

Report on the PhD thesis entitled  
**„Aliphatic polyester-based nanoparticles as drug delivery systems“**

presented by

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The PhD thesis of MSc. Alessandro Jäger is a comprehensive review on the design, preparation and characterization of biodegradable nanoparticles suitable for reversible encapsulation of drugs. These systems are promising for the drug delivery into the targeted cells of the human body and for a subsequent controlled releasing of the drugs in these cells.

Alessandro Jäger dealt particularly with: (i) the preparation of new type nanoparticles based on poly(butylensuccinate-co-butylenedilinoleate) (PBS/PBDL) copolymers and evaluating the parameters influencing the size, density and inner structure of the nanoparticles, (ii) encapsulation of a model hydrophobic drug into nanoparticles and evaluation of the influence of this process on the character and behaviour of the nanoparticles, (iii) loading nanoparticles with cytostatic drug DOX and covering them with hydrophilic poly(*N*-(2-hydroxypropyl)methacrylamide) (PHPMA).

The research of MSc Jäger was carried out thoroughly and precisely by using diverse advanced characterization techniques such as SLS, DLS, SAXS, Electrophoretic Light Scattering, SEC, TEM, cryoTEM, which enabled PhD candidate to achieve many interesting and valuable findings and to formulate important conclusions and hypothesis. Particularly, the finding that the size of nanoparticles can be precisely tuned in a large scale by the composition of the binary solvent mixture seems to be of high importance. Also the finding and the subsequent explanation on the gradual size change of the nanoparticles accompanying the drug release is to be highly evaluated.

The Thesis of Alessandro Jäger is written with sufficient theoretical background and relevant discussion and conclusions for each part. The research results were extensively published: Thesis contains three papers already published in international journals and one manuscript submitted for publication. Alessandro Jäger is the first and simultaneously corresponding author of three of these papers. Furthermore, Alessandro Jäger is author/co-author of eleven other published papers and two other submitted manuscripts that are not involved in the Thesis.

I have only marginal comments to the thesis:

- Author should specify which percentage (weight % or volume %) is used when the composition of the solvent mixtures is discussed.
- Polycondensation: the by-product removal from the reaction mixture does not drive the reaction equilibrium towards high  $K_p$  value as given on pp. 20. This process does not modify the  $K_p$  value; it only enhances the degree of conversion just to keep the  $K_p$  value constant.  $K_p$  value is modifiable by temperature change (decrease or increase in  $K_p$ , however, depends on the reaction enthalpy).

Besides, there are two topics that should be discussed by the author during the Thesis defence:

1. What is the reproducibility of the nanoparticle size and size distribution assuming that nanoparticles are prepared repeatedly from newly synthesized copolymers.
2. The preparation of nanoparticles and their covering with hydrophilic PHPMA was performed as a one pot synthesis during which, however, the PHPMA polymer penetrated into particles and (probably undesirably ?) modified the composition of these particles. Is it possible to divide the synthesis into two independent steps (particle preparation and coating of the prepared particles)? Have the author tried this approach?

As a conclusion, it is my pleasure to express a positive opinion for the PhD research work of MSc. Alessandro Jäger in order MSc. Alessandro Jäger to be awarded a PhD degree from Charles University in Prague.

In Prague, September 27, 2015

Doc RNDr. Jan Sedláček, Dr.