

Detailed responses to the Reviewers' comments

Thank you very much for your kind comments. We will try our best to revise the manuscript in order to improve its quality according to your suggestions and suit the requirements of the journal. Below are the itemized responses from authors to the comments of editor/reviewers (**BLUE** – Comments; **Black** – Authors response; **Red** – Revised text).

Reviewer #2:

In my opinion, the presented review of knowledge about nanomaterials synthesized using plant metabolites for biomedical purposes is very current and worthy of interest. Relatively little is currently known about the biomedical properties of nanoparticles, so studies of this type are an important step in the development of this field. Nevertheless, despite several necessary and interesting knowledge, the possibility of publishing this article in such a prestigious journal as "Pharmaceutics" requires improvement in content and editing.

Substantive suggestions:

1. Even though the title of the article does not suggest delving into the content related to the toxicity of nanostructures and theoretically such a topic does not have to be included in the proposed study, I believe that in the case of review articles on a given topic, information related to the possible negative effects of using nanomaterials for medical purposes should be more emphasized. Currently, little is known about the impact of using nanotechnology, and the mentions on this subject unfortunately clearly suggest that medicine is not yet ready for this type of innovation. I think that in addition to the superlatives of using nanotechnology in medicine, the authors should also critically discuss possible side effects.

Thanks for your valuable comments. All the above-mentioned comments are revised

2. In line 115, the authors use the term "Hybrids of plant extract and nanoparticle"... in my opinion, this is an abuse in this context and calling the use of plant metabolites for the simple reduction of metal ions to free atoms hybrids is incorrect.

According to the reviewer suggestions, we have modified that term of Hybrid and revised in the main manuscript

3. I believe that there is no need for a separate subchapter 4. Advances in plant-based nanotechnology applications are needed in the biomedical (line 399) since the entire article actually talks about it...

Thanks for your valuable comments. I agreed above-mentioned comments, so I removed that sub title

4. The title of chapter 5. Potential process of synthesizing nanoparticles (line 412) does not correspond to the content presented therein. The title suggests that the authors will present the mechanism of formation of nanostructures using plant extracts, while the chapter describes (very interesting!) possible reaction routes of nanomaterials in contact with the cells of a living organism.

Thanks for your valuable comments

5. The entire Conclusion chapter is basically about nothing. It describes the same problem in several ways, i.e. the need for further research on this topic. I believe that it should either be more concise or should be removed because it does not summarize the previous considerations.

Thanks for your valuable comments, I have removed that sentence, which reviewer mentioned in the comments section.

Editing suggestions:

1. Something is incorrect in the authors' e-mail addresses and markings **

Thanks for your corrections, Comments are revised and marked in main manuscript

2. In the abstract (line 22), the authors do not consistently describe the acronyms of nanoparticles and the word GtNPs is an obvious mistake.

Thanks for your corrections, Comments are revised and marked in main manuscript

3. Missing subscripts (e.g. line 16, 470, 471), extra space (line 562), lack of indentation of some paragraphs at the beginning

Thanks for your valuable comments and all above-mentioned comments are revised

4. The graphics are well put together, but I think that the font in the captions spoils the entire visual effect - I think that their visual quality needs to be improved.

Thanks for your valuable comments and all above-mentioned comments are revised

5. Table 1 needs to be edited to make it more readable - there are no spaces between the digit and the unit, the column should be widened to fit the entire word, the notation of significant digits should be standardized

Thanks for your valuable comments and all above-mentioned comments are revised

6. The paragraph on lines 288 to 304 has different spacing than the rest of the body manuscript.

Thanks for your valuable comments and above-mentioned comments are revised