Posudek vedoucího / konzultanta diplomové práce

Autor/ka práce: Veronika Měrková
Vedoucí/školitel/ka práce: PharmDr. Hana Jansová, Ph.D.
Konzultant/ka práce: Prof. Dr. Felix H. Schacher
M. Sc. Martin Raasch
Rok zadání: 2016
Rok obhajoby: 2017

Název práce:
Co2+ LOADED BLOCK COPOLYMER MICELLES:
PREPARATION AND THEIR UPTAKE INTO MACROPHAGES

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Doporučuji diplomovou práci k uznání jako práci rigorózní ☑

Slovní hodnocení, výrazné rysy autora/ky a práce:

V Hradci králové dne 16. 5. 2017

podpis
CHARLES UNIVERSITY
FACULTY OF PHARMACY IN HRADEC KRALOVE
Department: Institute of Organic Chemistry and Macromolecular Chemistry, Friedrich-Schiller-University Jena

Master’s degree program in Pharmacy
Mentor’s evaluation of Master’s thesis

Student’s name: Veronika Merkova
Thesis mentor’s name: Prof. Felix H. Schacher

Year of the thesis defense: 2017

Title of the thesis:
Co2+-Loaded Block Copolymer Micelles - Preparation and Uptake into Macrophages

The topic of the thesis was chosen by student (suggestion from my side after the student made contact via email)
Working with literature very good.
Language skills very good.
Student invention excellent.
The student was working independently.
Problems and issues were solved independently with mentor help.
Working in the lab was excellent.
Interpretation of the results correct with small corrections.
Processing of the thesis was correct with mentor corrections.
Graphical processing of the thesis very good.

I recommend Diploma thesis for the recognition as Rigorous thesis □.

Mentor’s comments both on the thesis and the student’s approach:
Please see separate document !

Evaluation of Master’s thesis: excellent
Recommendations for the thesis defense: recommended
In Hradec Králové 13.05.2017 in Jena

Mentor’s signature
Report on the Diploma thesis of Veronika Měrková

"Co^{2+}-Loaded Block Copolymer Micelles – Preparation and Uptake into Macrophages"

The aim of the master thesis of Mrs. Měrková was to evaluate whether core-shell-corona micelles can be used to safely deliver Co^{2+} ions into human macrophages and, further, whether the presence of Co^{2+} then induces any effect to the polarization state of these macrophages. This would open up new avenues in the treatment of inflammation-related diseases.

As model system, a PEO-b-PAGE-b-PtBGE triblock terpolymer was synthesized using sequential anionic ring-opening polymerization. Subsequent thiol-ene modification allowed the introduction of carboxylic acid groups to the middle block (PAGE_{COOH}). Self-assembly in water as selective solvent led to micelles with a PtBGE core, a PAGE_{COOH} shell and a PEO corona. Mrs. Měrková analysed these micelles using a combination of dynamic light scattering, electron microscopy, and zeta-potential measurements. Further, she managed to load different amounts of Co^{2+} ions into the negatively charged PAGE_{COOH} shell and was able to quantify the loading using ICP-OES studies.

Afterwards, fundamental studies regarding uptake and toxicity of the prepared micelles showed no significant influence on cell viability and sufficient uptake, although the actual mechanism of internalization is not yet clear. Although Mrs. Měrková could show that Clathrin-mediated endocytosis is probably not the dominating mechanism, further studies are necessary. In addition, she could demonstrate that also Co^{2+}-loaded micelles are not cytotoxic and that, depending on the micellar concentration used, different cytokines can be detected in the samples. Among others, the presence of IL-10 could be verified, which suggests that a polarization into M2 state of the macrophages was induced by internalization of Co^{2+}-loaded micelles.

In summary, Mrs. Měrková could successfully complete all individual steps of a challenging project and, although we will need some further studies to understand the underlying pro-
cesses, her work has most probably laid the foundation for a publication. Moreover, except transmission electron microscopy, she performed all intermediate steps on her own and was thus involved both in the laboratories of chemists and biochemists. Given her background, I was impressed how quickly she adapted to the new environment and how she could explain all results in several discussions.

The thesis is written in English language, contains a few minor mistakes, and is nicely illustrated. Taking into account the high level of self-motivation, the rather short time for the experimental work (October 2016 – January 2017), and the highly interdisciplinary topic of her thesis, I can rate Mrs. Měrková's work as **excellent** (1).

Prof. Dr. Felix H. Schacher