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Antiaging properties of 4-N-furfurylcytosine in cellular, yeast and mouse models

The aging process is a widespread phenomenon that significantly impacts the quality of life in organisms, leading to a gradual decline in functionality and an increased susceptibility to age-related diseases. The continuously growing population of elderly individuals presents one of the most pressing challenges of modern society, as emphasized by the United Nations' designation of 2020-2030 as the Decade of Healthy Aging.

This doctoral dissertation aimed to characterize the anti-aging properties of a novel compound, 4-N-furfurylcytosine (FC), which is a cytosine derivative modified with furfural at the N4 position. For this purpose, three well-established models in aging research were used: normal human fibroblasts, the unicellular organism *Saccharomyces cerevisiae* (yeast), and the complex organism *Mus musculus* (mice).

Based on the obtained results, it was found that FC is not a toxic compound and does not eliminate senescent cells. However, it mitigates senescence phenotype by reducing levels of the DNA damage and intracellular reactive oxygen species, enhancing mitochondrial quality, and activating the proteasome. Consequently, FC was classified as a senomorphic compound. The anti-aging efficacy was corroborated in the yeast model, where an extension of the chronological lifespan of yeast grown in the presence of FC was observed. This extension was linked to the inhibition of the TORC1-Sch9 signalling pathway and modulation of cellular metabolism. Mice supplemented with FC exhibited heightened locomotor activity and lower levels of oxidative stress markers in tissues, as well as reduced adipose tissue and increased muscle mass compared to control mice. These results led to the conclusion that FC significantly enhances the overall health of aged mice, notably by impeding the progression of sarcopenia.

In summary, the presented studies constitute the first comprehensive description of the biological activity of 4-N-furfurylcytosine, with a particular focus on its anti-aging properties, demonstrating the potential application of this compound.