Reviewer's report

Title: Antinociceptive activity of methanolic extract of Muntingia calabura leaves: Further elucidation of the possible mechanisms

Version: 2 Date: 27 November 2013

Reviewer: Lindsay Brown

Reviewer's report:

Major compulsory revisions:
The major question is – is this study a significant extension of previous studies by the same research group? The authors mention 4 related papers: Sani et al (2012), Zakaria et al (2006b, 2007a and 2007b). A quick look at these papers shows minor differences, such as aqueous vs methanol extracts, slightly different animal models of nociception, use of the same antagonists with the addition of one or two more. However, the conclusions are remarkably similar. The authors must be able to present solid arguments that the current manuscript represents significant advances in the understanding of the pharmacological responses to this extract.

Minor essential revisions:
Abstract, Results lines 7-10: Prazosin both reversed and did not reverse the MEMC antinociception – which statement is correct? In section 3.4.3, prazosin reversed the antinociception of phenylephrine but not MEMC.

Page 2 of Introduction, line 6: “ethnopharmacological”

Introduction page 2 line 10: What are “emmenogogue headaches”? Wikipedia defines emmegogues as “herbs which stimulate blood flow in the pelvic area and uterus; some stimulate menstruation”.

Section 2.4 Animals, line 1: insert “rats” after “Sprague-Dawley”

Section 2.5.3: Figure 3 suggests that the four potassium-channel blockers were given to different animals, yet the list in 2.5.3 says “and”. Were the drugs given as one injection, or to separate animals? If separate animals, then use “or” before tetraethylammonium chloride. The same comment applies to the opioid antagonists in section 2.5.5 and figure 9.

Section 2.5.7 line 1: Please give reference to “the previous report (2012)”.

Sections 3.1 – 3.5 should be combined and shortened as all are referring to the same tests for biological activity.

Section 3.2 line 2 and Discussion paragraph 1 lines 6 and 7: “dose-dependent”

Section 3.6: What are the identities of the 4 major peaks from HPLC? If they are
flavonoids as suggested by previous reports from this group, what is the advantage of this plant extract over use of the pure flavonoids such as rutin and quercetin, which are widely available and relatively cheap? What is the uniqueness of this plant extract, as flavonoids are remarkably widespread throughout the plant kingdom?

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.