Nanomedicine: Delevelopment of a series of experiments on the synthesis of smart nanocarriers

A. Fruntke†, L. M. Stafast †, C. Weber, U. S. Schubert & T. Wilke*

Introduction

The fight against inflammatory and viral diseases is currently of great importance in light of the corona pandemic. Active ingredients are needed in high concentrations at the site of infection, but they can cause severe damage outside and lead to the development of sepsis and ultimately death, in the worst case. The development of **smart nanomaterials** can resolve this contradiction by encapsulation of active substances in functionalized nanocarriers, transporting them to the targeted site and releasing them at the right time [1].

The objectives, research questions and central findings about this research offer **great opportunities for chemistry education**, as they allow to synergistically link current research contexts with classical chemistry education contents. In this contribution, experimental approaches that allow the topics of nanomedicine and smart drug delivery to be studied in the chemistry classroom are presented.

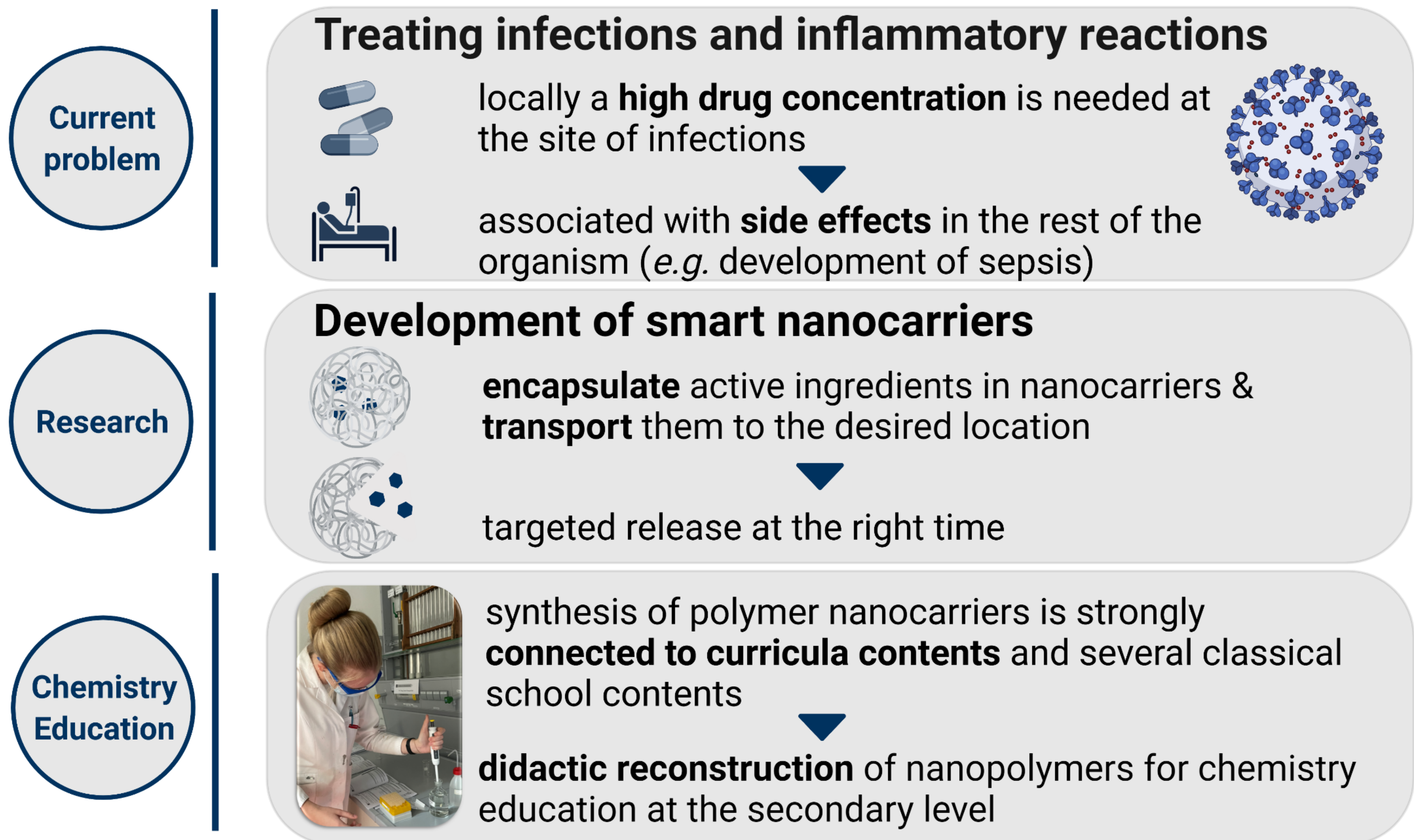

Fig. 1: Aim of the didactic reconstruction

Scientific Background

Different approaches to the synthesis of polyesters exist. The ring-opening polymerization (ROP) of lactones has prevailed over polycondensation in the context of polymers for biomedical use. Typical polyesters obtained via that method include polylactide as an exemplary homopolymer and poly(lactide-co-glycolide) as an exemplary copolymer. Typically, such polyesters are obtained