

## Fw: RPS 16-168 needs major major revision

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From: RPS Journal (rps@pharm.mui.ac.ir)

To: dewiffua96@yahoo.com; farisadrianto@gmail.com

Date: Sunday, 6 August 2017, 01:43 pm GMT+7

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Sent:Sun, 6 Aug 2017 09:56:20 +0330

Subject:Fw: RPS 16-168 needs major major revision

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Subject:RPS 16-168 needs major major revision

Dear author

Thank you submitting your article to RPS journal, your revised article was reevaluated to ensure that all comments have been taking in to account and the manuscript has been revised accordingly. Unfortunately your article can not be transferred to next step unless your manuscript is completely and fully revised scientifically and also from English point of view. I as Editor in Cheif of the

Journal, reviewd your article and realized that your article needs serious revision

Please go through all the comments carefully and one by one and address all the comments in your manuscript and return the revised article to us for reevaluation.

Editor in Cheif comments

1. The work lacks adequate novelty. So many Micro, macro, and nano carriers have been reported using chitosan and HA to target drugs to the desired tissues. The method also is very old and has no novelty or innovation and tablet or tablet-form composite seems inappropriate for bone damages and fractures.

2. The evaluation and assessment methods are not appropriately and logically selected and described. References given in the method section do not match with the methods described and unrelated to the described method.

3. Observations are all over the places and can not be explained or justified with variables such as the GA or

genipin content used in the implants.

4. So many problems and issues are associated with the discussion section. The observations are not correctly discussed and in some occasions are incorrect. Most often the results contradict each other. For instances dissolution profiles are not in accord with density, porosity and water uptake of the formulations. Statistical analysis are not described appropriately in the result and discussion sections. They are non-scientifically and nonstandard are presented in discussion section.

5. Overall, the paper does not follow a scientific approach and very poorly written in terms of English language and skills. Crammer errors and non scientific and incorrect phrases are abundant.

[REVIEWER]1:

In this manuscript, "The effect of different cross link agent glutaraldehyde and genipin incomposites to the physicochemical" , while I find some interests, I have several criticisms described below.

1. In the " Introduction" the authors should introduce the use of chitosan and hydroxyapatite for bone tissue engineering
2. The genipin and glutaraldehyde crosslinked the chitosan, what's the function of Bovine Hydroxyapatite in the implant? In the FTIR and XRD following BHA in the formulations is not clear and should be discussed.
3. Molecular weight of chitosan should be noted in the materials.
4. "Mechanism of crosslinking" should be transformed to the Result section.
5. For determining the prosity, the authors should display BET test. The implant has a hydrogel structure and adsorbs the water, so using water for prosity test is incorrect.
6. Equation 2 and Equation 4 are the same. This equation is used for determining the swelling ratio and should be omitted from prosity test.
7. For determining the swelling ratio, the duration time of immersion of implants in the buffer should be noted.
8. "Degradation test" should be changed to the "disintegration test".
9. The results of Degradation test were not shown.
10. Analysis of ciprofloxacin was performed at 3 wave lengths, the authors display about this method.
11. In "In vitro drug release study" the volume of release medium is very low (5 ml) in comparison to the sampling volume (1 ml), and 20% of the medium was replaced with fresh buffer at each sampling point time. This can cause error.
12. X and Y axis in Fig 3 should be corrected. Cumulative drug releasedpercent against time should be plotted not cumulative drug releasedconcentration. Indeed, number of days should not have decimal points.
13. The authors didn't discuss why different formula released the drug

with the same manner?

14. The SEM images were not uploaded correctly.
15. At the end of discussion the authors should conclude about the study.
16. At the lines number of 161, 238,260, please change “,” to “.”
17. At the line numbers of 105 please change the red point to black point.

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[REVIEWER]2:

The manuscript deals with investigating the effect of type and concentration of two crosslink agents, glutaraldehyde or genipin, on the physiochemical characteristics of the composite hydrogel of hydroxyapatite and chitosan. Please find the following comments to undertake a major revision:

- 1- the abstract needs re-writing with respect to the structure and the content. It also contains many typos and grammatical errors.
- 2- incomplete literature review! the papers on chitosan-hydroxyapatite hydrogel hasn't been addressed.
- 3- the aim of study has not been well defined at the end of the introduction section.
- 4- there are some ambiguous parts in the materials and methods section that needs to be revised or explained: homogeneous chitosan powder (homogeneous?), the compression pressure of 2 tons, mechanism of crosslinking section (unrelated to the materials and methods section), the calculation of hydrogel porosity, assay of drug content by extrapolating of the UV-Vis calibration curve constructed at 3 wavelengths, the mechanical strength of the implant which has only been tested in term of hardness in dry state.
- 5- some parts in the results section are related to the discussion. P values have only been presented in the discussion, so it is suggested to combine the results and the discussion sections.
- 6- there are some justifications that have to be re-considered: molecular dispersion of ciprofloxacin in the XRD experiment (or may be only an amorphous drug state), no free glutaraldehyde has been remained (FTIR of free glutaraldehyde at the corresponding amount is missing), etc.
- 7- the discussion section has been started with the non-significant density findings. It is recommended to begin this section with what the study is concerned about and also to discuss only about the most important findings.
- 8- there is no discussion about the drug release from the implant that should be included.
- 9- there is no interesting conclusion coming from the effect of type and the concentration of crosslinks on the physicochemical and the drug release properties.

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[REVIEWER]3:

The authors review the the effect of different cross link agent

glutaraldehyde and genipin in composites to the physicochemical characteristics and the release of

ciprofloxacin implant. This issue is of potential interest and pharmaceutical interest and inputs new insight to the understanding of the topic. However, a few points must be considered prior to publication.

1. There are numerous grammatical points and the manuscript requires a thorough English editing prior to publication.

2. The authors have discussed the availability of retard ciprofloxacin release. The clinical importance has been explained in the introduction. It would be better to describe the potential clinical benefits in the discussion section.

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From: RPS Journal (rps@pharm.mui.ac.ir)

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Date: Saturday, 16 September 2017, 03:14 pm GMT+7

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Subject:RPS 16168 editing phase

Dear author

Please modify the figure according to the comments.

Thanks

Assistant editor of RPS journal

Dr. Rabbani

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