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2,3-Dehydrosilybin A/B as a pro-longevity and anti-aggregation compound

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ABSTRACT

Aging is an unavoidable process characterized by gradual failure of homeostasis that constitutes a critical risk factor for several age-related disorders. It has been unveiled that manipulation of various key pathways may decelerate the aging progression and the triggering of age-related diseases. As a consequence, the identification of compounds, preferably natural-occurring, administered through diet, with lifespan-extending, anti-aggregation and anti-oxidation properties that in parallel exhibit negligible side-effects is the main goal in the battle against aging. Here we analyze the role of 2,3-dehydrosilybin A/B (DHS A/B)¹, a minor component of silymarin used in a plethora of dietary supplements. This flavanolignan is well-known for its anti-oxidative and neuroprotective properties, among others. We demonstrate that DHS A/B confers oxidative stress resistance not only in human primary cells but also in the context of a multi-cellular aging model, namely *Caenorhabditis elegans* (*C. elegans*) where it also promotes lifespan extension. We reveal that these DHS A/B outcomes are FGT-1 and DAF-16 dependent. We additionally demonstrate the anti-aggregation properties of DHS A/B in human cells of nervous origin but also in nematode models of Alzheimer's disease (AD), eventually leading to decelerated progression of AD phenotype. Our results identify DHS A/B as the active component of silymarin extract and propose DHS A/B as a candidate anti-aging and anti-aggregation compound.

ABBREVIATIONS

A β , amyloid beta; AD, Alzheimer's disease; DHS A/B, 2,3-dehydrosilybin A/B; CHO, Chinese hamster ovary; CM, conditioned medium; FGT-1, facilitated glucose transporter isoform 1, GLUT; IIS, insulin/IGF-1 signaling; IPTG, Isopropyl- β -D-1-thiogalactopyranoside; NBT, nitro tetrazolium blue; NRLB, non-reducing Laemmli buffer; NS, not significant; O₂^{•-}, superoxide anions; PMA, phorbol myristate acetate; RNAi, RNA interference; wt, wild type.

Keywords

2,3-dehydrosilybin A/B, Anti-aging, Anti-aggregation, Anti-oxidation, FGT-1, DAF-16

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