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HOSTS of the CONGRESS

On behalf of the Scientific and Organizing Committees, it is our great pleasure to invite scientists, researchers and practitioners of pharmacy and other related professionals to participate in the 6th Congress of Pharmacy in Macedonia with international participation which will be held on June 1-5 2016 in Ohrid, Macedonia. The hosts of the Congress are Macedonian Pharmaceutical Association and Faculty of Pharmacy, Ss Cyril and Methodius University.

We believe that scientific program including plenary lectures, oral presentations and poster sessions will result in enrichment of knowledge and exchange of experience among scientists, researchers and practitioners. The Congress will cover new challenges in all fields of pharmaceutical science and professional practice. It will provide an excellent opportunity for young scientists and researchers as well as renowned researches and practitioners to exchange opinions, introduce ground-breaking ideas and acquire new practical knowledge.

The exhibition of pharmaceutical companies and other companies belonging to the chain of suppliers of medicines and pharmaceutical products will be an integral part of the Congress.

The attractive and rich social program will create a perfect atmosphere for connecting with longtime fellows, building long- lasting friendships and memorable friendly gatherings.

We look forward to welcoming you in Ohrid, a beautiful Macedonian pearl, situated along the coast of Ohrid Lake in June 2016.

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Chair of the Scientific committee
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Generation and Combined Study on the Chemical Structure of Nitrofurantoin Radical Anion

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Introduction

Nitrofurantoin (N-(5-nitro-2-furfurylidene)-1-aminohydantoin) is antimicrobial compound, used extensively as a prophylactic for urinary tract infections in humans and animals (Maaland and Guardabassi, 2011). It is reported that the modes of action underlying DNA damage or cytotoxicity induced by nitrofurantoin in rodent liver and lungs may involve ROS generation by reduction to nitro radical anion (Suntres and Shek, 1992). A recent study showed that the drug exhibits carcinogenicity in the kidneys of male rats and the structure of the nitro furan plays a key role in the induced genotoxicity (Kijima et al., 2015).

Despite these drawbacks, new nitrofuran derivatives are still being developed as antimicrobial agents (Zorzi et al., 2014). Therefore, improved knowledge on the structure and reactivity of nitrofurantoin radical anion could help reduce the toxicity of the new nitrofuran antimicrobial agents.

This reports motivated us to generate electrochemically the nitro radical anion of nitrofurantoin and study its chemical structure by spectroscopic IR methods and DFT computations.

Material and Methods

The electrochemical generation of nitrofurantoin radical anion was performed in a special CaF_2 cell, provided with platinum electrodes build in the polyethylene spacer. 4.5 V were applied to the cathode in the solution cell containing 0.1 mol/l nitrofurantoin and equimolar amount of tetraethylammonium bromide in DMSo-d_6. The IR spectra were measured on a Brucker Tensor 27 FT spectrometer at a resolution of 2 cm^{-1} and 64 scans.

All theoretical calculations were performed using the Gaussian 09 package of programs. Geometry optimization and vibrational frequencies were performed by analytical gradient technique without any symmetry constraint at DFT B3LYP/6-311+G(2df,p)-IEFPCM level of theory.

Results and discussion

The initial IR spectrum of nitrofurantion in DMSO-d6 solution, containing tetraethylammonium bromide as electrolyte salt, showed that the asymmetric and symmetric stretching vibrations of the nitro group are observed at 1521 and 1350 cm-1. The stretching vibration of the N-C bond linking the nitro group to the furan ring is found at rather high wavenumber - 1211 cm-1, respectively. A few minutes after applying the current, the solution in cathode space became brown, and the bands of the anion radical of nitrofurantoin appeared in the IR spectrum. More prolonged electrolysis (75 min) caused strong increase of the bands of the anion radical, while the bands of the neutral compound vanished. Reversal in the polarity of the electrolysis cell resulted in gradual decrease of the IR bands of the radical anion and reappearance of the neutral molecule absorptions. After 75 min of reversed electrolysis the initial spectrum of the parent compound was completely restored without the presence of any additional IR bands. This fact unambiguously demonstrates that the observed spectral changes are due to the reduction of nitrofurantoin to radical anion and not to chemical transformation to other products.

The conversion of nitrofurantoin into radical anion is related to strong frequency decreases in the assymetric N-O stretching: $\Delta vas(NO2) = 220$ cm-1, strong frequency decreases in the symetric N-O stretching: $\Delta vs(NO2) = 209$ cm-1 and strong frequency increase in C-NO2 stretching: $\Delta v(C\text{-}NO2) = 273$ cm-1. Based on the calculated spin density, the odd electron is localized mainly on the nitro group (c.a. 70 %) and in smaller extends – on the furan ring (c.a. 30 %). The radical anion formation leads to simultaneous shortening of the C-N bond and lengthening of the N-O bonds.

Conclusion

The observed frequency shifts arising from the conversion of nitrofurantoin into radical anion are larger than those found with the conversion of dinitrobenzenes and cyanobenzonitriles. It is evidence

that larger structural variations in the nitrofuran moiety occur upon conversion into radical anion than in case of dinitrobenzenes and nitrobenzonitriles. The localization of the spin density over the nitro group is a sign for high reactivity of the formed nitrofurantoin radical anion and strong ability to initiate production of various ROS via electron donation.

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