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Active Hexose Correlated Compound Extends the Lifespan and Increases the Thermotolerance of Nematodes

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ABSTRACT:

Background: Active hexose correlated compound (AHCC) is the extract from cultured mycelia of *Lentinula edodes*, a species of *Basidiomycetes* mushroom. AHCC contains various polysaccharides, including partially acylated ⟨-1,4-glucan, which is one of its major constituents. The application of AHCC has been markedly increased in complementary and alternative medicine as a functional food because AHCC improved the prognosis of postoperative hepatocellular carcinoma patients. AHCC has anti-inflammatory and antioxidant effects, such as the suppression of nitric oxide production in hepatocytes. AHCC might affect resistance to environmental stress, which is assumed to play a pivotal role in the longevity of many organisms.

Objective: To investigate the effect of AHCC on longevity, we measured the lifespan of the nematode *Caenorhabditis elegans*, a model animal that is widely used to assess longevity. We also examined the effect of AHCC on resistance to heat stress, *i.e.*, thermotolerance.

Methods: The lifespan of *C. elegans* animals grown on media in the absence or presence of AHCC at 20°C was evaluated. Thermotolerance assays were performed at 35°C, the restrictive temperature of the animals. The effects of AHCC on lifespan and thermotolerance were analyzed with longevity mutants. Expression levels of stress-related genes, including heat shock genes, were measured by strand-specific reverse transcription-polymerase chain reaction after heat shock.

Results: Wild-type *C. elegans* animals exhibited a longer mean lifespan by up to 10% in the presence of AHCC in the growth media than animals in the absence of AHCC. Furthermore, AHCC markedly increased thermotolerance at 35°C. Epistasis analyses showed that lifespan extension by AHCC at least partly required two longevity-promoting transcription factors: DAF-16 (*C. elegans* homolog of FOXO) and HSF-1 (*C. elegans* homolog of heat shock transcription factor 1). After heat shock, AHCC activated the transcription of the heat shock genes, which are the targets of HSF-1. Similarly, the expression of hsf-1 mRNA was elevated following AHCC treatment. Recently, natural antisense transcripts were shown to regulate mRNA stability at the posttranscriptional level. In nematodes, AHCC increased the natural antisense transcript of the *hsf-1* gene.

Conclusion: AHCC conferred lifespan extension and thermotolerance to *C. elegans*. Our analyses suggest that the beneficial effects of AHCC on longevity are involved in the activation of at least two transcription factors, DAF-16 and HSF-1, most likely through an antisense transcript-mediated mechanism.

Keywords: longevity, heat stress resistance, HSF, FOXO, heat shock gene