Antiprionic activity of 6-aminoquinolones and their dimeric benzoquinone conjugates

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ABSTRACT

6-aminoquinolones (1a-h) and their dimeric benzoquinone conjugates (2a-h) had their anti-prion profile evaluated by two different assays. The first explored the ability of these substances to inhibit the formation of amorphous protein aggregates due to mechanical and thermal stimuli in solutions containing the cellular prion protein. All aminoquinolones (1) showed inhibitory ability with inhibition percentages varying from 21.4 to 63.1%. Although not all of the dimers (2) were active, three of them showed better activity than their monomeric analogues, with the best result achieved by 2e, with 79% inhibition. In the second assay the inhibitory capacity on the formation of mature prion fibers was evaluated. The best results were obtained with 2g and 2h dimers which led to changes in the kinetic and thermodynamic profiles of the fibrillation stage. The substances tested showed low cytotoxicity in concentration of 10 μM. Further studies are underway.

GRAPHICAL ABSTRACT

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