Author's response to reviews

Title: Potential of stratum corneum lipids liposomes for the topical delivery of 5-aminolevulinic acid in photodynamic therapy of skin cancer.

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The manuscript "Stratum corneum lipids liposomes from the topical delivery of 5-aminolevulinic acid in photodynamic therapy of skin cancer: preparation and in vitro permeation study was revised based on referees suggestion. The changes are listed below:

1- Dr Jose Parra:
We made in vitro retention experiments using tape- stripping method. We measured 5-ALA retained in SC and rest of epidermis + dermis. These results were very interesting because proved that 5-ALA was delivered preferencialy to the epidermis without SC + dermis, which is desirable for skin cancer treatment, ie the drug was delivery and retained in the skin tissue where skin cancer takes place.

2- Dr Arto Urtti
The explanation above answers part of Dr Urtti's major comments.
We used formalin (0.01% w/w) to preserve acceptor solution and the skin during in vitro experiment. This preservative is adequate because it maintains reasonable the skin integrity during long time experiments.
Hairless mouse skin is more permeable than human skin. However, the present study is comparative between two formulation. The results of skin permeation and retention will not be quantitatively similar to human skin, but we can have the same qualitative behaviour.

3- Dr Shuji Kitagawa
SCLLS did not retain 5-ALA in the SC (Figure 3), probably because is hydrophilic and the retention in the SC can depend on the lipophilicity of the drug. However, SCLLS delivered higher amount of 5-ALA into epidermis without SC + dermis, where is the target skin tissue for PDT of skin cancer. This behaviour can be due to SCLLS improve the partition and diffusion of 5-ALA in the SC. Because is a hidrophilic molecule, 5-ALA is partitioned to aqueous skin layers like viable epidermis and dermis. Liposomes obtained with phospholipids can provoked increase of skin permeability facilitating the transdermal transport, which is not adequate for topical PDT on skin cancer. In this aspect, SCLLS seems more interesting for this treatment.We did not make additional experiment but justified by published work.
We change the title taking of the expression "Potential of ....."
In the retention experiment we cleanned the skin with buffer solution in order to avoid possible enhancement of SCLLS penetration by methanol.
Further studies will include entrapment of 5-ALA ester derivative (more lipophilic molecules) into SCLLS. This can increase the encapsulation of the drug and more drug may be deliver into the skin. Even with low degree of encapsulation (due to 5-ALA leaks from the system) we had promising results.
The English revision was made.

General comments:

- We do not have competing interesting related to this paper.
- We did not receive any reimbursements, fees, funding, or salary from an organisation that may in any way gain or lose financially from the publication of this paper.
- We do not have any other financial competing interests.
- We have research competing interests on this publication.