Reviewer's report

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

**Version:** 1  **Date:** 27 March 2008

**Reviewer:** Ashraf B Abdel-Naim

**Reviewer's report:**

The manuscript by Garg et al. describes the neuroprotective effects of curcuma oil in an embolic forebrain ischemia paradigm. The authors have reported that curcuma oil has ameliorated the injurious neurological deficits associated with brain ischemia via modulation of an array of markers both biochemically and morphometrically. In deed, the work plan encompasses a plethora of investigations that were conducted in good shape. However the manuscript needs the following minor essential revisions

1. The authors conducted a large number of investigations using curcuma oil, though the active ingredient; the turmeric pigment (curcumin), is available and could have been used instead. The use of oily extracts is sometimes questionable due to the lack of accurate dosimetry. Besides, the kinetic disposition of oily preparations is usually subject to erratic calculations.

2. Why the control animals received pea nut oil as long as curcuma oil was used? The authors did not use a vehicle for the oil, so, why pea nut oil in particular?

3. On what basis such dose of oil was given? Did they carry out dose response study to rule out other doses? Was 500 mg/kg an optimal dose?

4. Why the authors have studied only forebrain ischemia without reflow. Reperfusion injury is crucial for the neurological deficits particularly when talking about oxidant stress in brain lesions.

5. Figure 8 has dulled resolution and adds nothing to the data armamentarium.

6. Figure legends are too long and much distracting. Enough details are available in methodology.

7. Authors emphasize on what is so called "therapeutic window" in their study. The authors have addressed only one dose of the oil (500 mg/kg).

8. Authors investigated the neurological deficits 24 h after injection of clot, though the optimal time for assessment of neurological deficits was 1 h according to the model of Zhang et al. (1997), which the authors reproduced in their manuscript. Why did not they assess the 1 h-point, even as a pilot trial?

9. Authors reported that curcuma oil has ameliorated the ischemic lesions one hour after administration (5 h After ischemia). From the kinetic viewpoint, curcumin is subject to extensive biotransformation during absorption, and, hence it has a low bioavailability, besides, the small fraction absorbed needs time (more
than 1 hour) to build up in plasma. Even, after absorption, very little amount of the substance accumulates in brain tissues compared to other body compartments. So the oral absorption of curcumin, let for, its oil is almost erratic. That is why, as aforementionbed, the use of curcumin instead of the oil would have been more apropriate.

10. As long as animals were used as self controls in the neurological deficits study, data were better to be analyzed using a paired-wise test instead of the independent one way AONVOA.

11. Authors should avoid using the adage of "therapeutic window" or "time window" because the study just entails only one dose of curcuma oil and most of observations were done 1 h or 24 h thereafter. More doses are required and much more time longevity is to be addressed.

12. Text suffers from syntax errors and erratic vocabulary.

13. What is the exact role of NO in membrane potential or neuronal damage? A paragraph in discussion section would be beneficial.

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

**Quality of written English:** Acceptable

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

**Declaration of competing interests:**

'I declare that I have no competing interests' below"