

Herbal extract GRAPE boosts homeostatic microglia and tempers (without suppressing) DAM activation in AD

P3-02

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GRAPE is a standardized plant-based traditional medicine extract that improves AD-related cognitive performance and neuropathology by reducing brain A β burden and reprogramming microglia toward expanded homeostatic states that preserve A β -clearing/lysosomal pathways while mitigating neuroinflammation.

INTRODUCTION	METHODS	RESULTS	CONCLUSIONS	REFERENCES
A prior retrospective cohort study demonstrated that GRAPE , a standardized herbal extract, when used as an add-on to conventional therapy, significantly improves cognitive function and slows disease progression in patients with Alzheimer's disease (AD) [1]. These clinical benefits motivate further investigation into its underlying cellular mechanisms. Microglia play a dual role in AD by facilitating A β clearance while also driving neuroinflammation, underscoring the need for multitarget modulation strategies such as GRAPE, whose precise effects on microglial states remain undefined.	GRAPE constituents were characterized by HPLC fingerprinting. Using APP/PS1 mice, we evaluated the effects of early GRAPE intervention on microglial phenotypes while preserving A β -handling capacity through an integrated approach combining behavioral testing, histopathology, biochemical A β assays, and single-cell RNA sequencing (scRNA-seq).	GRAPE treatment significantly improved memory performance, reduced cerebral A β deposition and insoluble A β 42 levels, increased amyloid plaque compaction, and alleviated neuritic dystrophy. scRNA-seq revealed an expansion of homeostatic microglia exhibiting surveillance-related signatures, together with moderated activation of disease-associated microglia (DAM) that preserved Aβ-clearing and lysosomal pathways . In addition, microglial located distal to A β plaques displayed increased morphological ramification, accompanied by reduced expression of proinflammatory cytokines.	Early GRAPE administration rebalances microglial states by restoring homeostatic programs and fine-tuning DAM activation without impairing A β clearance, thereby attenuating neuroinflammation and amyloid-associated pathology. These findings provided cellular-level mechanistic support for the cognitive benefits of GRPAE observed in clinical settings.	[1] Shi J, Ni J, Lu T et al. Adding Chinese herbal medicine to conventional therapy brings cognitive benefits to patients with Alzheimer's disease: a retrospective analysis. <i>BMC Complement Altern Med</i>. 2017;17(1):533 CONTACT Fuyao Li: Julia_light@msn.cn; 202302005@bucm.edu.cn  ALZHEIMER'S ASSOCIATION AAIC 26