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| Book Name: | [**Pharmaceutical Science: New Insights and Developments**](https://www.bookpi.org/bookstore/product/pharmaceutical-science-new-insights-and-developments-vol-1/) |
| Manuscript Number: | **Ms\_BPR\_4314** |
| Title of the Manuscript:  | **Exploring the potential of Chitosan-based nanoparticles as novel carrier for oral delivery of protein and peptide drugs** |
| Type of the Article | **Book Chapter** |

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| PART 1: Comments |
|  | Reviewer’s comment | Author’s Feedback *(Please correct the manuscript and highlight that part in the manuscript. It is mandatory that authors should write his/her feedback here)* |
| **Please write a few sentences regarding the importance of this manuscript for the scientific community. A minimum of 3-4 sentences may be required for this part.** | This manuscript highlights the significance of chitosan-based nanoparticles as innovative carriers for the oral delivery of therapeutic proteins and peptides, addressing critical challenges like poor permeability, stability, and enzymatic degradation. By exploring various preparation methods and emphasizing the unique advantages of chitosan, such as biocompatibility, biodegradability, and mucoadhesive properties, the study provides valuable insights for advancing protein drug delivery systems. |  |
| **Is the title of the article suitable?****(If not please suggest an alternative title)** | Yes |  |
| Is the abstract of the article comprehensive? Do you suggest the addition (or deletion) of some points in this section? Please write your suggestions here. | Yes. However, certain points need to be addressed.1. ‘So, the objective of this work was to explore the potential of chitosan nanoparticles….’—Being a book chapter, this section should be like ‘This chapter explores the potential of chitosan nanoparticles’.
2. The phrase *"impactful characteristics"* should be revised for scientific precision. Consider rephrasing to *"favorable properties"*.
3. A space needs to be added before ‘Chitosan and modified chitosan can be used as polymers…….’.
4. ‘…preparing the formulation of polymeric nanoparticles via different methods Ionic Gelation Techniques, Emulsion Solvent Evaporation Method, Emulsification Solvent Diffusion etc.’—don’t use any uppercase letters in the middle of the sentence.
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| **Is the manuscript scientifically, correct? Please write here.**  | Yes |  |
| **Are the references sufficient and recent? If you have suggestions of additional references, please mention them in the review form.****-** | Additional references need to be incorporated, including more recent citations, to enhance the manuscript's relevance and ensure it reflects the latest advancements in the field. |  |
| Is the language/English quality of the article suitable for scholarly communications? | Yes, but a lot of correction is needed. There are several grammatical errors and issues with sentence construction throughout the text. A considerable number of sentences require rephrasing for improved clarity and grammatical accuracy. |  |
| Optional/General comments | 1. Graphical abstract: ‘Chitosan nanoparticle containing protein’ should be ‘Chitosan nanoparticle containing protein drug’. Moreover, draw a vertical line before the section Chitin source, in order to separate two sections.
2. ‘……cancer treatment as well as for metabolic disorders[1].’—Use space before citation [1]. Follow this throughout the manuscript.
3. ‘However pharmacokinetic properties of this therapeutics…..’—‘this’ should be ‘these’.
4. ‘However pharmacokinetic properties of this therapeutics are the main drawback in the delivery aspect. However, the research on routes of administration other than parenteral continues’—Please don’t use ‘however’ in two subsequent sentences.
5. ‘Carrier-like chitosan is a potential candidate to provide protective conditions…….’— ‘conditions’ should be ‘environment’.
6. ‘The various natural sources are molluscs, insects, fungi, and yeasts.’—various sources of what?
7. Cite specific reference for ‘However pharmacokinetic properties of this therapeutics are the main drawback in the delivery aspect.’
8. Cite specific reference for ‘However, the research on routes of administration other than …………………. proteolytic activity and acidic condition of the gastrointestinal tract.’
9. Cite specific reference for this ‘Additionally, chitosan possesses various properties such as antimicrobial, antioxidant, analgesic, and antitumoral activities’.
10. In the title of the section 2 “Main text”, the word is not sufficient. The author should replace it with a word which has a broader definition.
11. ‘…….and peptides via various administration routes for diverse therapeutic applications’—mention some example for various administration routes.
12. ‘Protein absorption can be enhanced by chitosan.’—please make it clear and complete.
13. ‘Chitosan's potential to transport therapeutic compounds across organized epithelia including nasal, intestinal, ophthalmic, buccal, and pulmonary epithelia, has received extensive study’—rephrase it to increase clarity.
14. ‘Chitosan derivatives can be prepared by the modification of OH and NH2groups……’—use space after ‘NH2’. Moreover, use a bond before the functional groups. eg. —OH and —NH2.
15. Use space before ‘The majority of approaches for administering…………..’. There are a lot of issues with spacing. Please do modify those carefully throughout the manuscript.
16. No reference has been cited for ‘2.2 Several barriers for protein delivery via oral route’.
17. ‘………in the Peyer's patches region, which aids in the passage of nanoparticles.’—write the location of Peyer's patches region (small intestine).
18. No reference has been cited for Enzyme Barrier.
19. ‘…….breakdown in the GIT and enhancing the drug's oral bioavailability.’—describe the abbreviation GIT.
20. ‘..and M cells and the cell membrane is made of lipid bilayer.’—full form of M cell at its first appearance.
21. ‘….these barriers can be successfully overcomed.’—wrong word ‘overcomed’.
