New evidence on easing inflammation of brain cells for Alzheimer's disease

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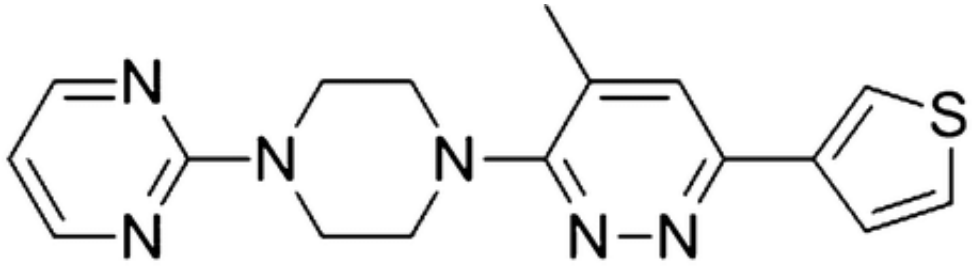

14

in vitro, BV-2 cell IC_{50} (IL-1β) = 2.4 μM;
in vivo, comparable to donepezil

New research proves the validity of one of the most promising approaches for combating Alzheimer's disease (AD) with medicines that treat not just some of the symptoms, but actually stop or prevent the disease itself, scientists are reporting. The study, in the journal *ACS Medicinal Chemistry Letters*, also identifies a potential new oral drug that the scientists say could lead the way.

Wenhui Hu and colleagues point out that existing drugs for AD provide

only "minimal" relief of memory loss and other symptoms, creating an urgent need for new medicines that actually combat the underlying destruction of brain cells. Research suggests that inflammation of nerve cells in the brain is a key part of that process. One medicine, Minozac, is in clinical trials. But Hu says Minozac still has more space to improve its efficacy. So the scientists sifted through compounds with a molecular architecture similar to Minozac in an effort to find more active substances.

The report describes success in doing so. They discovered one compound that appeared especially effective in relieving nerve inflammation and in improving learning and memory in lab mice widely used in AD research. "In general, this study not only proves that countering neuroinflammation is indeed a potential therapeutic strategy for Alzheimer's disease, but also provides a good lead compound with efficacy comparable to donepezil [an existing AD medicine] for further oral anti-AD drug discovery and development," the report states.

More information: "Identification of Aminopyridazine-Derived Anti-neuroinflammatory Agents Effective in An Alzheimer's Mouse Model" ACS Med. Chem. Lett., Article ASAP
DOI: 10.1021/ml3001769

Abstract
Targeting neuroinflammation may be a new strategy to combat Alzheimer's disease. An aminopyridazine 1b previously reported as a novel antineuroinflammatory agent was considered to have a potential therapeutic effect for Alzheimer's disease. In this study, we further explored the chemical space to identify more potent antineuroinflammatory agents and validate their in vivo efficacy in an animal model. Compound 14 was finally identified as an effective agent with comparable in vivo efficacy to the marketed drug donepezil in counteracting spatial learning and working memory impairment in an Aβ-

induced Alzheimer's mouse model.

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