

REVIEW OF DOCTORAL THESIS

Author: Quazi Tanminul Haque Shubhra

Title:

preparation and surface modification of magnetic PLGA nanoparticles for sustaining natural interferon release

Reviewer: Dr. Gyula Tolnai

The reviewed phd thesis dealing with a unique aspect of the synthesis, modification and application of a complex nanostructured device. This work focused to the following main topics: (i) development and optimization of a new and effective synthesis route for the creating magnetic nanoparticle based drug delivery systems with consecutive encapsulation and stabilization steps; (ii) investigation of interferon alfa release capacity of prepared systems by in vitro drug release experiments. Both topics are important for basic science and practical application and represents very modern directions in the field of nanomedicine.

The thesis consists of seven chapters. The introduction and the declaration of objectives as the first part of thesis. The last part is the references and the appendix. The thesis is written on 107 pages all together. The results and their interpretation of the thesis performed in the fourth chapter more than 40 pages!

The structure of thesis conforms to requests to the structure of a well-structured scientific thesis. The presentation of experimental results is adequate. All the figures and pictures are spectaculars and informative.

Because the author has performed sufficient research work on these fields thus the topic of thesis is absolutely current and relevant in the context of nanomedicinal research field.

The author has studied the appropriate number of relevant scientific sources and quoted in the thesis. The discussions of references cover all the related particular scientific areas particularly in case of description of microencapsulation methods. But the following sections are no less detailed and high quality. The author gave detailed description about the interfacial forces including DLVO and steric interactions which have primarily affect on the stability of prepared nanosystem. In addition Mr. Shubhra collected and analyzed the most important aspects of magnetic nanoparticles including physical characteristics and toxicology.

The aims and the applied experimental methods are clearly described. Mr. Shubhra represents the aims and methods with sufficient theoretical background. Experimental techniques are appropriate to the fulfillment of aims.

The author proposed three-phase synthesis method to produce the required drug delivery system for natural interferon alfa which can be effective medicine against viruses and carcinoma.

In first step magnetic nanoparticles were produced by coprecipitation of the iron salts with ammonia solution in the presence of oleic acid under inert atmosphere. This method is often

used for the synthesis of magnetite nanoparticles but in most cases the produced nanoparticles have broad size distribution and therefore very difficult or impossible to stabilize them in the given environment.

In second step the drug loaded magnetic nanoparticles were prepared by double emulsion solvent evaporation method. This is a very complicated and sensitive process. The successful implementation required high precision and strict control over the reaction conditions.

In third phase aqueous solution of poloxamer compounds were used for surface modification of the PLGA nanoparticle surfaces.

In my opinion, the major advantage and success of this work is the creation of a good (but very complex) idea and it's successful implementation.

The in vitro experiments showed that the prepared systems are capable to sustain the release of interferon and protect it from degradation.

This result clearly demonstrates the effectiveness of the work.

Of course, these results can still be enhanced but already in this state give significant contribution to the knowledge on development of nanoformulation processes and they have significant impact to practical utilization.

All the new scientific results (collected in five points) are clearly defined and acceptable.

Questions

I have two main questions to the author:

1) In the optimized process the mean size of PLGA/magnetic nanoparticles was between 100 and 200 nm. In contrast the individual particles have much smaller size around 20 nm which can be seen in the transmission electron microscopy image (p 44). Is it possible to encapsulate the individual particles or not?

2) The values of zeta potential of poloxamer-modified PLGA/NP's are very surprising (p 76). It would be necessary to show the measured zeta potential curves. Both the tendency of the changes and the very small value of standard deviation is unexpected. How to interpret the increased negative value of zeta potential when the stabilization capacity of poloxamer taking into consideration?

Conclusions

Overall, this PhD thesis has very good level. From what was said above, it is unquestionable that the author is able to understand, organize and realize high-quality research work in the relevant research area.

An interesting and relevant topics in the field of nanoscience particularly in nanomedicine are addressed. It is very well and clearly written. All the parts of experimental work are well planned and properly discussed. The explanations are suitable and focused on the relevant topics. Selected results of Mr. Shubhra have been published in excellent relevant scientific journals.

In my opinion, this thesis by Quazi Tanminul Haque Shubhra fulfils all the requirements for gaining the Ph.D. degree in the research field of molecular-and nanotechnologies, therefore it is recommended.

Budapest, 22. September 2014