22. Use citation after ‘……..makes it an appropriate drug carrier for parenteral administration.’.
23. Don’t use bold form for mentioning authors names like Rekha et al.
24. Cite Jin et al. here—‘ By employing optimal emulsion polymerization, Jin et al. created poly (butyl cyanoacrylate) nanoparticles’.
25. Use full form of CS—‘ Ionic gelation involves dissolving CS in acetic acid………..’.
26. ‘…..and agitating the mixture mechanically at room temperature’—use ‘stirring’ in place of ‘agitating’.
27. ‘….Sang et al. prepared CS NPs via the ionotropic gelation method’—wrong citation [15]. Cite Sang et al. at the end. Cite appropriate references for all. A lot of issues are there.
28. No references have been cited for Nanoprecipitation Method.
29. ‘This approach involves dissolving drugs and polymers in a polar solvent (ethanol, propanone, or DMSO).’—use full form of DMSO.
30. ‘Hydrophobic compounds were the original target of the method's development’—Not clear at all. Replace this sentence with ‘The method was originally developed to target hydrophobic compounds.’.
31. ‘….the emulsion was allowed to agitate for 8 hours’—use stir in place of agitate.
32. ‘To get rid of any leftover drug molecules, centrifuged followed by washing with distilled water.’— The sentence is incomplete and grammatically incorrect. Here's a corrected version: To remove any leftover drug molecules, the sample was centrifuged and then washed with distilled water.
33. ‘Again sonicated, resulting nanoparticles formation from pellets which were maintained at 80°C and lyophilized for overnight’—incorrect sentence.
34. Citation needed for ‘Supercritical fluids are ……………., then expanding the solution using a nozzle’.
35. ‘Elvassore et al.[17] used this technique to create insulin-loaded PLA NPs…..’—Use full form of PLA and NPs at its first appearance.
36. ‘…..results in the formation of the basic w/o emulsion.’—use full form of o/w.
37. Increase the resolution of the quality of the figures.
38. ‘…..a TPP cross-linking agent is typically utilized’—full form of TPP.
39. ‘The scientists think that M cells or cytosolic fluid where the nano-drug delivery method is primarily absorbed’— The sentence is unclear and grammatically incorrect.
40. ‘M cells have a much greater absorption of nanoparticle than intestinal cells’—replace with ‘M cells have a much greater capacity for absorbing nanoparticles compared to intestinal epithelial cells’.
41. ‘Peyer's patches is the first site of nanoparticle uptake….’—incorrect verb.
42. ‘A study by Hussain et al. has demonstrated an ideal particle…..’—A lot of anomalies are present in the reference citation. Hussain et al. should be cited.
43. No reference has been cited for ‘Nature of Nanoparticle’.
44. ‘According to Yoncheva et al. cysteine-modified….’—incorrect citation. Yoncheva et al should be cited.
45. ‘The primary pH-dependent vector used in the colon-targeting nanoparticle delivery method.’—incomplete sentence.
46. ‘…..preserve the activity of thesedrugs’—use space in between thesedrug.
47. No citation in Drug Delivery Specific for the Colon.
48. ‘The primary method of producing mucous membrane adhesion is extending the duration of drug residency in the mucous membrane. The bioavailability of protein drugs can be enhanced by mucous adhesives, which can also directly alter the mucous epithelium's permeability.’—cite reference.
49. Cite proper reference for ‘Protein Nanocrystallization Technology’ and ‘Nanoparticles of Cell-Penetrating Peptides’.
50. ‘pHPMA’ should be in uppercase.
51. ‘Oral absorption is significantly limited by the close proximity between the cells …………….. can potentially disrupt the intestinal barrier, regardless of specific targets’—please cite proper references for each sentences.
52. ‘Liu et al. reported their research on insulin in rats. The outcome was that absorption and degradation of that drug were affected by protease inhibitors. They discovered that the large intestine was more effectively affected by these protease inhibitors than the small intestine[23].’—the cited reference is different than the Liu et al.
53. ‘Soluble TMC has better mucoadhesive qualities…….’—the full form of TMC should be mentioned at its first appearance only.
54. ‘A large number of toxicity studies that are now accessible involve formulations…….’—use comma after ‘accessible’.
55. ‘In Vivo Toxicity’—no reference was cited. Include more studies here with proper ref.
56. ‘Thirteen clinical trials have been done on the oral administration of CS as a dietary supplement……—make a table to describe the details about the trials.
57. ‘Modified chitosan shows more toxic effect on COS-7 and MCF-7, elevated MW…’—describe what is COS-7 and MCF-7, and MW. Also write what kind of cell lines they are, like MCF-7 a breast cancer cell line.
58. ‘Sen et al.[30] explored the use of O-methylated….’—please verify, whether its Sen et al. or Biswas et al. As per ref list, it should be Biswas et al.
59. ‘Preparing vaccine-loaded CS-TM nanoparticles…..’—what is TM?
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| **PART 2:**  |
|  | **Reviewer’s comment** | **Author’s comment** *(if agreed with reviewer, correct the manuscript and highlight that part in the manuscript. It is mandatory that authors should write his/her feedback here)* |
| **Are there ethical issues in this manuscript?**  | *(If yes, Kindly please write down the ethical issues here in details)* |  |

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| **Reviewer Details:** |
| Name: | **Sabyasachi Banerjee** |
| Department, University & Country | **Gupta College of Technological Sciences, India** |