Reviewer’s report

Title: Neuroprotective Efficacy and Therapeutic Window of Curcuma oil: In Rat Embolic Stroke Model

Version: 1 Date: 27 March 2008

Reviewer: Yasuhisa Furuichi

Reviewer’s report:

Comments to the Author:
In this manuscript, the authors clarified the neuroprotective efficacy of Curcuma longa oil in embolic stroke model in rats even when administered 4 hours after ischemia, and more importantly showed that Curcuma oil produced neuroprotective effects via the anti-apoptotic effect and anti-oxidant effect by assessing various cascades of ischemic neuronal death. The findings are potentially interesting in terms of clinical therapeutic utilities for stroke. The manuscript is well-written as a whole, however, the conclusion drawn in the MS appeared to need more supporting data. Otherwise, appropriate revisions should be made on data interpretation and conclusion.

Major comments:
(1) The authors described that C. oil ameliorated the ischemia induced changes in the early lesion significantly as visualized by using diffusion-weight MR imaging (P2, L13) in abstract, and also described that we observed a significant decrease in lesion volume as observed with C. oil treatment in the discussion part (P21 L14). However, there are no results of statistical analysis in the lesion volume of MR imaging. The result of statistical analysis should be described in the result section, because it is very important to interpret the neuroprotective mechanism of C. oil. The authors mentioned that neuroprotective effects of C. oil could primarily be due to inhibition of iNOS because the time course of iNOS expression and the timing of drug treatment match well. However, lesion volume has already reduced significantly by the treatment of C.oil at 5 hours after ischemia when expression of iNOS would start. How do the authors interpret this discrepancy? If this drug possesses the ability to increase the cerebral blood flow or to lyse clots, this result would be reasonable. Therefore, the authors should show whether C. oil affects cerebral circulation and clot-lysis action or not in this experimental condition.

(2) It is unclear that anti-apoptotic effect, such as inhibition of cytochrome c release, caspase 3, caspase 1&4 and expression of Bax after 24 hours of ischemia, is due to the drug action or a result of the reduced early ischemic lesion, because ischemic damage was significantly suppressed by the treatment of C. oil at 5 hours as well as 24 hours after ischemia.

(3) If the authors use the term of “therapeutic window” in a stroke model, several
time point for drug treatment including the timing at immediately after ischemia should be tested. There is no data that C. oil is effective when administered immediately or 2 hours after ischemia in this model.

Minor comment:
(1) How did the authors select the dose of 500mg/kg in this study?
(2) (P22, L23) Characters are blue.
(3) (Figure 3) In Y axis, DAF2-DA is wrong. “DAF-2DA” will be correct.
(4) (P36 L3) In Figure legends, DHDCF-DA is wrong. “DCDHF-DA” will be correct.
(5) (P38 L15) In Figure legends, Bax is wrong. “Bcl-2” will be correct.

**Level of interest:** An article whose findings are important to those with closely related research interests

**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'