Reviewer's report

Title: Effect of Black Tea Extract on Herpes Simplex Virus-1 Infection of Cultured Cells

Version: 3 Date: 31 January 2013

Reviewer: Charles Isaacs

Reviewer's report:

The present study was undertaken to assess the effect of a black tea extract with approximately 80% theaflavins on the production of HSV-1 in cultured cells. The study showed that at BTE concentration of up to 13-14 mM there was no toxicity to Vero or A549 cells.

There are however a number of problems with the study:

1. It is difficult to accurately determine the concentrations of theaflavins used in this study and it would be helpful if the authors used calculations based on an average molecular weight of 716.6 as was done in reference #17 which examined the effect of BTE on HIV replication.

2. The authors state in the discussion that, “…individual theaflavins should be tested to determine their effectiveness in inhibiting HSV-1…” however this has already been done in a published study, Antimicrobial Agents and Chemotherapy, vol 55,ps 5646-5653,2011. The study showed that the digallate theaflavin was the most effective at inhibiting HSV-1, HSV-2 and other enveloped viruses.

3. The authors indicate that BTE inhibits HSV-1 at a number of steps in the viral replication process however, in most of these assays HSV-1 is incubated for 1 hour with BTE at a concentration which is sufficient to directly inactivate the virus and would therefore lower the MOI of HSV-1 producing a number of the results attributed to decreased adsorption, attachment, penetration and DNA replication. The reference indicated above shows that concentrations of 100um theaflavin-3,3’-digallate will inactivate multiple logs of HSV in an hour. Also, results in references 16 and 17 in this manuscript show that HIV is inhibited by BTE in the 1-30 um range through a direct effect on the virion. The authors in reference 17 state the effect of BTE on HIV reverse transcriptase is minor compared to the direct effect on the virion.

4. Most of the results presented in this manuscript show lack of toxicity and not efficacy. These studies should be repeated with purified black tea theaflavins at lower concentrations.

5. Much of the discussion and introduction are repetitive.

6. The figure legends for Figs 7 and 8 do not match up with how the figures are labeled.
Level of interest: An article of limited interest

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

I declare that I have no competing interests.