Nanomedicine: A Digital Learning Module for Chemistry Education

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Abstract

The awarding of the Nobel Prizes in Chemistry and Medicine in 2023 is closely related to nanotechnology. Katalin Karikó and Drew Weissman received the prize in the medical field for fundamental research on mRNA vaccines against Covid-19, where the mRNA is encapsulated in lipid nanoparticles to prevent premature degradation by enzymes [1]. With this in mind, we present a way to convey this topic in chemistry education for schools and student labs. For this, we use the innovative method of a digital differentiation grid [2], and for the specific context, we focus on nanomedicine, or more precisely: targeted drug delivery. Conventional pharmaceutical drug systems usually have a systemic effect and cause severe side effects throughout the body due to the high doses applied. However, at the site of infection, the dose is often insufficient for successful treatment. This problem can be solved by using targeted drug delivery systems (DDS). Similar to mRNA vaccines, the active pharmaceutical ingredients are wrapped in nanoparticles and protected, thus preventing early release. The active ingredient is only released at the required location induced by pre-defined stimuli, such as pH or temperature. Within the learning module, various experiments and exercises about DDS are conducted, allowing students to gain insight into this current research topic [3]. The structure is based on a differentiation grid, enabling the topic to be approached individually depending on learning requirements [2]. Moreover, we use iPads and eBooks that include further digital elements to enhance students' motivation and engagement with the topic.

Keywords: *nanotechnology, nanomedicine, medicine, drug delivery*

1. Introduction

The application of drugs in the form of nanoparticulate drug delivery systems (DDS) offers a great potential for targeted and personalized treatment for a wide range of diseases, such as sepsis or tumor diseases. By loading polymer nanoparticles with active pharmaceutical ingredients (API) and releasing them in a targeted manner at the diseased organ or tissue in response to stimuli, the required dose and bioavailability can be optimized. Overall, in contrast to systemic drugs, there are fewer side effects and complications, while the treatment is more efficient [4,5].
Based on a series of best-practice experiments for chemistry lessons on the topic of DDS, in which students experimentally follow the complete process, from polymer synthesis, formulation and loading to targeted release, this publication presents a further developed digital learning module on the topic of nanomedicine.
The aim is to enable pupils with different learning requirements to take an independent look at this innovative subject area. Tablets support the learning module and enable additional interactive tasks and aids. First tests of the learning module show positive trends.

2. Series of experiments as the central element of the learning module

The basis for the differentiation matrix is a previously developed three-part test series by Fruntke, Behnke, Stafast et al [3,6] (Figure 1).

