LW-AFC, a new formula derived from Liuwei Dihuang decoction, ameliorates cognitive deterioration via modulating the hippocampus transcriptome in senescence-accelerated mouse prone 8 strain, a mouse model of Alzheimer’s disease

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Alzheimer's disease (AD) is a neurodegenerative disease which cannot be effectively prevented, halted or cured. The senescence-accelerated mouse prone 8 (SAMP8) strain is considered a robust experimental model for developing preventative and therapeutic treatments for AD. LW-AFC is a new formula derived from the classical traditional Chinese medicinal prescription Liuwei Dihuang decoction. Our studies showed LW-AFC had ameliorative effects on spontaneous locomotor activity, object recognition memory, spatial learning and memory, passive and active avoidance impairment in SAMP8 mice. Effects of LW-AFC on learning and memory improvement in SAMP8 mice were better than memantine and donepezil. We conducted a genome-wide survey of gene expression in the hippocampus in mice from the senescence accelerated mouse resistant 1 (SAMR1) strain, from SAMP8 and from LW-AFC treated SAMP8. The results showed that LW-AFC reversed the transcriptome in the hippocampus of SAMP8 mice. The specific investigation of altered gene expression in subtypes defined by cognitive profiles indicated that the systemic lupus erythematosus pathway, spliceosomes, amyotrophic lateral sclerosis and the insulin signaling were involved in the improvement of cognitive ability by LW-AFC. The expression of genes Enpp2, Etnk1, Epdr1, and Gm5900 in the hippocampus were correlated with that of LW-AFC's ameliorating cognitive impairment in SAMP8 mice. Because LW-AFC is composed of polysaccharides, glycosides and oligosaccharides, we infer that LW-AFC has direct or indirect effects on altering gene expressions and regulating pathways in the hippocampus of SAMP8 mice. These data are helpful for the enhanced identification of LW-AFC as new therapeutic modalities to AD.