Nanomaterials in Cancer Therapy – a Model Experiment for Chemistry Education

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Abstract

With the continuing COVID-19 situation, science has moved closer to the focus of society, with research into new vaccines and therapeutic options being the central focus. It seems therefore appropriate to take up this current interest in science and medicine, which has been intensified by media, and to address medical topics in STEM lessons to motivate students [1]. Beyond COVID-19, however, research continues into many areas such as cancer or anti-inflammatory strategies [2]. A promising approach for the treatment of both examples (and many more) is related to nanotechnology. Nanomaterials can be used as a transport system for active ingredients and transport them more specifically to the location where they are intended to work. It is therefore known as "drug delivery" or "drug targeting" [2,3]. But the nanomaterial itself can also be used as an active ingredient or adjuvant for a therapy. Magnetite nanoparticles (Fe_3O_4) are an important material for both approaches. Due to their outstanding magnetic properties, their good biocompatibility and good availability, they are subject of many research projects and offer great potential for modern medical solutions either as part of a carrier system or, for example, to induce heat to damage cancer cells [4]. The synthesis of magnetite nanoparticles with educational means is already sufficiently documented and ferrofluids are already available for purchase at low cost on the Internet. This results in the potential combination of medicine and nanotechnology, which provides a wide range of learning opportunities for STEM education. In this contribution will be shown how magnetite nanoparticles can be synthesized with simple school chemicals and stabilized as ferrofluids. Subsequently, the ferrofluid will be used in a model experiment to illustrate the hypothermic treatment of tumor cells and first practical experiences with students in the student laboratory will be presented.

Keywords: *nanotechnology, ferrofluid, medicine*

1. Introduction

Current medical research, in particular the development of a vaccine for the coronavirus, has been observed by society with great expectations. But other research projects not related to corona are not less important or exciting. Research is continuing to look for a cure for cancer and Alzheimer's disease or on combating multi-resistant germs, with a wide variety of approaches being pursued. One example is nanotechnology. The corresponding nanomaterials have not only established themselves for use in products for end consumers and industry, but they hold great potential for medicine too [1]. In addition to silver, which is also important as a non-nanomaterial for medicine, magnetite nanoparticles are being investigated for medical purposes. If nanoscale magnetite is bound to an enclosed active ingredient, it will be transported directly to the intended site of action with the aid of an appropriate magnetic field due the magnetite's superparamagnetic properties. This is referred to as "drug delivery" or "drug targeting".

But nanoscale magnetite can be used as an active agent itself too. When it is placed into a magnetic field that changes the orientation of the field at a certain frequency (also referred to as an alternating or oscillating magnetic field), the magnetite heats up so much that a tumor can be consequently damaged or even destroyed. If the tumor is damaged, other agents can better act on the tumor. In this way nanoscale magnetite can support other active ingredients [4].

Since the phenomenon of induction heat is already an exciting topic for its own, this offers the option of a promising expansion of the subject area, which will be explored in the following.

2. Objectives

For students in STEM classes, evaluation competence is of great importance, since they should be able to evaluate scientific results in everyday life contexts based on their knowledge. Current research topics, which chances and risks are still to be assessed, provide a great context to develop or promote this competence. The nanosciences has emerged as an especially suited field for this. Many different materials and contexts have already been successfully used for this, like potential harms and chances of zinc oxide or titanium oxide nanoparticles from sunscreen [5]. Magnetite nanoparticles are sometimes prepared in schools as they show impressive magnetic properties; the application as active agents in tumor therapy, however, has not yet been developed for chemistry education so far. The next chapters describe a simple ferrofluid synthesis with a subsequent model experiment for its application in tumor therapy.

3. Didactic Reconstruction

For local hyperthermal treatment, a water-based ferrofluid is initiated into the affected tissue. The ferrofluid consists of magnetite nanoparticles dispersed in water with the aid of a stabilizer. Without the stabilizer, the particles would agglomerate and lose their useful properties. The affected tissue is now placed in an alternating magnetic field, generated by a strong induction coil operated with alternating current. Depending on the strength of the magnetic field, the frequency of the current and the nature of the nanoparticles (such as how much energy is required for an alignment), heating of these particles occurs.

