

REVIEW of PhD Thesis

PhD thesis: “Drug self delivery systems for enhanced targeted cancer therapy”

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The present PhD thesis deals with the construction of drug self-delivery systems for targeted cancer therapy to be used without any carriers. The research subject which was treated by the PhD candidate is greatly interesting, because it concerns a very serious disease that affects many people but also with the manufacture of self-delivery systems.

The plan of the thesis is classical with an abstract, a theoretical part and an experimental part. The cancer treatment methods such as surgery, radiation therapy, immunotherapy, hormone therapy, stem cell transplants, chemotherapy are presented and discussed in the theoretical part. Undesirable side effects due to the incorporation of drug molecules as well as the drug resistance was also discussed in this part .

However, the experimental part includes the preparation of nanoparticles with different drug ratios (different molar ratios of irinotecan hydrochloride to curcumin) and different content of surfactant. The effect of molar ratio of irinotecan hydrochloride to curcumin on the distribution of nanoparticles was discussed. The stability of surfactant stabilized irinotecan hydrochloride and curcumin nanoparticles (SICN) prepared under various conditions were characterized by Dynamic Light Scattering (DLS). The optimization of SICN formulations was carried out by using the particle sizes, surface charges and size distribution of SICN under various conditions.

The effect of surfactant (poloxamer 105) content on the nanoparticles shapes and size distribution was also investigated.

The main Carrier based drug delivery systems with different compositions and structures and Drug self-delivery systems were presented. In vitro evaluation of the cytotoxicity and in vivo evaluation were carried out including the anticancer effects and the reduced side effects due to nanoparticles formulation. Natural and synthetic materials used in drug delivery systems to modify the properties of therapeutic agents were also presented with their respective chemical structures and characteristics.

The thesis shows very interesting results and the theoretical part was built on extensive literature and research works (300). The testing methods are quite well explained and the interpretation of the obtained results is adequate.

The PhD candidate is a co-author of two papers which were published in scientific journals with impact factor and one patent. The presented thesis is part of a scientific project on polymeric materials and biomaterials to be used in medicine.

Comments and remarks:

- Many sentences are too long and/or incorrect (ex. the sentence “In the theoretical part, of these drug delivery systems” in section Introduction on page 10, the sentence “The particle sizes, surface charges were took as the evaluation parameters” in

section 6.2.1 on page 73, the third sentence in abstract “Both *in vitro* and *in vivo* tests for further clinical trials”, etc ...);

- The abstract is too short and incomplete, which made the reading of the thesis quite difficult;
- The concept of “optimization of nanoparticles” (page 29) does not make sense. One can optimize the properties of nanoparticles or their formulations;
- Titles of y-axis and x-axis are missing in some figures (ex. figures 7.1,);
- Figures were reproduced from published papers without permission;
- There was a lack of uniformity in the writing of references;

It should be pointed out that these comments and remarks do not alter in no way the quality of the work presented.

The following questions are addressed to the candidate for which answers are expected during the defence of the thesis:

1. How the conditions (parameters) were selected for the preparation of the drug self-delivery systems?. On which basis the nanoparticles formulations were optimized?;
2. DSC results of Figure 2.1-11: The appearance of a melting temperature (endothermic peak) at 177°C attributed to curcumin and a glass transition at 140°C should be explained;
3. Based on the obtained results, which formulation (s) could be selected for the manufacture of Drug self-delivery systems?. Arguments should be used to motivate the selection;
4. What would be the stability of SICN nanoparticles formulations over time?;
5. Why particles with dimensions much larger than 100 nm were considered as nanoparticles?.
6. Which similar systems could be investigated for which additional applications?.

Haijun Xiao’s doctoral thesis fulfils all formal requirements imposed by PhD degree regulations at Faculty of Technology (Tomas Bata University in Zlin).

Based on above, I recommend the defence of the thesis in front of the examination committee to obtain the PhD degree.

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