CHRONIC ADMINISTRATION OF BERBERINE INHIBITS Aβ PRODUCTION, PLAQUE FORMATION, GLIOSIS AND COGNITIVE DETERIORATION IN A TRANSGENIC MOUSE MODEL OF ALZHEIMER'S DISEASE

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Introduction: A prominent feature of Alzheimer’s disease (AD) is the accumulation of amyloid-β peptide (Aβ) derived from abnormal processing of amyloid precursor protein in senile plaques. Accordingly, reduction in the potentially toxic Aβ has emerged as one of the most important therapeutic goals in treating AD. One potential source of phytotherapeutic agents is berberine (BBR), an alkaloid from Coptis Chinensis.

Aims: To test the therapeutic effects of BBR in transgenic Alzheimer mice (TgCRND8).

Methods: Two months old TgCRND8 mice (n=15) received BBR (25 and 100mg/kg/day) or tap water by oral gavages until 6 months. To assess hippocampus-dependent spatial learning and memory, mice were trained and tested in a Morris water maze. Immunohistochemistry was performed to determine the Aβ load and microgliosis. ELSIA was performed to quantitate the Aβ1-40 and Aβ1-42 levels.

Results: Four months treatment of TgCRND8 with low dose (25mg/Kg/day) and high dose (100mg/Kg/day) of BBR showed significant reductions of 37% and 24% of mean plaque number per mouse, respectively. In the SDS-soluble fraction, the reduction in Aβ1-40 and Aβ1-42 levels was 35% (P< 0.05) and 23% (P>0.05), respectively, whereas in the formic acid fraction, the corresponding reductions were 49% (P< 0.05) and 43% (P=0.05). There is a significant decrease in iba-1-positive microgliosis between control and BBR-treatment. Further, there was a significant decrease in escape latency in water maze when BBR was orally administrated as compared with the Tg-control group (P< 0.01).

Conclusions: Based on our results, BBR deserves further exploration as a promising therapeutic agent for AD.