Multi-target strategy and new drug development of traditional Chinese medicine for Alzheimer’s disease therapy

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Abstract: Alzheimer's disease (AD) is a multifactorial complex disease. The failure of recent development of AD therapeutic agents in clinical trials is partly due to their single-target effect. The multi-target therapeutic characteristics of traditional Chinese medicine (TCM) have advantages over the single-target treatment. Shen-wu capsule (SW) is a new compound containing 6 kinds of traditional Chinese herbs. 2,3,5,4’-Tetrahydroxystilbene glucoside (TSG) is a main component extracted from Polygonum multiflorum, which is also a major ingredient of SW capsule. The results from our experiments showed that in 7 kinds of AD or dementia animal models SW and TSG improved learning and memory ability; decreased cholinergic cell death in hippocampus; decreased Aβ content and β-secretase expression; inhibited microglial activation and decreased IL-1β and TNFα content; inhibited tau protein hyperphosphorylation and increased expression of protein phosphortase 2A (PP2A); increased the ratio of cholinacetyl-transfetase (ChAT) / cholinesterase (AchE) and M-receptor density; enhanced expression of nerve growth factor (NGF) and brain derived neurotrophic factor (BDNF), and their receptors TrkA and TrkB; protected synaptic structure and functions and increased expression of synaptophysin; and inhibited the overexpression and aggregation of alpha-synuclein in hippocampus and cerebral cortex. These results demonstrate that SW and TSG can act on multiple targets in the complicated pathogeneses of AD. Completed phase III clinical trial of
SW in China demonstrated that SW treatment effectively improved cognitive impairment in patients with mild to moderate AD. These results suggest that a multi-target strategy may be beneficial in AD therapy.

**Key Words:** Alzheimer’s disease; multi-target; traditional Chinese medicine; tetrahydroxystilbene glucoside.