

Structure-activity relationships of sulfonamides derived from carvacrol as new agents for the treatment of Alzheimer's disease

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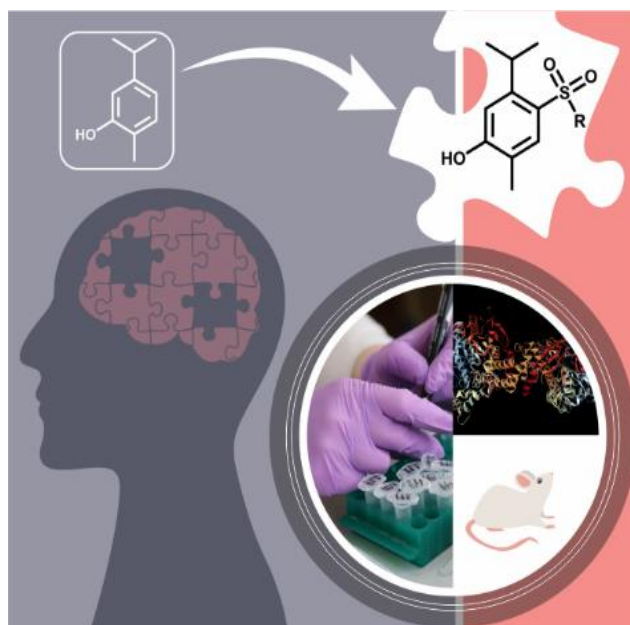
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ABSTRACT

Alzheimer's disease (AD) is a neurological disorder whose treatment needs new therapies.¹ Five sulfonamides derived from carvacrol,² a natural small-molecule product with drug-like properties, were evaluated with respect to their effects on the cognitive deficits of animals with streptozotocin (STZ)-induced Alzheimer's disease (AD). *In vitro* assays were performed using the acetylcholinesterase (AChE) and the data were combined with molecular modeling investigations for the establishment of structure-activity relationships (SAR). The memories of animals treated with compounds derived from morpholine (**1**), hydrazine (**3**) and 2-phenol (**5**) were improved. Compound **3** was the most promising, yielding excellent results in the inhibitory avoidance test. Moreover, the compounds did not exhibit any deleterious effects on the animals' ambulation. In short, compounds **1**, **3** and **5** can reduce STZ-induced deficits and show potential for the treatment of AD. These compounds produce significant anxiolytic and antioxidant effects and have favorable pharmacokinetics profile and drug-like properties.

GRAPHICAL ABSTRACT



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REFERENCES

- Oliveira, A. S.; Meier, L.; Zapp, E.; Brondani, D.; Brighente, I. M. C., & Sá, M. M. *J. Braz. Chem. Soc.*, **2019**, 30(5), 1045-1054.
- Oliveira, A. S.; Llanes, L. C.; Brighente, I. M. C.; Nunes, R. J.; Yunes, R. A.; Máximo Junior, N. M.; Baumgart, A. M. K.; Aust, A. N. and Cruz A. B. *Journal of Biosciences and Medicines*, **2016**, 4, 105-114.