PHYSICAL CHEMISTRY 2012

11th International Conference
on Fundamental and Applied Aspects of
Physical Chemistry

Under the auspices of the
University of Belgrade

Proceedings

The Conference is dedicated to
Professor Ivan Draganić

September 24-28, 2012
Belgrade, Serbia

ISBN 978-86-82475-27-9 ***Volume*** **1**
ISBN 978-86-82475-28-6 ***Volume*** **II**

Title: PHYSICAL CHEMISTRY 2012 (Proceedings)
Editors: S. Anić and Ž. Čupić
Published by: Society of Physical Chemists of Serbia, Studenski trg 12-16, 11158, Belgrade, Serbia
Publisher: Society of Physical Chemists of Serbia
For Publisher: S. Anić, President of Society of Physical Chemists of Serbia
Printed by: "Jovan" Priting and Publishing Company; 200 Copies;
Number of pages: 6+ 497; **Format**: B5; Printing finished in September 2012.

Text and Layout: "Jovan"

200- *Coppy printing*

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D-19-P

DETERMINATION OF PIROXICAM IN PHARMACEUTICAL BASED ON AN OSCILLATING CHEMICAL REACTION

N. Sarap[1], N. Pejić [2], J. Maksimović[3]

[1]*Institute of Nuclear Science Vinča, Radiation and Environmental Protection Department, University of Belgrade, Mihajla Petrovića Alasa 12-14, P.O. Box 522, 11000 Belgrade, Serbia*
[2]*Faculty of Pharmacy, University of Belgrade, Vojvode Stepe 450, 11000 Belgrade, Serbia, e-mail:nata@pharmacy.bg.ac.rs*

Abstract
A novel procedure for kinetic determination of piroxicam (PX) by the concentration perturbations of the Bray-Liebhafsky (BL) oscillatory chemical system was proposed. The response of the BL matrix in a stable non-equilibrium stationary state close to the bifurcation point, to the perturbation by different concentrations of PX, is followed by a Pt-electrode. Under the optimized reaction conditions, the linear relationship between maximal potential shift ΔE_m, and PX concentration was obtained in the concentration range 6.8×10^{-5} mol L^{-1} – 1.7×10^{-3} mol L^{-1} with a detection limit of 3.5×10^{-5} mol L^{-1}. The method had a rather good sample throughput (ST) of 45 samples h^{-1} with the recovery RCV = 103.7 %. Applicability of the proposed method to the direct determination of PX in pharmaceutical formulation (injections) was demonstrated.

Introduction
Piroxicam (PX), is a non-steroidal anti-inflammatory drug from oxicams family with analgesic and anti-pyretic activities. This effective analgesic and anti-inflammatory agent is used in the treatment of rheumatoid arthritis, osteoarthritis, ankylosing spondylitis, and acute pain in musculoskeletal disorder and acute gout.
For determination of PX in various real samples, apart from potentiometric, voltametric and fluorimetric techniques, chromatographic and spectrophotometric techniques have been used most extensively [1]. Some of those methods are cumbersome, time-consuming or not enough sensitive. Therefore, some new methods based on relatively simple and inexpensive equipment were desirable. Regarding that, the kinetic method based on employing the analyte pulse perturbation technique (APP) to the Bray-Liebhafsky (BL) oscillatory reaction [2] as very nonlinear system, as well as using the potentiometric monitoring of analyte perturbation, promise alternative to some instrumental methods due to its low cost instrumentation, and relatively rapid detection procedure. The applied method, which has already been described [3], provides simple, effective and convenient method to assay the pharmaceutical samples.

Experimental

The BL matrix was conducted in the CSTR. Peristaltic pumps controlled the flows (inflow and outflow) of reactants (KIO_3, H_2SO_4 and H_2O_2). The chosen dynamic structure for perturbation analysis is stable non-equilibrium stationary state in vicinity of the bifurcation point that was found under the following experimental conditions: the mixed inflow concentration of reactants $[H_2SO_4]_o = 9.7 \times 10^{-2}$ M, $[KIO_3]_o = 5.9 \times 10^{-2}$ M, $[H_2O_2]_o = 1.50 \times 10^{-1}$ M, specific flow rate, $j_o = 2.95 \times 10^{-2}$ min^{-1} and T = 67.0 ± 0.2 °C. Temporal evolution of the BL matrix was recorded by means of a Pt electrode and double junction Ag/AgCl electrode interfaced to a PC-AT 12 MHz compatible computer *via* a PC-Multilab EH4 16–bit ADC. Perturbations of matrix system were performed with 50 μL of the methanol standard solution of PX.

Results and Discussion

From the obtained dynamic structures observed under the above described conditions and the found bifurcation point ($[H_2SO_4]_0 = 9.65 \times 10^{-2}$ mol L^{-1}) [4] we have selected the non-equilibrium stable stationary states of the matrix that will be used for perturbation with PX (the non-equilibrium stationary states that are realized for $[H_2SO_4]_0 = 9.7 \times 10^{-2}$ mol L^{-1}).

