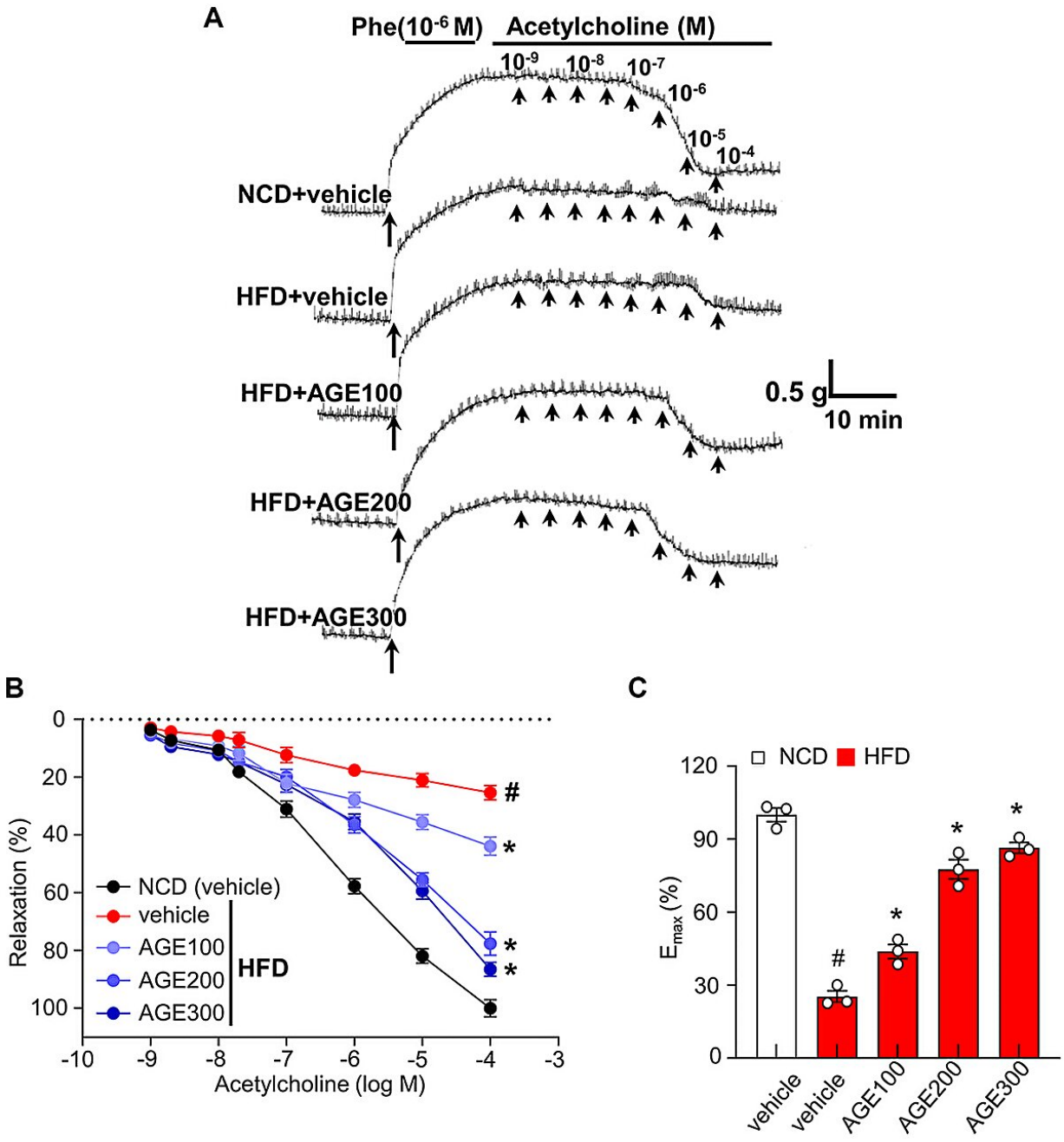
Medicinal herb found to inhibit acetylation of eNOS in vascular dysfunction

December 29 2023



AGE enhances endothelial relaxation in aorta rings. (A) Representative traces under specified conditions. (B) Percentage of relaxation proportional to Ach concentration. (C) Maximum relaxation by Ach (10^{-4} M) in aorta from Figure 1B. Results are expressed as percent relaxation ± SEM. Abbreviations: Phe: phenylephrine; NCD: normal chow diet; HFD: high fat diet. Credit: *Aging* (2023). DOI: 10.18632/aging.205343

Angelica gigas NAKAI (AG) is a popular traditional medicinal herb widely used to treat dyslipidemia due to its antioxidant activity. Vascular disease is intimately linked to obesity-induced metabolic syndrome, and AG extract (AGE) shows beneficial effects on obesity-associated vascular dysfunction. However, the effectiveness of AGE against obesity and its underlying mechanisms have not yet been extensively investigated.

In this new study, researchers from Jeonbuk National University and Jeonbuk National University Hospital supplemented 40 high fat diet (HFD) rats with 100–300 mg/kg/day of AGE to determine its efficacy in regulating vascular dysfunction. The paper, titled "Angelica gigas extract inhibits acetylation of eNOS via IRE1α sulfonation/RIDD-SIRT1-mediated posttranslational modification in vascular dysfunction" was published in *Aging*.

"The primary aim of this study is to examine the inhibitory effects of AGE on dyslipidemia-associated vascular dysfunction, with a focus on its potential mechanisms of action," state the researchers.

The vascular relaxation responses to acetylcholine were impaired in HFD rats, while the administration of AGE restored the diminished

relaxation pattern. Endothelial dysfunction, including increased plaque area, accumulated reactive oxygen species, and decreased nitric oxide (NO) and endothelial nitric oxide synthase (eNOS) Ser1177 phosphorylation, were observed in HFD rats, whereas AGE reversed endothelial dysfunction and its associated biochemical signaling.

Furthermore, AGE regulated endoplasmic reticulum (ER) stress and IRE1α sulfonation and its subsequent sirt1 RNA decay through controlling regulated IRE1α-dependent decay (RIDD) signaling, ultimately promoting NO bioavailability via the SIRT1-eNOS axis in aorta and endothelial cells.

Independently, AGE enhanced AMPK phosphorylation, additionally stimulating SIRT1 and eNOS deacetylation and its associated NO bioavailability. Decursin, a prominent constituent of AGE, exhibited a similar effect in alleviating endothelial dysfunctions. These data suggest that AGE regulates dyslipidemia-associated vascular dysfunction by controlling ROS-associated ER stress responses, especially IRE1α-RIDD/sirt1 decay and the AMPK-SIRT1 axis.

"Ultimately, this study presents clearly evidence that AGE is a promising natural product-based functional food/herbal medicine candidate for preventing or regulating hyperlipidemic cardiovascular complications," state the researchers.

More information: Geum-Hwa Lee et al, Angelica gigas extract inhibits acetylation of eNOS via IRE1α sulfonation/RIDD-SIRT1-mediated posttranslational modification in vascular dysfunction, *Aging* (2023). DOI: 10.18632/aging.205343