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

Xuejuan Zhang[1]

1 Jinan University

Potential competing interests: No potential competing interests to declare.

Al-Hussaniy *et al.* reported a review about “Protein and Peptide Drug Delivery Nanocarriers”, elucidated the various nanocarrier systems available, their mechanisms of action, and their potential in enhancing the bioavailability, stability, and targeted delivery of protein and peptide drugs. However, the content of this article is not closely related to the theme, which lacks logical coherence and persuasiveness. A major revision is needed before the final acceptance.

General Comments:

1. There are some logical problems in the introduction part. The content between sentences lacks coherence. Please carefully reconsider and revise this section for clarity. For example, 1) the authors describe the therapeutic potential of protein and peptide drugs, followed by a discussion on the limitations of existing delivery forms. However, the subsequent introduction of two properties influencing nanocarrier drug delivery appears somewhat illogical;
   2) "Peptides and proteins are essential for contemporary biomolecular applications, particularly in the diagnostic domain." In this sentence, the authors emphasize the diagnostic domain but fail to elaborate further. Moreover, the application of proteins and peptides in the diagnostic domain does not seem to be the main focus of this manuscript.
2. As the title described, this is a review of "Protein and Peptide Drug Delivery Nanocarriers", but there is not much description of this part in the paper, which lacks focus.
3. When presenting various types of nanocarriers for the delivery of proteins and peptides, it would be more convincing to cite appropriate examples as supporting evidence.
4. While "nanocarriers for protein and peptide drug delivery" indeed represents a current and vibrant research area, the content presented in this article appears somewhat dated, failing to capture the recent advancements in nanocarrier delivery systems. Numerous studies have focused on enhancing delivery efficiency by addressing challenges such as crossing biological membranes and refining drug targeting. For instance, the incorporation of cell receptor targeting ligands like folic acid and hyaluronic acid, cell-penetrating peptides, or antibodies such as Herceptin and transferrin onto the surface of nanocarriers has been extensively explored.

Specific Comments:

1. In the sentence “The size of the nanoparticles and a high surface-to-volume ratio are two physical and chemical characteristics that often set apart drug delivery methods at the nanoscale”, neither the size nor the surface-to-volume ratio is the chemical characteristics of nanoparticles.

2. The word “nanoemulsion” is repeated in the sentence “Exciting techniques include mucoadhesive polymers, microspheres, nanoparticles, nanoemulsion, and nanoemulsion” in the first paragraph of “Potential Nanocarriers Approaches”.
3. In Table 1, Minocycline isn’t a protein-based drug, which can not be put in the table.
4. In Figure 1 and Figure 2, both the pictures and texts are not clear, please provide high-resolution pictures.
5. In the "Polymeric nanoparticles" part, defining polymeric nanoparticles will enhance readers' comprehension. Additionally, please elaborate on how polymeric nanoparticles can achieve precise drug delivery.
6. In Figure 3, it will be better to add the brief preparation process of polymeric nanoparticles in the illustrated section.
7. In the last sentence of the part of “Solid Lipid based Nanoparticles”, what does the abbreviation SLN represent? It is not mentioned throughout the article, please add it.
8. Please italicize occurrences of "in vivo" and "via" in the manuscript.