

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

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**Potential competing interests:** No potential competing interests to declare.

It was a pleasure for me to read and review the review article "[Review Article] Nanocarriers for Protein and Peptide Drug Delivery". The review is very important as it collects most of the available experimental results on nanocarriers available for peptide and protein delivery. Therefore, in my opinion, it requires few major treatments.

"Exciting techniques include mucoadhesive polymers, microspheres, nanoparticles, nanoemulsion, and nanoemulsion", the repetition of nanoemulsion must have been a typing mistake. Please rectify and replace with other nanocarrier systems.

"following: I extending the half-life of proteins with poor pharmacokinetic" Please write the numbering in roman small letter and close it with a parenthesis.

"Although it is also possible to deliver them orally, the oral bioavailability of this medication is very low due to its poor absorption, but the release of its active ingredients in the gastric tract after the effect of several degradative enzymes." What does the authors mean by "this medication"? In this line, the authors mean to discuss the shortcoming of oral administration of microsphere which are nanocarriers rather than medications. And the structure of sentence has some missing information. Please correct it.

For table 1, the table captions must contain "*protein based drugs*". There must be some applications for Arestin and Suprecur, please mention them in application column. Arestin is preferably used in dentistry for gum diseases and Suprecur for hormonal treatment and several other applications. Please fill the nil cells in table.

"Nanoemulsion is a thermodynamically stable, isotropic, transparent or translucent particle with a particle size of 1 to 100 nm formed spontaneously from water, oil, surfactants, and co-surfactants. It is a homogeneous dispersion system". Is nanoemulsion a particle or a homogenous dispersion system? Please rectify.

"Nanoemulsion has many advantages that are unparalleled by other preparations" the para must have the numbering in roman small letters. Please be sure to be consistent in formatting throughout the document or manuscript. Please correct them to improve the overall quality of manuscript.

Figure 1 is more of a written text rather than an illustration. Figures or illustrations are added to enhance the understanding of text in graphical form to attract more readers. Please convert it into text. Or please merge it with figure 2.

“Different techniques are used to prepare natural and synthetic polymers into polymeric nanoparticles. The following table lists some of the frequently used natural and man-made biodegradable polymers. Different techniques are used to prepare natural and synthetic polymers into polymeric nanoparticles. The following table lists some of the synthetic biodegradable polymers and natural polymers that are often employed.” There is repetition of two sentences. Please delete them. Please be sure that all man made polymers are synthetic.

The caption for table 2 does not fits properly to the content within the table. The caption mentions the polymeric nanoparticles whereas the table only mentions the polymer used in the synthesis of nanoparticles. Please correct the caption for table 2. This is misleading in by opinion.

Here figure 3 is missing the explanation to diagram. Please add the details about the method of preparation of polymeric nanoparticles in the caption to figure. Please add details for the purpose of using syringe pump and how are the nanoparticles formed by the addition of its components/chemicals.

“To overcome the drawbacks of liposomal drug administration, solid lipid nanoparticles were introduced in 1990 as an alternative to liposomes and emulsions”, What were the limitations that lead to introduction of SLNs in market? Please mention few limitations of liposomes in first sentence and then continue with the SLNs in order to make connection.

“This review has 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.” After carefully reading the manuscript, I find that the manuscript has not completely align to the aim mentioned here. The manuscript gave a brief description of major types of carrier system employed for delivery of peptides and proteins but did not focus on bioavailability, stability and targeted delivery of proteins and peptides. Please mention the developed formulations in terms of all the nanocarriers covered in the manuscript. Please ensure to add experimental results from past 5 years only. Please include more publications for proteins and peptides made by utilizing nanotechnology, including the marketed and researched products and those that are in clinical trials as well. Inclusion of 2-3 recent publications for each type of nanocarrier, mentioning their impact in enhancing the therapeutic efficacy of incorporated proteins and peptides.

Are keywords based on MESH terminologies?

Liposomes are not novel carriers but are widely used for delivery of drugs. I wonder why they have been totally neglected while making this manuscript. Please make a separate heading for liposomes mentioning the limitations of conventional liposomes that incorporated proteins and peptides and how these limitations were overcome from past few years. Also mentioned few FDA approved liposomes carrying proteins and peptides (if available) in form of a table.

The authors are advised to remove all the self-citations and the reference of high cited works or scientists expert in this field should be added