Review of: "Targeting Alzheimer's disease hallmarks with the Nrf2 activator Isoeugenol"

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Potential competing interests: No potential competing interests to declare.

The authors have worked on isoeugenol, as an activator of Nrf2 and having potential to treat AD. Different in vivo and in vitro tests are conducted targeting the transcription factor nuclear factor erythroid 2–related factor 2 (Nrf2) as a master controller of metabolism, neuroinflammationa and proteostais in AD.

This work was conducted in vitro (in mice microglia cells exposed to LPS and neuronal cells overexpressing the human APP with Swedish mutation, N2a-APPswe) and in vivo (in the AD double transgenic mice, APP/PS1, intranasally administered with Isoeugenol), at an early (6-month-old animals) and late (11-month-old animals) AD stage.

Overall, the results showed that Isoeugenol exhibit a good pharmacokinetic and pharmacodynamic profile. Isoeugenol activates Nrf2 and displays antioxidant and anti-inflammatory effects and reduced the levels of Aβ peptides in in vitro and in vivo models of AD. In addition, its positive effect on metabolism was also demonstrated in vivo, as it reduced the triglyceride and LDL cholesterol levels in treated AD mice. Importantly, Isoeugenol improved the memory deficits observed in APP/PS1 mice, which was more evident in older animals (11-month-old), reinforcing its potential in ameliorating AD hallmarks, even at a late stage.

The article is having multiple studies placed on one table, causing a lot of confusion and showing an asymmetric data. The authors might reconsider the title in order to address all the studies provided, or the authors may only include the data related to Nrf2 activation.

Introduction

a. The information about the AD is too long, the introduction must be precise and to the point.
b. The results must not be added in the introduction part.

Methods

Phramcokinetic Studies

a. Why was the brain samples homogenized in NaCl? Usually the brain samples are homogenized in the solvents of mobile phase.
b. The detail of HPLC method development and validation is not provided.