the stability constants of the Q–TiOx complex at different pH values, the following solutions were prepared: quercetin in 50 % ethanol $[Q] = 5.0 \times 10^{-4}$ mol dm⁻³ and a solution containing both quercetin $[Q] = 5.0 \times 10^{-4}$ mol dm⁻³ and potassium tityloxalate $[K_2[TiO(C_2O_4)_2]] = 2.5 \times 10^{-5}$ mol dm⁻³ in 50 % ethanol. The UV-VIS absorption spectra were recorded at different pH values. In the case of pure quercetin, 50 % ethanol was used as the blank. For the second solution, a 50 % ethanolic solution of pure quercetin, at the same pH, temperature and ionic strength as in the mixture, was used as the blank.

Procedures for the spectrophotometric determination of quercetin via Q–TiOx complex. As quercetin is often conjugated to vitamin C in pharmaceutical complex formulations, two procedures for were designed the determination of quercetin via the Q–TiOx complex, one in the absence (A) and the other in the presence of ascorbic acid (B).

Procedure A

Stock solutions of quercetin in absolute ethanol, $[Q] = 1.69 \times 10^2$ $\mu\text{g mL}^{-1}$ and potassium tityloxalate in water $[K_2[TiO(C_2O_4)_2]] = 2.83 \times 10^3$ $\mu\text{g mL}^{-1}$, were prepared. To construct the calibration curve for quercetin a series of standard stock solutions of the complex, in which amount of quercetin was varied from 0.67 $\mu\text{g mL}^{-1}$ to 18.6 $\mu\text{g mL}^{-1}$, whereas the concentration of potassium tityloxalate was kept constant at $[K_2[TiO(C_2O_4)_2]] = 3.54 \times 10^2$ $\mu\text{g mL}^{-1}$, were prepared by mixing appropriate volumes of the standard stock solution of quercetin (V_1), absolute ethanol (V_2), water (V_3) and the standard stock solution of potassium-tityloxalate (V_4). The standard solutions were prepared in 20 mL volumetric flasks, the reaction were mixed in the order given above, and the fol-

lowing relations were obeyed $V_1 + V_2 = 10$ mL and $V_3 + V_4 = 10$ mL. The volumetric flasks were filled to the mark with 50 % ethanol. The values of the pH and ionic strength were adjusted according to the procedure previously described in details.¹⁸

Procedure B

In addition to the stock solutions of quercetin and potassium tityloxalate, in the same concentrations as given in Procedure A, a stock solution of ascorbic acid, $[C_6O_6H_7] = 1.88 \times 10^2 \mu\text{g mL}^{-1}$ was prepared. To construct the calibration curve for quercetin the determination of a series of standard stock solutions was prepared in the same manner as described in procedure A, except that a constant volume of the ascorbic acid solution was added (V_3), to all of them, giving a final concentration of ascorbic acid, $[C_6O_6H_7] = 17.17 \mu\text{g mL}^{-1}$. These standard solutions were allowed to stabilize for at least 20 min and the measurements were performed only after this time had elapsed.

Sample preparation from pharmaceutical formulations. For quercetin determination in *Quercetin + C* capsules, twenty capsules were weighed and the average value per capsule was calculated. An amount equivalent to the average weight of two capsules (containing 500 mg of quercetin and 1400 mg of Vitamin C, according to the manufacturer's declaration) was weighed, dissolved in absolute ethanol to a volume of 1000 mL, shaken for 15 min in an ultrasonic bath and filtered through a Whatman N° 1 filter paper. The filtered solution was collected in a clean 1000 mL volumetric flask and filled to the mark with absolute ethanol to compensate for the evaporated solvent. Then, 16.9 mL were pipetted into a 100 mL flask, and diluted with absolute ethanol to the mark. From this solution, 2.0 mL aliquots were transferred and further treated in accordance with procedures A and B. The whole procedure of sample preparation was repeated five times, and the amount of quercetin in the sample was determined as the average of five measurements.

