Review of: "[Review Article] Nanocarriers for Protein and Peptide Drug Delivery"

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Potential competing interests: No potential competing interests to declare.

Nanocarriers for Protein and Peptide Drug Delivery Reviewed By: Dr Bibhu Prasad Panda, Ph.D The proposed review article entitled 'Nanocarriers for Protein and Peptide Drug Delivery' was found to be more interesting and scientifically relevant to the present era of biological therapeutic development and delivery. On review of the proposed manuscript, it is suggested to include an extensive literature review on topics with relevant citations, such as how nanocarriers are ideal for protein and particle drug delivery, specifically in targeting delivery, the present and future of the delivery system, and development and regulatory challenges that could have been scientifically more justified in addressing the scientific reader community.

It is also suggested to the author and coauthors to restructure, include relevant subtopics, review, and do a second thorough proofreading of the contents and language of the manuscript by a neutral expert reviewer before making the final submission.

I appreciate the authors for making a bold attempt to address the most challenging and advanced topic of Nanocarriers for Protein and Peptide Drug Delivery, which needs a thorough scientific analysis and review proposed for consideration.

A few specific suggestions are proposed for the implementation and improvement of the quality of the manuscript.

1. Make it clear that 'Nanocarriers for Protein and Peptide Drug Delivery' and 'Protein and Peptide as Nanocarriers for Drug Delivery'. These are two different topics that have great potential and scope in their respective delivery domains.

2. It is suggested to include these delivery systems for protein and peptide delivery: viral vectors, biomimetic nanoparticles, exosomes, protein nanoparticles, and DNA-based nanoparticles.

3. Confirm the relevance and appropriateness of references cited throughout the content (on cross-referencing, references nos. 4, 6, 7, 14, 36, 37, etc. are found irrelevant and not related to protein peptide drug delivery).

4. Confirm the statement with the appropriate citation: 'As an alternative, natural biodegradable polymers, including proteins, offer more desirable characteristics in terms of safety and biocompatibility. Thus, for biological treatment, natural protein-based nanoparticles are becoming more and more popular.

5. Rephrase the sentence: 'Exciting techniques include mucoadhesive polymers, microspheres, nanoparticles, nanoemulsions, and nanoemulsion'.

6. Most of the methods discussed in the manuscript, such as mucoadhesive polymers, microspheres, nanoparticles, and nanoemulsions, do not cover how proteins and peptides could be delivered.

7. Justify the statement with an appropriate citation. Therefore, nanoemulsion has received widespread attention as a drug carrier. Nanoemulsions are essential in the preparation of oral and topical dosage forms that enable optimum transport of proteins and peptides.

8. Confirm the inclusion of only protein and peptide drug information in Table 1. (Pharmaceutical Drugs and Their Trade Names, Companies, Routes, and Applications)

9. Cite appropriate references in the 'Protein-based Nanoparticles' section.

10. Discuss in detail how 'Animal Proteins and Plant Protein Sources' could be developed as a protein and peptide delivery system with proper citations.

11. Rephrase and confirm the statement and content of Table 2. (Polymeric Nanoparticles for Targeted Drug Delivery (Both Natural and Synthetic Polymers))

12. Confirm the nature of albumin in Table 2.

13. Confirm the illustration in Figure 3 with a citation. (Figure 3 illustrates the fundamental conventional method of protein-conjugated polymeric nanoparticles.)

14. Rephrase and confirm the statement in 'Conclusion and Future Trends' section: The problems associated with peptide/protein-based medication delivery in the contemporary period may be effectively resolved by combining the two methods.

15. Typographic corrections are suggested.

• The use of nanoparticle technology in protein delivery can be applied to the following: I extending the half-life of proteins with poor pharmacokinetic properties in vivo;

• Exciting techniques include mucoadhesive polymers, microspheres, nanoparticles, nanoemulsions, and nanoemulsions [8]