

Review of the doctoral thesis of Vladimir Sincari, M.Sc. "Self-assembled polymer systems responsive to external stimuli for biomedicine"

Thesis of Vladimir Sincari deals with the synthesis of well-defined diblock copolymers via (micro wave-assisted) RAFT for preparation of diverse stimuli-responsive (pH, ROS) polymersomes suitable for anti-cancer treatment. Microfluidics was used for fabrication of uniform polymersomes. Further, most of the samples were tested in vitro or in vivo for their anti-cancer action. Thesis is scientifically valuable contribution to the field with clearly distinguishable drive towards applications. However, the impact and scientific qualities are somehow weakened by the style of Theses and inconsistencies in its formal presentation.

Thesis is a result of 6 years long study at IMC/CU under supervision of Dr. P. Štěpánek and Prof. M. Hrubý. It is based on 5 papers in prestigious journals with IF (4 already published and 1 under consideration, where VS is the first author two-times and the second author three-times). All the papers are attached to the Thesis. Thesis is written in English, it has 110 pages and 176 references, and the text is divided to 6 chapters: 1. Introduction into the field of interest, 2. Aims, followed by chapters 3.-6. repeating in a slightly modified way texts of the papers. Thesis is summarized in 7. Conclusions.

While the overall message of Thesis is clear and understandable, the text is quite difficult to read, it contains relatively high number of errors and typos such as: wrong link to publication No.1 (page 9); inconsistent indentation of paragraphs, which sometimes consist only of one sentence; unfortunate positions of Figures and figure captions in the text; different and inconsistent fonts of chapter and sub-chapter headings; using of nonsensical terms (polydisperse, monodisperse, disperse, ...), etc.

The introductory parts resemble a continuous flow of thoughts, where pieces of information are too often not referenced to related literature. Even if Thesis contain general Introduction (chapter 1), the parts presenting results (chapters 3-6) contain sometimes but not always their own introductory parts, which is confusing. This is because the chapters are only slightly edited manuscripts. It makes no sense, because the papers in a more readable form are attached. This is the reason why the anti-plagiarism program detected of 47% similarity with already published documents. Chapter 1.10 about experimental techniques used in Thesis is not very convincing, it would be better to describe the techniques on acceptable level or omit it at all.

The attached papers have quite long line of co-authors. I would like to ask for clarification of the contribution of Vladimir Sincari, M.Sc. to presented results during the Thesis defense.

Despite my criticism, Thesis represents the valuable contribution to the field of polymeric drug-delivery systems, and I would like to state that Vladimir Sincari, M.Sc. met all legal requirements relating to Doctoral degree graduates. I recommend this thesis for his Ph.D. defense.

I have several questions and comments to general discussion:

1) The term “self-assembly” is mentioned even in the title of Thesis. I am wondering if the term is appropriate for systems created by kinetic effects and “tricks” with microfluidic devices. It means that the self-assemblies were not result of equilibrium.

2) In Figure 33(C,D), structural changes upon addition of DOX to polymersomes could be observed. I would like to ask about impact of drug loading to overall shape, dispersity, morphology and stability of the system.

3) Uniformity of prepared nano- or micro-particles is very important for the evaluation of the obtained results. I would like to ask about factors that can influence the size of the vesicles, the “wall” thickness, and the system uniformity.

4) In chapter 6, poly[2-(diisopropylamino) ethyl methacrylate] blocks were synthesized. I would like to ask on the long-term stability of this polymer in solution. It was observed for similar systems that amino groups can cause self-hydrolysis of ester groups. Was it observed in this case?

In Prague, 28th October 2022

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