A similar phenomenon is known from the kitchen while cooking with induction. Analogously, a magnetic pot or pan is placed on the field and analogously exposed to an alternating magnetic field, causing it to heat up. Although there are many parallels in both processes, there are nevertheless serious differences. For example, the pot is ideally ferromagnetic, while the nanoparticles in the ferrofluid are superparamagnetic. Simplified, a non-magnetized ferromagnet consists of various elementary magnets that have the same orientation in magnetic domains. By applying a magnetic field, all elementary magnets of all domains now align themselves with it. After the magnetic field is removed, the alignment remains for a certain time and hold its own magnetic field. In case of magnetite nanoparticles, each particle represents its own magnetic domain. If these are brought into a magnetic field, their elementary magnets and thus the domains align with it, but the particles are also able to align themselves with the field by rotation. If the magnetic field is now removed, this order is lost again. Compared to the pot, the material does not retain an own magnetic field; it has no remanence. In an alternating magnetic field both materials change their magnetic orientation regularly and heat up due to the magnetization losses. These are based, among other things, on the so-called hysteresis losses, which occur during steady remagnetization, and the eddy current losses, which occur due to electrically induced currents. In the case of nanoparticles, there is an additional effect: not only can the magnetic orientation within the particle change, but the entire particle can rotate according to the constantly changing field direction, thus generating additional heat (see Fig. 1) [4].

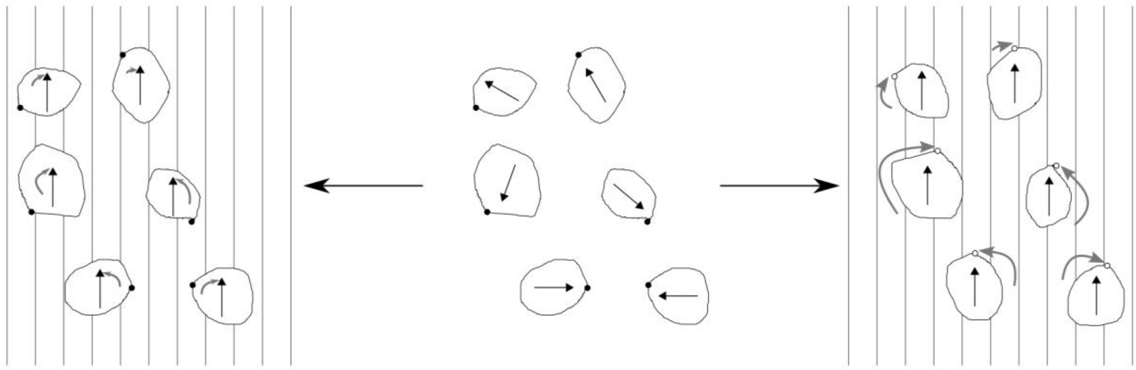

Fig. 1: In an external applied magnetic field the spin (left) and the whole nanoparticles align (right) to it.

This exciting subject area, located between physics and chemistry, provides a suitable context for an introduction to nanotechnology with insights into current medical research. According to empirical findings, the medical context is particularly interesting for female students [1] while nanoscience education appeals to both genders equally [6].

Therefore, there are at least two experiments on the subject. On the one hand the synthesis of the ferrofluid and on the other hand a model experiment to determine the heating of a ferrofluid in an oscillating magnetic field.

3.1 Synthesis of Ferrofluids

Many instructions are already published for the synthesis of ferrofluids, and some are now also commercially available at low cost. Best results were obtained with an adapted variant of Berger et. al. [7], which has also been used for further nanoscience teaching projects such as magnetic nanocomposites [8]. The synthesis consists of two steps.

- In the first step magnetite nanoparticles are prepared and stabilized to obtain a ferrofluid. For this, 3.5 g of iron(II) sulfate and 2.0 g of iron(III) chloride are dissolved in 25 mL of water. To this, 100 mL of a 2 M ammonium hydroxide solution is added over the course of about 5 minutes with vigorous stirring.
- During the addition, the initially yellow liquid quickly turns deep black. After the base has been completely added, the solid can be fixed to the bottom by means of a strong neodymium magnet and the liquid poured off. By adding water again and then decanting analogously, unreacted educts and interfering products are removed.