RESULTS AND DISCUSSION

Potentiometric determination of the stability constants of the Q–TiOx complex

Characteristic titration curves obtained for the titration of the Q–TiOx complex with NaOH solutions of different ionic strengths are presented in Fig. 1.

The average number of ligands (\bar{n}) that binds to one metal ion was calculated for each point of all the titration curves from the equation:

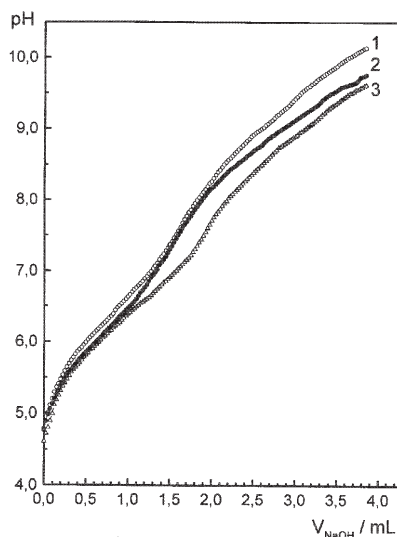


Fig. 1. Titrations curves of the Q–TiOx complex obtained at $T = 26.0$ °C for different ionic strengths: $I = 5.0 \times 10^{-4} \text{ mol dm}^{-3}$ (1), $I = 3.0 \times 10^{-2} \text{ mol dm}^{-3}$ (2) and $I = 6.0 \times 10^{-2} \text{ mol dm}^{-3}$ (3).

$$\bar{n} = \frac{c - \alpha[Q]}{c_M} \quad (1)$$

where c is the initial concentration of the protonated ligand (*i.e.*, quercetin), corrected at each point on the titration curve for the volume change caused by the addition of the standard alkali, $[Q]$ is the free quercetin concentration and c_M is the initial metal ion concentration (*i.e.*, potassiumtitanxyoxalate). α is calculated from: $\alpha = 1 + c_H K_{1Q} + 2c_H^2 \beta_{2Q}$, where c_H is the concentration of hydronium ions and K_{1Q} and β_{2Q} are the dissociation constants of quercetin alone.¹⁹

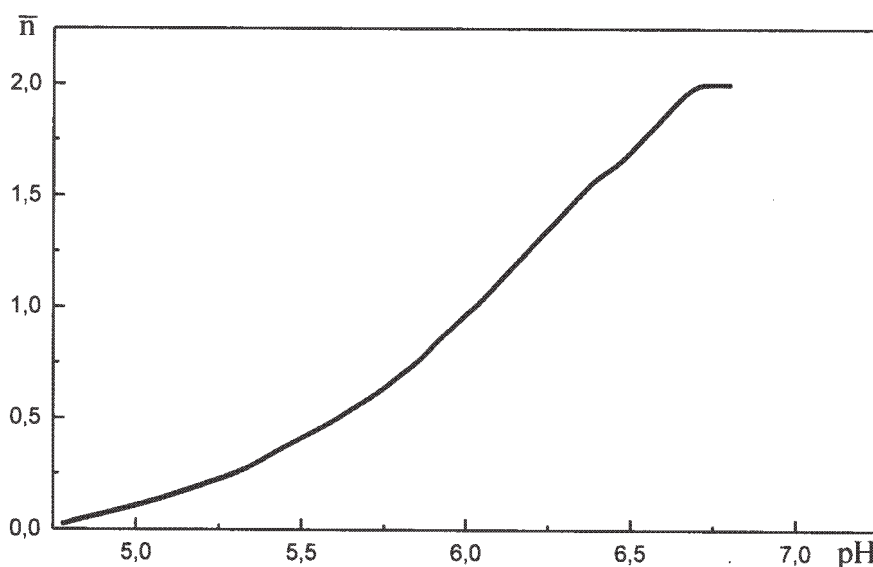


Fig. 2. The complex formation curve, $\bar{n} = f(\text{pH})$ obtained at $T = 26.0\text{ }^\circ\text{C}$, $I = 5.0 \times 10^{-3}\text{ mol dm}^{-3}$, $[Q] = 2.5 \times 10^{-3}\text{ mol dm}^{-3}$, $[K_2[\text{TiO}(\text{C}_2\text{O}_4)_2]] = 6.3 \times 10^{-4}\text{ mol dm}^{-3}$.

