

-----Original Message-----

from: XXX YYY <xxx@yyy.zzz>

to: Managing Editor

date: Thu, Jan 17, 2013 at 1:31 AM

subject: RE: Request for final decision for manuscript number 2012 ORAJ 2442

Dear Dr ZZZ

Re: Formulation and physical characterization of a novel sustained-release ophthalmic delivery system for sparflaxacin: the effect of the biological environment

Overall the text is well written, the study is well designed and performed.

The agent is a promising possibility in the context of ocular infection.

The authors acknowledged the following points in their rebuttal. However, they don't address them as limitations in the text, which they should, or carry out the work as suggested by previous reviewer Mahmoud Al Omari .

1.Again, to prove complex formation and suitability of the analysis techniques (DSC, IR, and SEM), the author needs to prepare the physical mixture after treating each component (Drug, CD) separately with the same spray-dried procedure.

2.The author needs to run also the dissolution using physical mixture prepared from spray-dried drug and CD.

3.Again, gel formulations in the present work can be done by simple procedure without using spray drying any more. So I recommend to prepare the same formulas (FM1, FM2, FM3 and FM4) using non-treated components (Drug and CD).

In addition I would like to add some recommendations of my own

Line 457 Change to .highly significant.

Line 305 The method was performed by filling 1 ml of the each in-situ gel formulation in the dialyzer body with care to avoid presence air bubbles inside the preparation

Change to: The method was performed by filling 1 ml of the each in-situ gel formulation in the dialyzer body with care to avoid air bubbles inside the preparation

Line 348

In thermogram of the physical mixture of drug with HP- β -CyD, unchanged broad band due to the HP- β -CyD dehydration, while the sharp endothermic drug peak was decreased in its intensity but not completely disappeared, this may be due to partial inclusion of drug with cyclodextrin by the physical mixing process.

This is confusing.

Does the author mean?

In the thermogram of the physical mixture of drug with HP- β -CyD, there is an unchanged broad band due to the HP- β -CyD dehydration, while the sharp endothermic drug peak was decreased in its intensity but did not completely disappear, this may be due to partial inclusion of drug with cyclodextrin by the physical mixing process.

Line 562

It is important to know the gelling time of all the prepared formulations, as if the gel takes long time to be formed in the eye, it may be drained out of the eye before its formation, so decreased ocular bioavailability.

This is confusing

Does the author mean?

It is important to know the gelling time of all the prepared formulations, because if the gel takes a long time to form in the eye, the drug may be drained out of the eye before gel formation occurs, leading to decreased ocular bioavailability.

Line 736

These results indicate that, this formulation approach could be developed and used in future to treat intra-ocular infections with a reduced dosing frequency.

This is over reaching somewhat.

Perhaps the authors could say:

These results indicate that, this formulation approach could be developed and trialed in the treatment of intra-ocular infections with a reduced dosing frequency.

I believe that with the above changes, the manuscript should be accepted for publication.

XXX YYY

Note: Modification was done in this email ONLY to hide the identity.