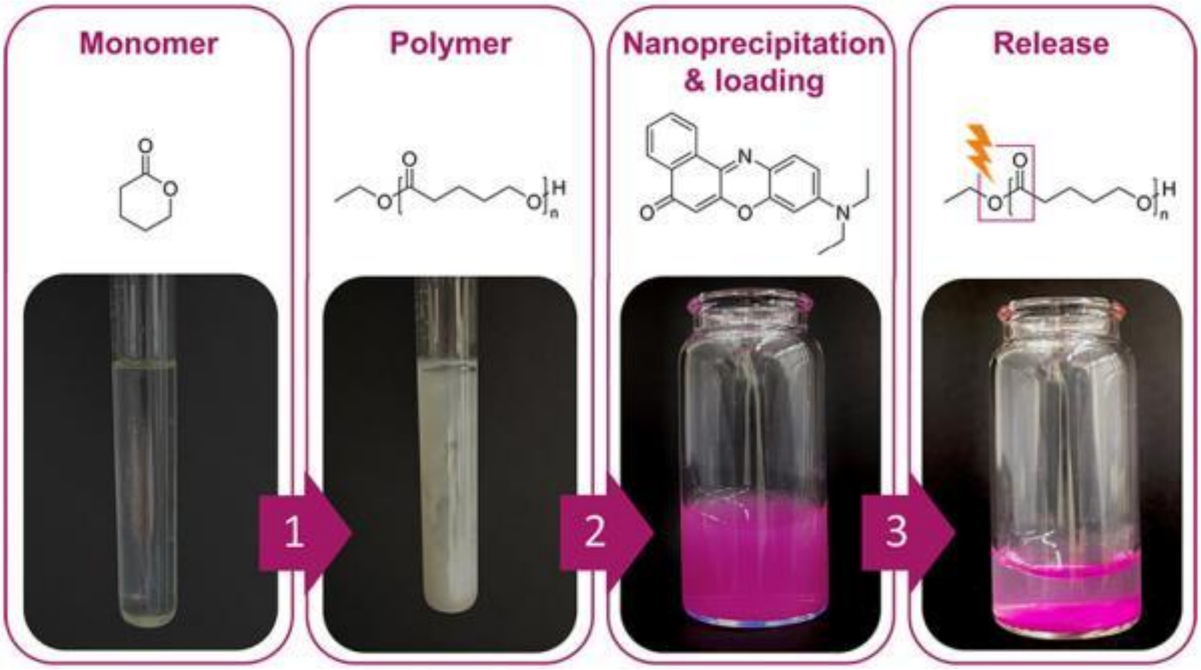

Figure 1. Overview of the test series on the topic of drug delivery systems [3].

In a first step, the students independently synthesize the polymer poly-δ-valerolactone (PδVL), which is a simple polyester. The experiment only takes a few minutes and is easy to follow visually. The colorless, liquid monomer δ-valerolactone (δVL) reacts by adding the initiator ethanol and the catalyst 1,5,7-triazabicyclo[4.4.0]dec-5-ene (TBD) in a ring-opening polymerization to the white, wax-like polymer PδVL.
In the second step, the synthesized hydrophobic PδVL is used as a starting material for nanoprecipitation to formulate the particles. For this purpose, the polymer is dissolved in the solvent acetone and then injected into water (Figure 2).

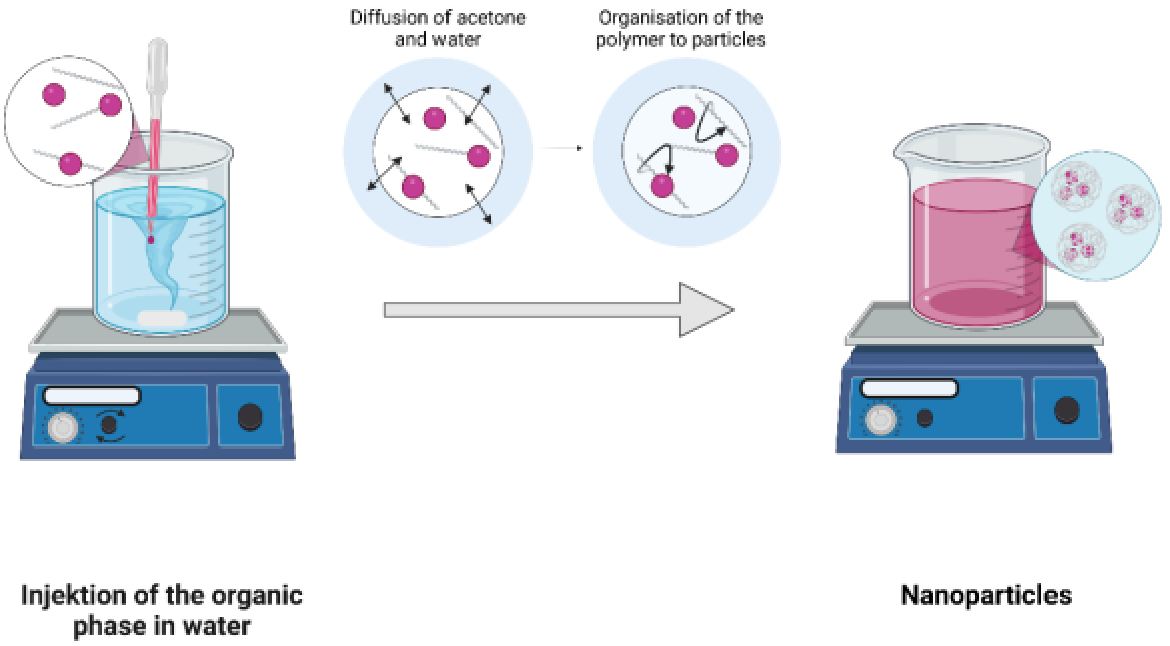

Figure 2. Formulation of the polymeric nanoparticles [6].

