Reviewer’s report

Title: Antinociceptive, muscle relaxant and sedative activities of gold nanoparticles generated by methanol extract of Euphorbia milii

Version: 2  Date: 31 December 2014

Reviewer: Iris Bell

Reviewer’s report:

This study presents a “green” method for biosynthesizing gold nanoparticles using Euphorbia milii methanol extract and testing their physical chemistry properties and behavioral effects on mice. Overall this is a valuable empirical study that should interest readers of this journal. The question is well-defined and the methods, including statistics, are generally appropriate and well-described.

However, there are some questions that the authors might clarify or address to improve the usefulness of the paper for other investigators.

Major Essential Revisions

1. Although the authors utilized well-respected methods for characterizing the synthesized nanoparticles, they did not mention evaluating zeta potential values. In view of their important experimental manipulations with pH and salt concentrations to test particle stability, it is somewhat surprising that they did not also report on the zeta potential measurements in addition to the other data collected as another objective indication of comparative particle stability.

2. Along a similar vein, given the source material was gold, it is surprising that they did not also assess the nanoparticle properties using x-ray diffraction (e.g., [1]). The authors may want to comment on why they chose to use or not use specific techniques for characterizing the synthesized nanoparticles.

3. Given the omission of comments, I presume that the authors’ institution does not require prior review and approval of the study procedures by a research animal welfare protection committee, but if so, this may need to be stated and the humane treatment of the animals during the study be addressed in some manner.

Minor Essential Revisions

4. It would be helpful for the authors to mention somewhere in an appropriate place in the Results and/or Discussion the usual bulk dose of the herb used in herbal medicine to treat people in order to put the doses of the nanoparticles tested into perspective.

5. In the Introduction, it may help to introduce the concept of improving bioavailability and biological effects at lower doses with nanoscale forms of an agent earlier in the Introduction.
6. Moreover, in the Introduction, it may be helpful to highlight the advantages of herbal agents as multi-target treatments, as contrasted with conventional synthetic drugs [2].

7. In the Introduction, the authors mention the tumor-promoting data with the herbal agent that they used. Somewhere in the Discussion they may want to address this point as a potential disadvantage of this specific plant in treating patients with infections. This agent may also have some anticarcinogenic effects as well. What are the conditions that foster versus treat cancers? Is the tumor induction a long-term effect that is not a concern for short term use? Most of the other effects of the herbal agent appear to be positive, and the lack of comment on this notable negative effect would seem indicated.

8. In the Methods section, it would be helpful to state the size of the filters used in the synthesis of the nanoparticles. This is potentially important given evidence that glassware can release sufficient glass or silica particles from the inner walls especially during agitation to affect immunogenicity of proteins in solution, even after careful filtration [3-5]. This can lead to bioactive silica micro- and nanoparticles in addition to any other intended nanostructures in the solution.

Discretionary Revisions

9. Although it is acceptable that they did not test the original herbal extract along with the nanoparticles for effects on the same outcome measure for pain. They did do so in evaluating other behavioral outcome measures. Thus, it seems like a surprising omission. It also seems curious that they did not address the head-to-head comparison of doses of bulk form herbal extract versus nanoscale form needed to produce comparable effects, given evidence with other nanoscale forms involving other herbal agents reduce the dose needed by at least one or more orders of magnitude [6, 7].

References


**Level of interest:** An article of importance in its field

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

I am currently carrying out research on natural product nanoparticles found in homeopathic remedies via two separate grants from private foundations (AlterMed Research Foundation and the Lotte and John Hecht Memorial Foundation). The types of materials described in the current paper are on herbal-derived products (gold nanoparticles made using a plant herbal extract), not on homeopathic products. Thus, while the general topic area is one which I actively studying, there is no direct conflict of interest.