Reviewer’s report

Title: "Dimethyl Sulfoxide Blocks Herpes Simplex Virus-1 Productive Infection In Vitro Acting at Different Stages with Positive Cooperativity. Application of Micro-array Analysis"

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Reviewer: Mr Kenneth Simmen

Level of interest: A paper whose findings are important to those with closely related research interests

Advice on publication: Accept after discretionary revisions

1-This manuscript by Aguilar et al describes a study of the effects of DMSO on HSV infection. As such, the conclusions of the study (that DMSO acts to block HSV infection at IC50 concentrations of 0.7 to 2%) are certainly of interest to all those researchers engaged in antiviral research and compound screening. The methods employed include classical time-of-addition assays, as well as the recently developed HSV/cellular gene microarray the authors have reported in 2001.

DISCRETIONARY REVISIONS

2- Fig1 - y axis should presumably read (PFU x 10^7) instead of 10^-7?
3- the authors used DMSO in the study, but did not specify the particular chemical supplier of the DMSO used in the assays, or whether they used DMSO from different manufacturers; this detail may be of interest to readers performing antiviral testing.

4- Fig Legend to Fig 3 refers to "HDD" cells: these are presumably the human foreskin fibroblasts (HFFs) described in the text on p14/15 and defined in the Methods (p6). HDD should be defined in Legend or text, or corrected to HFF.

5- Fig 6 + p13: the authors interpret the expts in Fig.6 as effects on virion stability. In the absence of any biochemical experimentation to substantiate this interpretation, I would suggest that the term virion stability be replaced with virion infectivity, which is a more accurate description of what is assayed.

6- p14/15: the array analysis was performed with human fibroblast infections using the 4% DMSO concentration determined earlier to be effective at blocking HSV replication (Figs 1+3) with little (20%) effect on cell viability in Vero cells. In switching to HFF cells, the authors did demonstrate that DMSO had an antiviral effect in those cells (1.4% IC50) comparable to that in Vero cells (2%). However, my concern is that having profiled the antiviral effect in HFFs, they did not furnish any cytotoxicity data in human fibroblasts. I would recommend that such data be provided (if available), as it was for Vero cells (Fig2). As the array work is based on an assumption that the 4% DMSO was
non-toxic, and that all changes in viral gene expression are therefore solely due to the antiviral effects of DMSO, it is important to address this point.

7- p18 "all these actions are observed at conditions in which DMSO does not have any significant cytotoxic action" - see (6) above; not clearly addressed in HFFs.

Editing suggestions:

The text contains numerous typos and inconsistent spellings of the same words: I list these below and would suggest that a copy-editor looks at these in detail......

adenine arabinoside (p3/4)
Cidofovir (p3/4)
Idoxouridine (p3/4)
galactosidase (p6)
expressed (p8)
uCi (p9)
Data analysis (p10)
software (p10)
ref 31 Virology (p28)

Competing interests:

None declared.