It is important to ensure that the solvent is miscible with water. The fluorescent dye Nile red is used to load the particles instead of an API.
This can also be dissolved in acetone and added to the polymer solution before injection. Due to the low boiling point of acetone, the solvent evaporates at room temperature. The process is faster by stirring and slightly heating the sample to 50 °C. The hydrophobic polymer forms the nanoparticles in the water and the dye, which is also hydrophobic, is encapsulated.
Finally, in the third step of the test series, the focus is placed on the release as a result of increasing the pH value. Alkaline ester hydrolysis follows by adding sodium hydroxide solution. As a result, the particles are degraded, and the encapsulated Nile red dye is released. This can be observed optically due to the bad solubility of Nile red in water [6].

3. Development of a digital differentiation matrix

In order to enable pupils of different abilities to familiarize themselves with the topic of DDS, the newly developed approach of digitally differentiated learning modules was applied. This approach has already received a positive response in other research projects [7]. The aim is to get pupils interested in the innovative topic of nanomedicine in a variety of ways. The learning module is designed for upper secondary schools.
A 3x3 differentiation matrix [8] builds the basis of the learning module. It contains fields of varying thematic and cognitive complexity. Students can decide by themselves which field they work within the matrix. The stations in the lab are set up in multiple ways for this purpose.
Similar to a coordinate system, the matrix is divided into x-axis and y-axis. On the x-axis, the complexity increases thematically. That means that aspects of the topic, that are easier to understand are on the left, while the more complex aspects can be found on the right. The y-axis is based on the first stages of Bloom's learning taxonomy, to which fields were constructed accordingly [9]: Knowing, understanding, and applying. Thus, the overall complexity increases from field A1 (easiest) to C3 (most difficult). Within the fields, a distinction is made between two main formats: experiments and task fields. The first are based on the series of experiments described, while the tasks involve working on theoretical aspects by using digital materials. The students work on the module in pairs.
To give students an overview of their individual progress in the completed learning fields, the differentiation matrix is provided as a kind of content overview embedded in e-books. Each student is provided with an iPad for this purpose. The individual fields can then be accessed via the matrix, which takes the students to the linked material including tasks, instructions and help cards. A sample solution for independent checking is also included.

3.1 Implementation of the differentiation matrix using the example of nanomedicine

The learning module covers various basic aspects for students about nanomedicine / DDS. Three subject areas are listed along the y-axis. In column A "Nanoparticles in medicine", basic contents are presented. In topic field B, the focus is on the background and the methods of preparation of polymer nanoparticles. The C fields deal with the loading and targeted release of API.

The following content is included in the individual subject areas:

Subject area A:

- **A1:** Definition and size of nanoparticles.
- **A2:** Transport of API using DDS.
- **A3:** In this station, the students can become doctors themselves. They should select suitable DDS and justify which one is possible for treatment.

Subject area B:

- **B1:** Polymers, their production and their everyday use.
- **B2:** Experimental station: At this station, students can synthesize a suitable polymer for a DDS and check the properties.
- **B3:** Experimental station: At this station, nanoparticles are synthesized from the polymer.

Subject area C:

- **C1:** Nanoprecipitation method for the formation of nanoparticles is explained in more detail.
- **C2:** Experimental station: Formulation of a DDS: Use of the nanoprecipitation method, loading with the dye (instead of API) Nile red.
- **C3:** Experimental station: Investigation of the degradation of nanoparticles and pH-sensitive release.

Figure 3 shows an overview of the matrix.