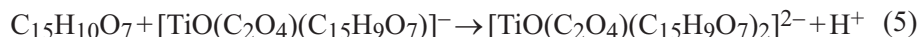
The resulting complex formation curve is shown in Fig. 2 from which the maximal value for the average number of ligands is determined to be $\bar{n} = 2$. This implies that two stability constants, partial and cumulative, exist for the same temperature and ionic strength. In a previous work,¹⁶ the maximum number of ligand (N) for the Q-TiOx complex was found to be two ($N = 2$). Therefore, the following relation between the average ligand number (\bar{n}) and the stepwise formation constant can be applied:²⁰

$$\frac{\bar{n}}{(\bar{n} - 1)[Q]} = \frac{(2 - \bar{n})[Q]}{\bar{n} - 1} \beta_1 - K_1 \quad (2)$$

where K_1 and β_2 are the partial stability constant and the cumulative constant of the complex, respectively, according to Irving and Rossotti.²¹ Thus, the overall reaction between quercetin and the tianyoxalate anion is:



and the stepwise equilibrium reactions are:



The stepwise formation constants, K_1 and K_2 , corresponding to the stepwise equilibrium reactions (4) and (5), respectively, can be calculated from equations (6) and (7).

$$K_1 = \frac{[\text{TiO}(\text{C}_2\text{O}_4)(\text{C}_{15}\text{H}_9\text{O}_7)]^-}{[\text{C}_{15}\text{H}_{10}\text{O}_7][\text{TiO}(\text{C}_2\text{O}_4)_2]^{2-}} \quad (6)$$

$$K_2 = \frac{[\text{TiO}(\text{C}_2\text{O}_4)(\text{C}_{15}\text{H}_9\text{O}_7)_2]^{2-}}{[\text{C}_{15}\text{H}_{10}\text{O}_7][\text{TiO}(\text{C}_2\text{O}_4)(\text{C}_{15}\text{H}_9\text{O}_7)]^-} \quad (7)$$

and the cumulative stability constant β_2 , for the overall reaction, is:

$$\beta_2 = K_1 K_2 = \frac{[\text{TiO}(\text{C}_2\text{O}_4)(\text{C}_{15}\text{H}_9\text{O}_7)_2]^{2-}}{[\text{C}_{15}\text{H}_{10}\text{O}_7]^2 [\text{TiO}(\text{C}_2\text{O}_4)_2]^{2-}} \quad (8)$$

If equation (2) is solved graphically, by plotting $\frac{\bar{n}}{(\bar{n}-1)[Q]} = f\left(\frac{2-\bar{n}[Q]}{\bar{n}-1}\right)$ (9)

are obtained from the straight line dependence the values of β_2 , from the slope, and $-K_1$, from the intercept (Fig. 3). The values of the thermodynamic stability constants (β_2^0), are obtained by extrapolating $\log \beta_2 = f(I^{1/2})$ to infinite dilution. The values of the partial (K_1), cumulative (β_2) and thermodynamic stability constants (β_2^0) for the Q-TiOx complex determined in this way are given in Table I.

Therefore, the values of the thermodynamic parameters ΔG , ΔH and ΔS for the complex formation were determined. Changes in the standard free energy were es-

