Reviewer's report

Title: Pleurotus ostreatus opposes mitochondrial dysfunction and oxidative stress in acetaminophen-induced hepato-renal injury

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Reviewer: Hartmut Jaeschke

Reviewer's report:

The authors investigated the effect of feeding a mushroom powder (Pleurotus ostreatus) to mice for 10 days and, after 12 h fasting, administered a dose of 500 mg/kg acetaminophen. The animals were sacrificed after 24 h and a number of liver and kidney-related parameters were measured. The mushroom powder-fed animals showed complete protection against APAP-induced liver injury. The authors concluded that the mushroom powder protected due to its antioxidant properties.

Major Compulsory Revisions:

Although the use of this particular mushroom powder as protective agent is novel, there are a number of significant concerns with the study:

1. The almost complete protection suggests that components of the mushroom powder may have inhibited metabolic activation of APAP. As the authors pointed out, the formation of the reactive metabolite is a critical initiating event. If this is blocked, all subsequent events are prevented. To test this, the authors need to at least look at GSH depletion at 1 h after APAP administration and measure protein adducts at this time. Without this information, the conclusions that ingredients of the mushroom powder acted as antioxidant is not justified.

2. The authors did not characterize the mushroom powder. Without understanding the chemical composition, it is almost impossible to reproduce the findings and any conclusions regarding antioxidants being involved is not justified. The authors need to analyze the major components of this powder.

3. The accuracy of some of the measurements appears questionable. For example, what does µM/mg protein mean (Figure 2A,B)? GSH or MDA levels are normally reported as nmol/mg protein or µmol/g liver wt. The numbers reported by the authors, especially the fact that the MDA levels reach concentrations equivalent to control GSH levels appears questionable. These data need to be recalculated.

4. Introduction (last sentence of 2nd paragraph): “…leading to apoptosis [4].” First, the cited review does not claim that APAP-induced cell death is due to apoptosis. Second, the authors themselves describe necrosis in their histology sections.

Level of interest: An article whose findings are important to those with closely related research interests
Quality of written English: Needs some language corrections before being published

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

Declaration of competing interests: no conflicts of interest to report