Author's response to reviews

Title: Evaluation of the in vitro skin permeation of antiviral drugs from penciclovir 1% cream and acyclovir 5% cream used to treat herpes simplex virus infection

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Version: 4 Date: 24 February 2009

Author's response to reviews: see over
Title: MS: 8370183982091332
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Version: 4 Date: 24 February, 2009

Author’s response to reviews

To: Scott Edmunds PhD
Senior Editor
BMC-series Journals

Dear Dr Edmunds,

Please find below our answers to reviewers, who enabled us to increase the clarity of this manuscript. We amended the introduction and the conclusion.

Thank you for considering publishing this revised version of our manuscript in BMC Dermatology.

With best regards,

Nathalie Hasler-Nguyen, PhD

Reviewer’s report

Title: Evaluation of the in vitro skin permeation of antiviral drugs from penciclovir 1% cream and acyclovir 5% cream used to treat herpes simplex virus infection
Version: 3 Date: 4 February 2009
Reviewer: John J Docherty

Reviewer’s report:
Thank you for the opportunity to comment once again on this paper. I appreciate the changes the authors made to their discussion by deleting those parts that dealt with an actual infection in viable tissue. However, there continues to be a problem with the way this paper portrays itself. My previous comments about
their model being non-viable applies to all of the manuscript. For example the first two pages of the “Introduction” (which by the way is too long) describes in great detail drug activity in viable tissue such as phosphorylation, inactivating DNA pol., inhibition of viral DNA synthesis, competitive inhibition etc., etc., etc. It’s not until the reader has read almost two pages of the “Introduction” do we get to the last sentence of the second paragraph (“Thus, in vitro…”) do the authors begin to indicate what their intentions are. In the last paragraph of the “Introduction” they state that “…skin permeation was assessed using human skin…”. For the readers sake they should clearly state here that it was non-viable human cadaver skin

Answer: we deleted the mode of action of the molecule in the introduction in order to focus only on the in vitro skin permeation and the molecular modeling. We feel the wording cadaver might be too crude so we prefer to keep non viable human skin and in vitro skin permeation assay.

There is nothing experimentally wrong with this paper but because of the use of non-viable tissue I question the significance of the work and interest to the reader. If the authors had done the studies they mention in the last sentence of their discussion this paper would be considerably more relevant.

Answer: the relevance of this work is the fact that it represents a valuable approach to in vivo percutaneous absorption study and it is a convenient means for evaluating the permeation characteristics of two drug analogues from comparable formulations. As stated now in the conclusion the molecular modelling enabled for the first time to reveal difference between acyclovir and penciclovir on the surface properties. This observation might support that penciclovir has the tendency to have a higher paracellular passage through the stratum corneum resulting in a tendency to reach higher concentration in deeper epidermal layers.

Performing the assays with viable human skin infected or not with HSV-1 would have been more relevant however surgical tissues supply is very restricted and limit the possibility of experiments when compared to human skin excised at autopsy.