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

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Potential competing interests: No potential competing interests to declare.

1. As the delivery protein and peptides are the main focus of the study, the main hurdles for their delivery can be highlighted as their high molecular weight and low stability which leads to poor absorption and low bioavailability.
2. Be specific about the “trustworthy scientific sources” like pubmed, sciencedirect, web of science, etc.
3. Discuss in the introduction about the challenges in the delivery of proteins and peptide either physiological or anatomical barriers and then discuss how the nanocarrier systems overcome the challenges posed
4. Explain each naosystem approach with 2 or more case studies focusing on how that particular nanosystem overcome the barriers and delivered proteins and peptides.
5. The word "therapeutics" can be used instead of "drug" or "medication" to make it easier for the reader and to avoid confusion between chemical drugs and peptide drugs.
6. Table 1; column: route of administration should be well defined, “3-month depot suspension”, “Unit dose cartridge” are not route of administration and be specific about the injection, either subcutaneous or intravenous, recheck the abbreviation s/c. Expand the abbreviation in the manuscript for the first time appeared and if the abbreviation appeared in table, then the expansion can be addressed at the bottom of the table. Arestin is used as adjuvant for the reduction of pocket depth patients with adult periodontitis. Suprecur is subcutaneous injection and clinically approved for the treatment of hormone-responsive cancers, sex hormone-dependent uterine diseases including endometrial hyperplasia, endometriosis, and uterine fibroids.
7. Page 3, line 3, nanoemulsion was repeated twice
8. Page 3, Microsphere heading, line 2 was not clear to understand
9. Microsphere does not fall under the category of “Potential**Nanocarriers** Approaches”, they are microparticles
10. Please refer to the following articles for the clarity of microemulsion and nanoemulsion: https://doi.org/10.3390%2Fbioengineering9040158, https://doi.org/10.1039/C2SM06903B
11. How do nanomeulsion “reduces the enzymatic hydrolysis of the drug in the body, and can form a protective impact on drugs and improve the absorption of drugs in the gastrointestinal tract”
12. Liposomes fall under the category of vesicular systems but not particulate (nanoparticles) systems
13. “In general, protein nanoparticles exhibit numerous benefits, including biocompatibility, biodegradability, and versatility compared to other nanosystems. More specifically, because of their remarkable biocompatibility, stability, rigid structure, well-defined pore structure, programmable shape, and customizable surface chemistry, mesoporous silica nanoparticles (MSNs) have attracted a lot of interest in protein delivery” these lines look like discussing about the

protein based nanoparticle but suddenly jump into the mesoporous nanoparticles

14. Ensure the quality of figures are good publication potential, especially figure 1
15. The figures used in the manuscript should be free of copy right, ensure the figure 2 does not contains images subjected to copy right
16. Ensure the synthetic polymer mentioned in table 2 are polymers but not just proteins
17. Page 8, as the “e” subheading discussion is about both the solid and nanostructed liquid nanoparticle, change the heading title to “Lipid based nanoparticles”
18. Page 9, “The problems associated with peptide/protein-based medication delivery in the contemporary period may be effectively resolved by combining the two methods” please specify what are the two methods