After washing several times, about 0.3 g of Tetrabutylammonium hydroxide solution (“TBAH”) is added and stirred well. If the magnet is held about 3 cm away from the mixture, Rosensweig lines indicate the presence of superparamagnetic nanoparticles (Fig. 2).

Fig. 2 from left to right: Solution upon addition of ammonia, sedimentation of nanoparticles with the magnet, washed nanoparticle dispersion, ferrofluid stabilized with TBAH.

3.2 Tumor therapy: hyperthermia model experiment

For the measurement, two snap-cap vials are placed on an induction plate. One vial is filled with the ferrofluid and water, the other with the same amount of water. A thermometer or temperature probe is now held in each of them. Now the field can be switched on and the temperature is measured in both vials. After 20 minutes with a power of 3.500 W, a clear trend can be seen: the ferrofluid heats up more than the reference. By using Styrofoam plates, the influence of external factors is reduced (*e. g.* radiated heat) and the effect can be intensified. The measurement with the LabPi measuring station has proven itself well in the student laboratory, since not only the initial and final temperature, but also the course of the curves can be compared. Although the aluminum coating of the sensor also heats up during operation due to the magnetic field, the effect is the same for the reference and therefore negligible.

Fig. 3: Experimental setup: Induction hob with both vials. The left one contains a ferrofluid, the right one only water. Temperature measurements are acquired with LabPi measuring stations.

4. Practical Experience

While the synthesis is mainly chemical in nature, the model experiment is very good to incorporate in physics lessons. However, the knowledge of induction and eddy currents is very important for this, so it is typically addressed in secondary level K-12 grades.
Both experiments have been piloted with students during a summer school; the synthesis has also been included in a laboratory practical course of the teacher training program at the Friedrich-Schiller-University in Jena. In both cases, the experiments were carried out successful by students and described as exciting and motivating. When the pandemic situation allows further evaluation, this experiment series will be carried out in regular chemistry and physics lessons and implemented into teacher formation.
The didactic potential of nanomedicine will be enhanced by and linked with further research areas and contexts, such as polymer chemistry for *e. g.* targeted drug delivery [2,3] or smart material design [8].

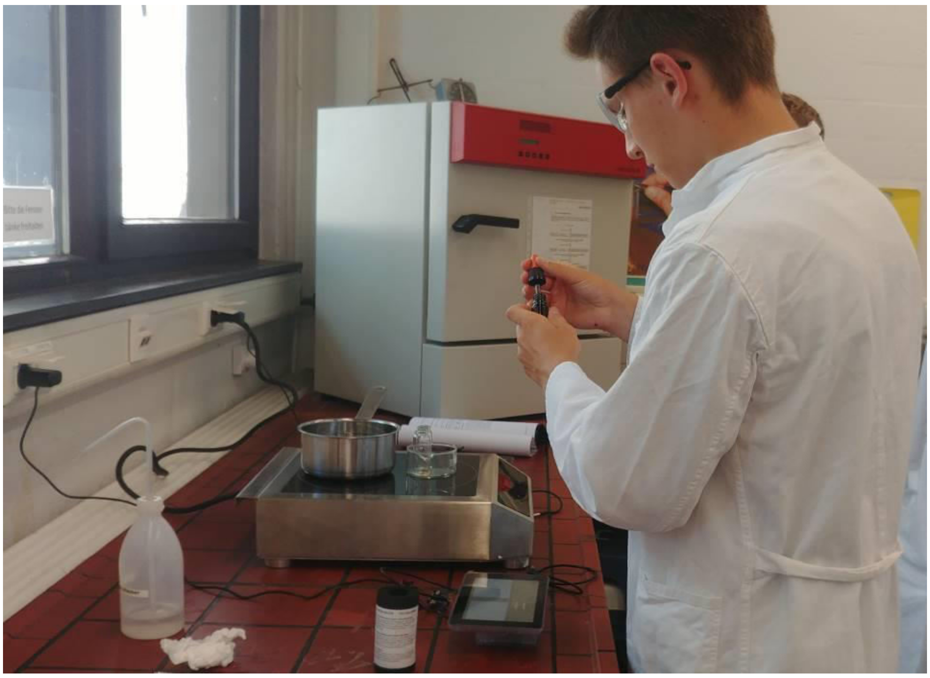

Fig 4.: Students in the lab preparing samples for the model experiment.

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