The APP used for quantitative determination of PX, is based on potentiometric monitoring of the response of the non-linear matrix to perturbations induced by different concentrations of PX (Fig. 1.). The maximal change in potential (in mV), that is used as indicator of the perturbation strength, is defined as the difference $\Delta E_m = E_p - E_s$, where E_p is the maximal potential value attained after the perturbation is performed and E_s is the potential corresponding to the stable stationary state before the perturbation is performed (Fig. 1.). In the PX concentration range between 6.8×10^{-5} mol L^{-1} and 1.7×10^{-3} mol L^{-1}, the regression equation of the standard series calibration curve is $\Delta E_m = -5.6 - 1.9 \times 10^4 c_{PX}$ (r = 0.995). The detection limit of the method is 6.5×10^{-5} mol L^{-1}.

In order to study the validity of the proposed method, it was applied to the determination of PX in injections (Pfizer, Greek). The Table 1 shows the obtained results; it can be seen that the RCV is 103.7 % indicating that the developed method is free from interference and it provides accurate results.

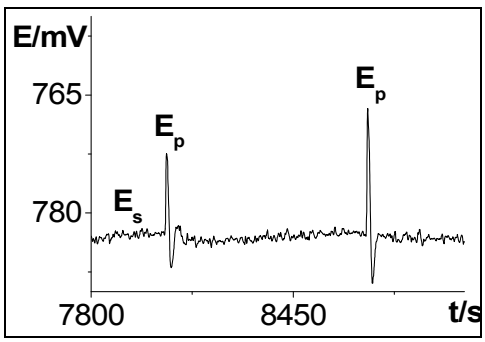

Figure 1. Typical response curves obtained after perturbing the stationary state in the BL reaction by addition of different concentrations of PX (from left to right): 2.9×10^{-4} mol L^{-1} and 7.7×10^{-4} mol L^{-1}.

Table 1. Precision and recovery of PX in pharmaceutical dosage form.

Sample[a]	Claimed (mg/mL)	Concentration found	RSD (%)	RCV (%)
PX-injection	20	20.62	1.3	103.7

[a]Sample also containing: benzyl alcohol, ethanol, hydrochloric acid, nicotinamide, propylene glycol, monobasic sodium phosphate, sodium hydroxide and water for injection

Conclusion

The proposed method for the determination of PX is fast (45 samples h^{-1}), accurate (RSD is 1.3 %) and precise (RCV = 103.7 %). It was proved to be very appropriate for routine analysis of pharmaceuticals without any pretreatment of the samples apart from their dissolution; it could be also used for their quality control.

Acknowledgement

The present investigations were partially supported by The Ministry of Sciences and Education of Serbia, under Projects 172015 and III43009.

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CIP Volume I

CIP - Каталогизација у публикацији
Народна библиотека Србије, Београд

544(082)
621.35(082)
66.017/.018(082)

MEĐUNARODNA konferencija iz fundamentalne i primenjene fizičke hemije (11 ; 2012 ; Beograd)
Physical Chemistry 2012 : proceedings. #Vol. #1 / 11th International Conference on Fundamental and Applied Aspects of Physical Chemistry, September 24-28, 2012, Belgrade ; [editors S.[Slobodan] Anić and Ž.[Željko] Čupić ; organized by Society of Physical Chemists of Serbia ... et al.]. - Belgrade : Society of Physical Chemists of Serbia, 2012 (Belgrade : Jovan). - VI, 498 str. : ilustr. ; 24 cm

"The Conference is dedicated to Professor Ivan Draganić" --> nasl. str. - Tiraž 200. - Bibliografija uz svaki rad.

ISBN 978-86-82475-27-9
1. Društvo fizikohemičara Srbije (Beograd)
a) Физичка хемија - Зборници b) Електрохемијско инжењерство - Зборници c) Наука о материјалима - Зборници
COBISS.SR-ID 193432332

CIP Volime II

CIP - Каталогизација у публикацији
Народна библиотека Србије, Београд

544(082)
621.35(082)
66.017/.018(082)

MEĐUNARODNA konferencija iz fundamentalne i primenjene fizičke hemije (11 ; 2012 ; Beograd)
Physical Chemistry 2012 : proceedings. #Vol. #2 / 11th International Conference on Fundamental and Applied Aspects of Physical Chemistry, September 24-28, 2012, Belgrade ; [editors S.[Slobodan] Anić and Ž.[Željko] Čupić ; organized by Society of Physical Chemists of Serbia ... et al.]. - Belgrade : Society of Physical Chemists of Serbia, 2012 (Belgrade : Jovan). - VI str., 499-782 str. : ilustr. ; 24 cm

"The Conference is dedicated to Professor Ivan Draganić" --> nasl. str. - Tiraž 200. - Bibliografija uz svaki rad. - Registar.

ISBN 978-86-82475-28-6
1. Društvo fizikohemičara Srbije (Beograd)
a) Физичка хемија - Зборници b) Електрохемијско инжењерство - Зборници c) Наука о материјалима - Зборници
COBISS.SR-ID 193433356