Reviewer's report

Title: Pharmacokinetics of quinacrine in the treatment of prion disease

Version: 1 Date: 26 October 2004

Reviewer: Armin Giese

Reviewer's report:

General

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Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

None

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Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

1.) The authors should include the concentrations of quinacrine obtained in liver and spleen in the abstract. The actual numbers are important to put brain levels into perspective.

2.) The authors should indicate more clearly that the EC50 concentration of quinacrine for suppression of PrPSc in cell culture (300 nM) relates to the concentration added to the cell culture media and that the effective concentration in the cells may be significantly higher due to intracellular accumulation of quinacrine.

3.) The authors should use only one way of giving concentrations of quinacrine (preferably µg/g, avoid using "nM" for the results from cell culture experiments) so that the reader can compare the values obtained in different tissues and experimental models (cell culture vs. animals) more easily.

4.) page 6, 7th line from the bottom: missing character in the concentration of the standard solution.

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Discretionary Revisions (which the author can choose to ignore)

I think that the results of this study indicate that quinacrine penetrates into the brain inefficiently (compare levels in brain tissue to levels in liver and spleen). Considering that there will probably be significant intracellular accumulation of quinacrine in the cell culture experiments cited by the authors (so that the actual intracellular EC50 may be well above 300 nM), I personally think that the author’s conclusion "The documented extensive brain tissue penetration is encouraging suggesting quinacrine might be useful in the treatment of prion disease." (p. 3) is not justified by the data presented and should be modified (the same applies to some similar statements in the "results and discussion" and "conclusions" sections). However, it is up to the reader to make up his/her own mind in this regard. The data presented it definitely relevant in this respect.

What next?: Accept after minor essential revisions
Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: No

Declaration of competing interests:

None