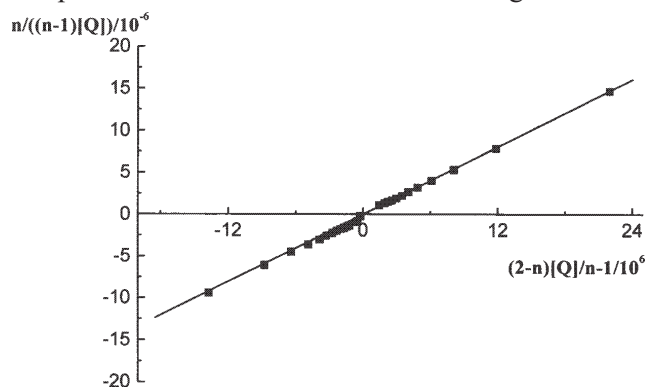


Fig. 3. Graphic presentation of function (9) obtained at $T = 26.0$ °C, $I = 5.0 \times 10^{-4}$ mol dm $^{-3}$, $[Q] = 2.5 \times 10^{-3}$ mol dm $^{-3}$ and $[K_2[\text{TiO}(\text{C}_2\text{O}_4)_2]] = 6.3 \times 10^{-4}$ mol dm $^{-3}$.

timated from the average value of the thermodynamic stability constants, $\Delta G = -RT \ln \beta_2^0$, whereas the values of ΔH and ΔS were estimated from the linear dependence of the logarithm of the thermodynamic stability constant (β_2^0) on the inverse temperature, $\log \beta_2^0 = f(1/T)$, implicitly assuming that they were not temperature dependent in the investigated range. In this way, the values $\Delta G_{299} = -68 \text{ kJ mol}^{-1}$, $\Delta G_{307} = -71 \text{ kJ mol}^{-1}$, $\Delta G_{132} = -71 \text{ kJ mol}^{-1}$, $\Delta H = 41 \text{ kJ mol}^{-1}$, and $\Delta S = 0.4 \text{ kJ mol}^{-1} \text{ K}^{-1}$ were obtained, showing that the reaction between quercetin and potassiumtitanoyloxalate is thermodynamically favorable, and occurs spontaneously in the investigated temperature interval.

Spectrophotometric determination of the stability constants of the Q-TiOx complex

In a 50 % ethanol-water solution, quercetin and potassiumtitanoyloxalate form a 2:1 complex having a distinctive yellow-orange color.¹⁶ To calculate the concentration stability constants for the Q-TiOx complex at different ionic strengths the Bjerrum's method²² modified in a manner described earlier in detail,^{15,18} was applied. The cumulative stability constants of the Q-TiOx complex are given in Table I. As can be seen the agreement with the stability constants obtained potentiometrically is good.

TABLE I. Stability constants for the Q-TiOx complex

$T/^\circ\text{C}$	$I/\text{mol dm}^{-3}$	Potentiometric		Spectrophotometric
		Partial stability constant $\log K_1$	Cumulative concentration stability constant, $\log \beta_2$	Cumulative concentration stability constant, $\log \beta_2$
26.0	0	5.5	12.0*	11.8
	5.0×10^{-4}	5.5	12.0	11.8
	3.0×10^{-2}	5.3	11.9	10.9
	6.0×10^{-2}	5.2	11.8	10.8
34.0	0	5.6	12.1	11.9
	5.0×10^{-4}	5.6	12.1	11.9
	3.0×10^{-2}	5.5	11.7	11.3
	6.0×10^{-2}	5.5	11.6	11.2
39.0	0	5.6	12.2	12.1
	5.0×10^{-4}	5.5	12.2	12.0
	3.0×10^{-2}	5.4	11.6	11.4
	6.0×10^{-2}	5.2	11.5	11.0

*The thermodynamic stability constant, β_2^0

Analytical application

After evaluating the thermodynamic data and verifying that a sufficiently stable complex between quercetin and potassium titylooxalate is formed at all the investigated temperature as well as ionic strengths it was reaffirmed that the previously determined conditions, 50 % ethanol as solvent, $\lambda = 430$ nm, pH 7.2 ionic strength $I = 7.5 \times 10^{-5}$ mol dm⁻³ and temperature $T = 23.0$ °C, are the most suitable for the spectrophotometric determination of quercetin *via* the complexing reaction between quercetin and potassium titylooxalate. Under those conditions, both procedures, A and B gave a linear relationship between the absorbance and the concentrations of quercetin over the same concentration range $0.85 \mu\text{g mL}^{-1} - 16.9 \mu\text{g mL}^{-1}$, and with the highest sensitivity. Compared to procedure A, procedure B requires a longer time, because the standard solutions have to stabilize for at least 20 minutes. Namely, in the presence of ascorbic acid, the absorbance of the Q–TiOx complex changes rapidly during the first 20 minutes, and remains constant thereafter (Fig. 4). This is due to the well-known capability of quercetin to reduce the ascorbyl radical – the so-called ascorbate protective function.²³ The parameters of the linear calibration curves ($A = Xc + Y$, where A is the absorbance of a 1 cm layer, X is the slope, Y is the intercept, and c is the concentration of quercetin in $\mu\text{g mL}^{-1}$), as well as the corresponding correlation coefficients (r) are given in Table II, together with the molar absorption coefficients (a), Sandell's sensitivity (S) and the limits of detection (d).