by ROP using Sn(II) catalysts. However, modern organocatalysts such as triazabicyclodecene (TBD) or diazabicycloundecene (DBU) facilitate shorter reaction times at milder reaction conditions. Moreover, less by-products are formed [2].The monomers δ-valerolactone and δ-caprolactone were selected here as δ-lactones are naturally occurring, cheap and non-toxic. The syntheses in scientific research were performed in a glovebox as well as under semi-inert conditions. The obtained polyesters were then used to prepare nanoparticles by nanoprecipitation [3].

Didactic Reconstruction

The aim of the experiments was to transfer the syntheses of potential polymeric nanocarriers from research laboratories with professional equipment under inert conditions to chemistry classes, using only student laboratory equipment and simple chemicals. Fig. 2 shows the didactic simplifications based on the scientific syntheses.

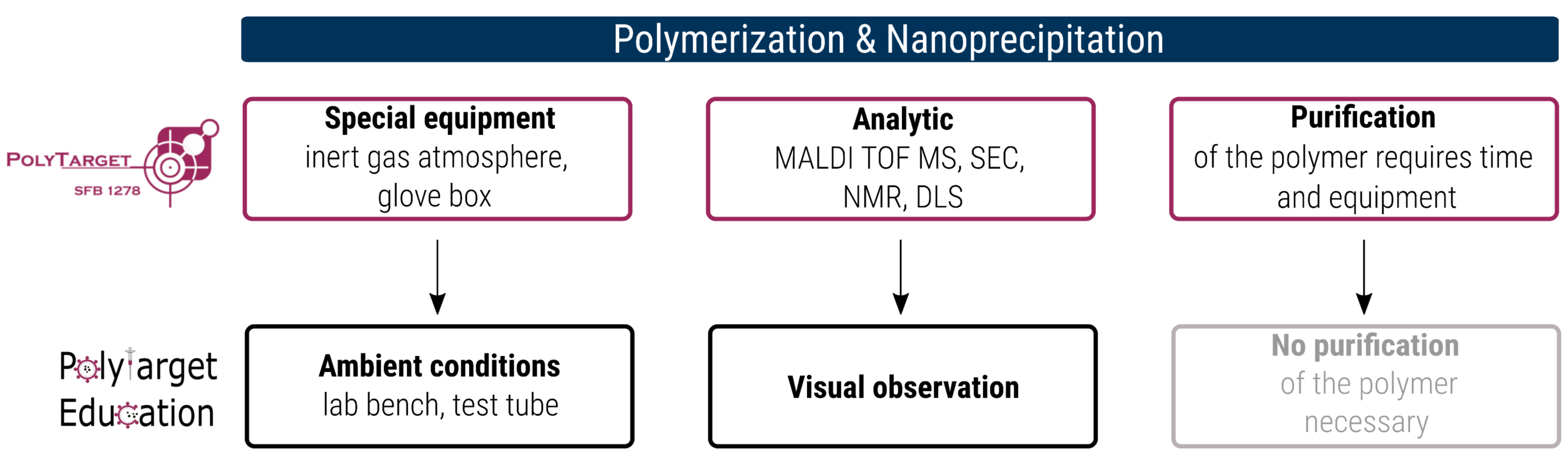

Fig. 2: Summary of the didactic simplifications made based on the research experiments

Results and Practical Experience

Based on the adjustments on the experiments mentioned above, a procedure for the nanocarrier synthesis was developed and piloted with a group of students during the Jena Summer School (Fig.3). In this context, the feasibility and robustness of the experiments was confirmed.

Fig. 3: Participants of the Jena Summer School 2021

The students independently **synthesized poly(δ-valerolactone),** whereby an optical change from a clear colorless liquid to a white, viscous liquid could be observed within a few minutes (Fig. 4).

