

OPEN PEER REVIEW REPORT 1

Name of journal: Neural Regeneration Research

Manuscript NO: NRR-D-21-00908

Title: Icarin Ameliorates Memory Deficits through Regulating Brain Insulin Signaling and Glucose Transporters in 3×Tg-AD Mice

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COMMENTS TO AUTHORS

The manuscript investigated the beneficial effects of an herbal extract "Icarin" in an animal model of Alzheimer's disease (AD).

The study involves a series of behavioural and neurochemical assessments performed in WT and AD mice after at the end of a drug regime lasting 5 months. The authors show that Icarin is able to preserve locomotion and exploratory behaviours, as well as spontaneous alternation in the Y-maze (here used to assess memory function). In addition, they provide histological and neurochemical evidence to suggest that the brain insulin-glucose metabolism is perturbed in AD mice and these detrimental effects are prevented by ongoing supplementation with the herbal extract.

In general, this is an interesting and complete piece of work that shows how certain herbal constituents may indeed prevent brain deterioration caused by AD.

Major comments/issues:

1. Oral gavage is a well-established route of delivery for drugs. However, this reviewer is slightly concerned about the continuous daily administration of the drug (dissolved in 0.5% Tween-80) for five months. Did the authors observed any unexpected side effects or fatalities?

Other minor comments/issues:

2. Is Icarin was previously known to regulate brain glucose homeostasis? What was the rationale to believe that this herbal constituent could restore impaired glucose signalling?

3. Figure 3 - I recommend the authors to add some indication (arrowheads) in panel A to indicate which cells were counted as neurons in panel B, as Nissl stain is not the optimal staining method to distinguish neurons from neighbouring glia.

4. Figures 3-5 - Please indicate the molecular weights next to the corresponding blots.