

# Lactic acid and glucose-responsive micelles of poly( $\epsilon$ -caprolactone)-*b*-poly(ethylene oxide) block copolymers with phenylboronic ester as a sensitive blocks connector

Mariusz Uchman<sup>1\*</sup>, David Vrbata<sup>1</sup>

<sup>1</sup>*Department of Physical and Macromolecular Chemistry, Faculty of Science, Charles University in Prague,  
Hlavova 2030, 128 40 Prague 2, Czech Republic*

\**uchman@natur.cuni.cz*

Synthesis, self-assembly and responsiveness to glucose and lactic acid of a novel biocompatible and biodegradable block copolymer micelles that contains phenylboronic ester as a blocks linker between the hydrophobic poly( $\epsilon$ -caprolactone) (PCL) and the hydrophilic poly(ethylene oxide) (PEO) is described herein. Synthetic procedure to prepare successfully PCL block with pendant phenylboronic acid (BA) combines ring-opening polymerization (ROP) of  $\epsilon$ -CL initiated by 4-hydroxymethyl(phenylboronic) acid pinacolate and pinacol deprotection step. The second block glucose terminated PEO was obtained by 1,3-dipolar cycloaddition Cu(I)-catalyzed alkyne-azide reaction of  $\alpha$ -methoxy- $\omega$ -propargyl PEO and 1-azido-2,3,4,6-tetra-O-acetyl glucopyranoside. All new compounds were evaluated by <sup>1</sup>H NMR spectroscopy and SEC analysis. PCL and PEO blocks were connected in NaOH acetone solution and this feature has been confirmed by fluorescence measurements using Alizarin Red as a model compound as well as by <sup>1</sup>H NMR spectroscopy. The block copolymer was transformed into physiological relevant phosphate-buffered saline (PBS) solution via dialysis and self-assembled nanoparticles were characterized by static and dynamic light scattering (SLS, DLS) and cryogenic transmission electron microscopy (cryo-TEM). Furthermore remarkable sensitivity of nanoparticles can be triggered by addition of a surplus of glucose or lactic acid (simulating acidic cytosolic or endosomal conditions in tumor cells) that binds to BA competitively. The latter feature has been confirmed by fluorescence and light scattering measurements [1].

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- [1] A. Matuszewska, M. Uchman, A. Adamczyk-Wozniak, A. Sporzynski, S. Pispas, L. Kovacik, M. Stepanek, *Biomacromolecules*, 2015, **16**(12), 3731.