Both procedures, A and B, were tested for precision, sensitivity and reproducibility. The precision was established by repeated assays ($n = 5$) using three dif-

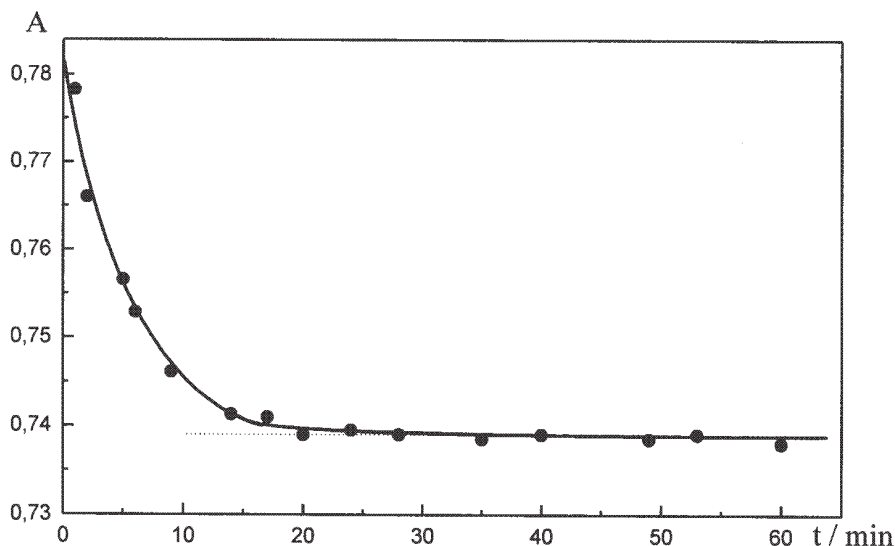


Fig. 4. Absorbance at $\lambda = 430$ nm of the Q–TiOx complex in the presence of ascorbic acid. $[Q] = 8.45 \mu\text{g mL}^{-1}$, $[K_2[TiO(C_2O_4)_2]] = 354 \mu\text{g mL}^{-1}$, $[C_6O_6H_7] = 17.17 \mu\text{g mL}^{-1}$, $T = 26.0$ °C, $I = 7.5 \times 10^{-5}$ mol dm⁻³ and pH 7.2.

ferent concentration of quercetin that are within the Beer's law limits, Table III. The standard deviations 0.05 – 0.09 and RSD values less than 3 %, indicate high precision and reproducibility.

Applicability of both procedures was tested for Quercetin + C capsules, Table III. Both the proposed procedures for the spectrophotometric determination of quercetin are applicable. Although the recovery values lie within the required range of $\pm 5\%$ (Ph EUR 97), procedure A is of lower accuracy and is not recommendable in the case of high dosage drugs. Procedure B gives excellent accuracy and is recommendable for quercetin determination in the presence of vitamin C.

