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New tacrine dimers with antioxidant linkers as dual drugs: Anti-Alzheimer's and antiproliferative agents

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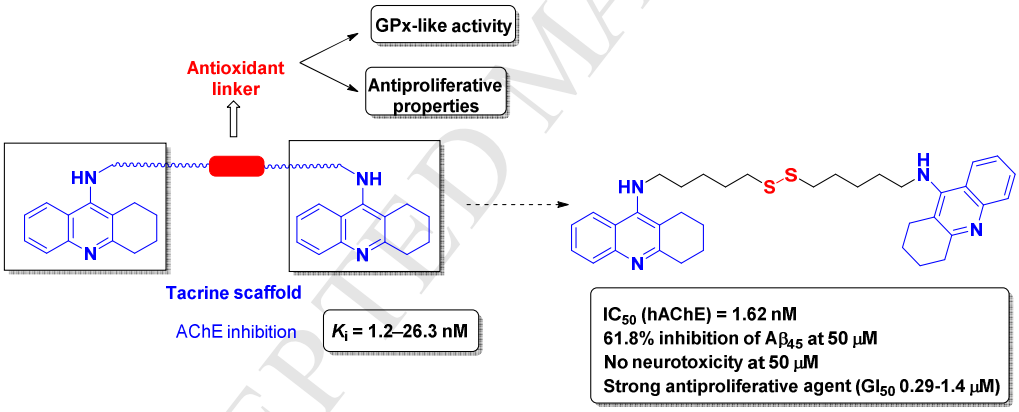
Graphical abstract



Highlights

- Tacrine homo- and heterodimers bearing linkers with antioxidant properties were accessed
- Symmetrical chalcogenides were strong AChE inhibitors (1.2–26.3 nM), up to 19–fold increase compared to parent tacrine
- Good selectivity compared to BuChE (up to 290-fold) was found
- Good inhibition of $A\beta_{42}$ aggregation was achieved; lead compound did not display neurotoxicity.
- Symmetrical chalcogenides were potent antiproliferative agents (0.12–0.95 μM, up to 306-fold more potent than 5-fluorouracil)