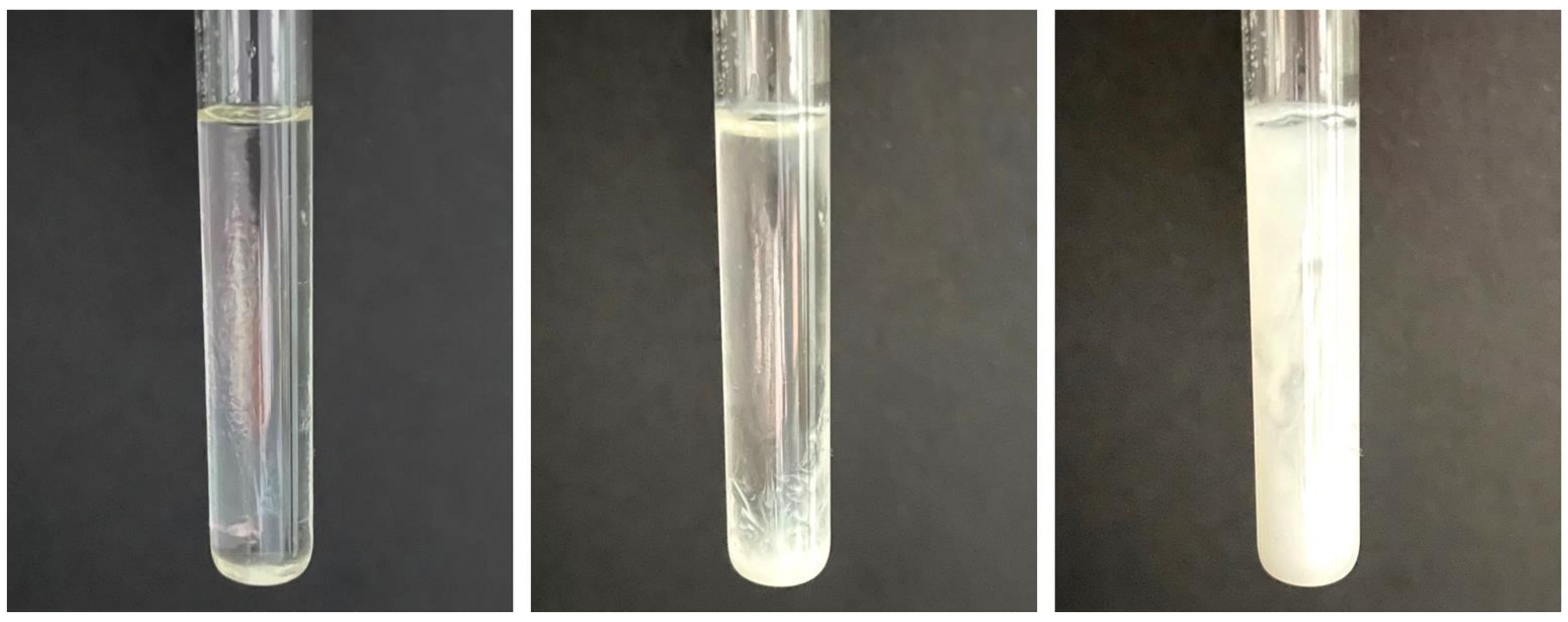

Fig. 4: ROP of δ-Valerolactone: start of the reaction (left), reaction after 1 minute (middle), reaction after 7 minutes (right)

The polyester was then used for **nanoprecipitation**, which takes advantage of the insolubility of the hydrophobic polymer in an aqueous medium (Fig. 5). It can be deduced that the experimental procedure can be utilized by students, as no difficulties were encountered during the performance. Thus, it is possible to produce suitable biocompatible nanocarriers within a student experiment, despite the limitation to common school (laboratory) equipment and conditions involving the use of non-toxic and inexpensive chemicals.

Fig. 5: ROP of δ-Valerolactone: start of the reaction (left), reaction after 1 minute (middle), reaction after 7 minutes (right)

References

[1] A. Fruntke, M. Behnke, L. M. Stafast, T. Träder, E. Dietel, A. Vollrath, C. Weber, U. S. Schubert, T. Wilke, "Target drug delivery: Synthesis of smart nanocarriers for school chemistry education", *J. Chem. Ed.* **2022**, *in preperation.* [2] A. Löfgren, A.-C. Albertsson, P. Dubois, R. Jérôme, "Recent Advances in Ring-Opening Polymerization of Lactones and Related Compounds", *J. Macromol. Sci. C: Polymer Reviews.* **1995**, 35/3, 379–418. [3] Y. Liu, G. Yang, D. Z. Y. Hui, K. Nigam, A. P.J. Middelberg, C.-X. Zhao, "Formulation of Nanoparticles Using Mixing-Induced Nanoprecipitation for Drug Delivery", *Ind. Eng. Chem. Res.* **2020**, 59/9, 4134–4149.

Antonia Fruntke
Research Assistent
Friedrich Schiller University Jena
Chemistry Education
August-Bebel-Str. 2, D-07743 Jena
antonia.fruntke@uni-jena.de

PolyTarget SFB 1278

All authors would like to thank the DFG (project number 316213987, SFB 1278 "PolyTarget", project Ö01, A04 and A06) and Tom Träder for support in the development of the experimental series.

FRIEDRICH-SCHILLER-UNIVERSITÄT JENA