TABLE II. Analytical parameters for the determination of quercetin concentrations at $T = 23.0\text{ }^{\circ}\text{C}$ and $\lambda = 430\text{ nm}$

Procedure	A	B
Regression equation *		
Slope, x	0.0738	0.0809
Intercept, y	0.0074	0.0071
Correlation coefficient, r	0.999	0.998
Molar absorptivity/ $10^{-4}\text{ dm}^3\text{ mol}^{-1}\text{ cm}^{-1}$	2.50	3.04
Sandell's sensitivity/ $\mu\text{g cm}^{-2}$	0.0135	0.0111
Limit of detection**/ $\mu\text{g mL}^{-1}$	0.67	0.72

* $A = xC + y$, where C is the concentration in $\mu\text{g mL}^{-1}$; ** Defined as the concentration that produces a signal-to-noise ratio of 3

TABLE III. Precision and recovery of quercetin concentration in bulk drugs capsules

Sample	Procedure	[Q]/ $\mu\text{g mL}^{-1}$	Found \pm Sd/ $\mu\text{g mL}^{-1}$	RSD	RC/(%)
Quercetin bulk drug	A	1.05	1.09 ± 0.06	2.02	103.80
		7.72	7.74 ± 0.06	0.60	100.25
		15.20	15.33 ± 0.09	1.30	100.85
	B	1.05	1.02 ± 0.05	1.80	97.14
		7.72	7.70 ± 0.05	0.50	99.74
		15.20	15.17 ± 0.08	1.20	99.80
Quercetin + C capsules	A	8.45	8.83 ± 0.45	2.80	104.49
	B	8.45	8.42 ± 0.09	0.40	99.64

Acknowledgment: We gratefully acknowledge the financial support of the Ministry of Sciences, Technologies and Development of the Republic of Serbia (Grant No. 1458).

ИЗВОД

ОДРЕЂИВАЊЕ КВЕРЦЕТИНА У ФАРМАЦЕУТСКИМ ПРЕПАРАТИМА
ПРЕКО РЕАКЦИЈЕ СА КАЛИЈУМ-ТИТАНИЛОКСАЛАТОМ. ОДРЕЂИВАЊЕ
КОНСТАНТИ СТАБИЛНОСТИ КВЕРЦЕТИН-ТИТАНИЛОКСАЛАТНОГ
КОМПЛЕКСА

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Предложен је брз, једноставан и тачан метод за одређивање кверцетина у фармацеутским сировинама и дозираним облицима. Метод је базиран на спектрофотометријском одређивању комплекса формираног између кверцетина и калијум-титанилоксалата у 50 % етанолу. Одређене су константе стабилности кверцетин титанилоксалатног комплекса потенциометријски и спектрофотометријски на различитим температурама ($T = 26,0\text{ }^{\circ}\text{C}$, $34,0\text{ }^{\circ}\text{C}$, $39,0\text{ }^{\circ}\text{C}$) и јонским јачинама ($I = 5,0 \times 10^{-4}\text{ mol dm}^{-3}$, $3,0 \times 10^{-2}\text{ mol dm}^{-3}$, $6,0 \times 10^{-2}\text{ mol dm}^{-3}$) и израчунати су термодинамички параметри. Како се кверцетин уобичајено налази заједно са витамином С у дозираним облицима, предложене су две процедуре за одређивање кверцетина: без и у присуству аскорбинске киселине. У обе предложене процедуре, Веер-ов закон важи у области $0,85\text{ }\mu\text{g mL}^{-1} - 16,9\text{ }\mu\text{g mL}^{-1}$ кверцетина. Према првој процедури, моларни апсорпциони коефицијент кверцетин-титанилоксалатног комплекса је $a = 2,49 \times 10^4\text{ mol}^{-1}\text{ dm}^3\text{ cm}^{-1}$, Санделова осетљивост методе је $S = 1,35 \times 10^{-2}\text{ }\mu\text{g cm}^{-2}$, а лимит детекције је $d = 0,67\text{ }\mu\text{g mL}^{-1}$. Према другој процедури, $a = 3,04 \times 10^4\text{ mol}^{-1}\text{ dm}^3\text{ cm}^{-1}$, $S = 1,11 \times 10^{-2}\text{ }\mu\text{g cm}^{-2}$ и $d = 0,72\text{ }\mu\text{g mL}^{-1}$. Предложени метод је примењен за одређивање кверцетина у дозираним облицима.

(Примљено 10. маја, ревидирано 9. јула 2004.)

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