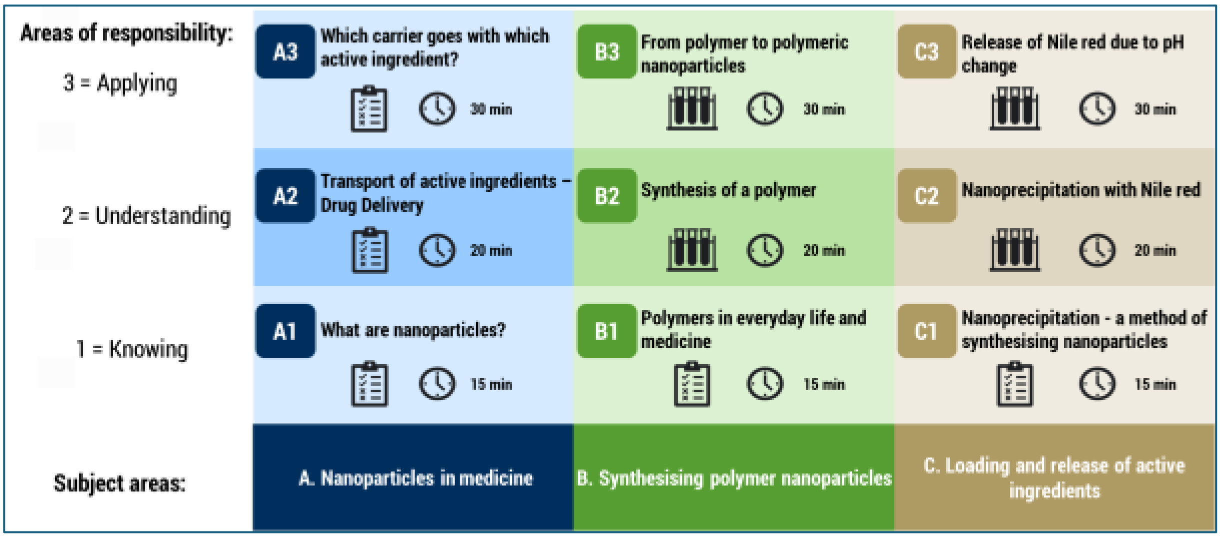

Figure 3. Overview of differentiation matrix on the topic of nanomedicine [2].
The aim is for students to work on at least four fields within a three-hour school lab course.

3.2 Experience in practical implementation

The learning module was piloted with pupils (N=20) in a laboratory course and with teachers (N=20) in two teacher training courses. (Figure 3).

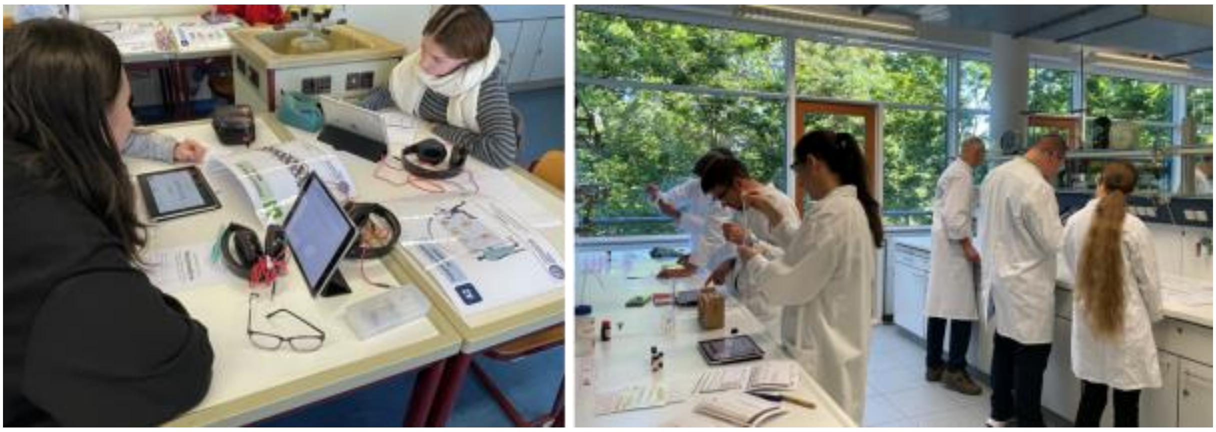
Figure 4. Piloting of the learning module. left: in a student laboratory course, right: within a teacher training course.

The feedback so far has been predominantly positive, while a more detailed evaluation is still pending. The integration of the series of experiments into the digitally differentiated learning module is described as purposeful and multifaceted. The various insights into the different areas of DDS are emphasized. The students describe the range of interactive aids and learning videos as very helpful.
The availability of a WiFi signal and tablets in the classroom set should be mentioned as technical requirements. The materials required essentially correspond to typical school equipment; the chemicals δ-valerolactone and Nile red are commercially and widely available at low cost.

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