

4<sup>th</sup> Annual Conference and Expo on **Biomaterials**

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**Argatroban immobilization on Cu-modified PVC and PU**Liana Azizova<sup>1</sup>, Volodymyr Chernyshenko<sup>2</sup> and Lyuba Mikhalovska<sup>1</sup><sup>1</sup>University of Brighton, UK<sup>2</sup>Palladin Institute of Biochemistry of the National Academy of Sciences of Ukraine, Ukraine

Thrombosis induced by biomaterials after their contact with blood is a main reason of medical device failure. To make material surface more thromboresistant different approaches have been undertaken. NO generating biomaterial has proven to play a crucial role in the prevention of thrombosis by inhibiting the platelets activation/adhesion. However, immobilization of the direct thrombin inhibitors onto material surface makes material more thromboresistant by preventing thrombin-mediated blood clotting. The aim of this research was to immobilize argatroban a direct thrombin inhibitor with reliable and predictable anticoagulant effect onto PVC and PU polymers. Both polymers were first imprinted with Cu ions for the catalytic generation of NO (this research was reported earlier). Argatroban was immobilized on the Cu-modified PVC and PU using the polydopamine ad-layer via the Michael addition/Schiff base reaction. The amount of argatroban bound to the polymer surface was measured (spectrophotometric determination at 334 nm) as 11.92 nmol/cm<sup>2</sup> on PVC and 13.10 nmol/cm<sup>2</sup> on PU surface. Assay using thrombin-specific chromogenic substrate was performed to evaluate the thrombin inhibition capacity of argatroban-modified polymers. It was found that both Argatroban-modified polymers inhibit thrombin activity in PBS. In order to confirm the NO generation catalyzed by Cu/Arg-modified PVC and PU samples after incubation with 100 μM GSNO/GSH in the PBS during 1h was examined using ArrowSTRAIGHT™ nitric oxide measurement system (Lazar Research Laboratories, Los Angeles, CA, USA). The Cu/Arg-modified PVC and PU generate NO with the rate 1.27-1.66×10<sup>10</sup> mole/cm<sup>2</sup>·min which is within the physiological level. From the data obtained it's possible to conclude, that immobilization of Argatroban to the Cu-modified polymers showed combine abilities: i) generate NO caused by Cu ions and ii) have capacity to inhibit thrombin formed in the blood via surface immobilized argatroban.

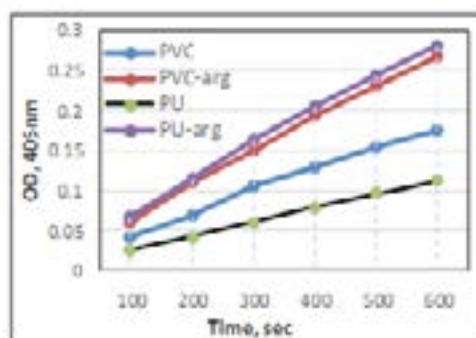


Figure 1: Generation of pNa from chromogenic substrate S2238 by 0.4 NIH/ml of thrombin that was pre-incubated with PU or PU modified with Argatroban during 20 min. The remnant thrombin activity is being measured.

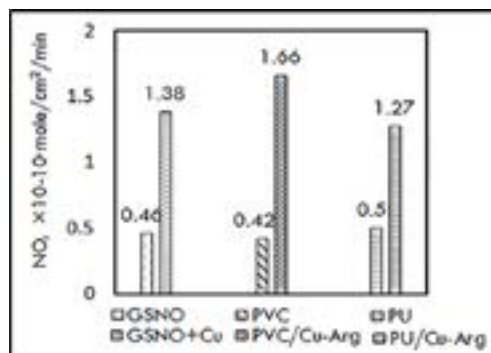


Figure 2: NO generation after incubation of Cu/Arg-modified PVC and PU with 100 μM GSNO/GSH in the PBS during 1h.

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## Recent Publications

1. K Kulyk, B Palianytsia, J D Alexander, L Azizova, M Borysenko, M Kartel, M Larsson and T Kulik (2017) Kinetics of valeric acid ketonization and katenization in catalytic pyrolysis on nanosized SiO<sub>2</sub>, γ-Al<sub>2</sub>O<sub>3</sub>, CeO<sub>2</sub>/SiO<sub>2</sub>, Al<sub>2</sub>O<sub>3</sub>/SiO<sub>2</sub> and TiO<sub>2</sub>/SiO<sub>2</sub>. ChemPhysChem 18:1943.
2. L R Azizova, T V Kulik, B B Palianytsia and N A Lipkovska (2015) Thermal and hydrolytic stability of grafted ester groups of carboxylic acids on the silica surface. J Therm. Anal. Calorim 122:517.
3. Liana Azizova, Tetiana V Kulik, Borys B Palianytsia, Aleksandr E Zemlyakov, Viktoriya N Tsikalova and Vasiliy Ya Chirva (2005) Investigation of chemical transformations of thiophenylglycoside of muramyl dipeptide on the fumed silica surface using TPD-MS, FTIR spectroscopy and ES IT MS. Nanoscale Research Letters 9:234.
4. T V Kulik, L R Azizova, B B Palyanytsya, A E Zemlyakov and V N Tsikalova (2010) Mass spectrometric investigation of synthetic glycoside of muramyl dipeptide immobilized on fumed silica surface. Mater Sci Eng B. 169:114.
5. A E Zemlyakov, V N Tsikalova, L R Azizova, V Ya Chirva, E L Mulik, M V Shkalev, O V Kalyuzhin and M V Kiselevsky (2008) Synthesis and Biological Activity of Aryl S-β-Glycosides of 1-Thio-N-Acetylmuramyl-L-Alanyl-D-isoglutamine. Russ. J. Bioorg. Chem. 34:223.

## Biography

Liana Azizova received her Master degree at Taurida National V.I. Vernadsky University in 2005. She got PhD in Surface Chemistry in 2013. She has her expertise in the area of surface chemistry, surface characterization, catalytic reactions on the surface of inorganic oxides, their kinetics and mechanisms and synthesis of hybrid organic-inorganic nanocomposites. It includes the development of biocompatible coating materials and composites for biomedical application. In particular, modification of polymer and nanosized oxides surfaces by biologically active compounds and biopolymers (polysaccharides, glycopeptides, carboxylic acids), adsorption and determination of a structure of an adsorption layer of biomolecules on a surface of inorganic oxides. Also, she dealt with heterogeneous catalytic reactions on the surface of inorganic oxides, their kinetics and mechanisms. Another area of her activity is mass spectrometric investigation of biomolecules interaction with inorganic oxide surfaces and thermal transformations of biomolecules on inorganic oxide surfaces using thermal analysis.

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