**Cannabigerol as a Potential Gerotherapeutic Agent:**

**Evidence from *Caenorhabditis elegans***

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**Background and aims.** Ageing is a complex biological process that involves the gradual deterioration of molecular and cellular function which leads to suboptimal health, morbidity and mortality. Gerotherapeutic agents are molecules that target ageing biology to delay ageing and promote healthy longevity, has increasingly focused on natural products with bioactive properties. Cannabigerol (CBG), a non-psychoactive cannabinoid found in the cannabis plant, has recently attracted growing attention due to its broad spectrum of potential health benefits, including anti-inflammation, antioxidant and neuroprotective effects (Li et al., 2024). However, its role in modulating ageing and lifespan has not been well defined. *Caenorhabditis elegans* (*C. elegans*), a widely used model nematode for ageing study, offers a valuable system to investigate the biological impact of CBG on age-related processes, including stress resistance, lifespan and health span. This project aims to investigate the gerotherapeutic potential of CBG by assessing its impact on lifespan, health span and stress tolerance in *C. elegans*.

**Methods.** Wild-type *C. elegans* N2 used in this study. Strains were provided by the Caenorhabditis Genetics Center (CGC), University of Minnesota. All strains were maintained on nematode growth medium (NGM) agar plates seeded with *E.coli* s OP50 at 20℃ for lifespan and health span assays. For the thermotolerance assay, worms were incubated at 37℃ for 4 hours and followed by 30 min recovery period at 20℃, after which survival was scored. Lifespan were conducted with age-synchronized N2 worms, with treatment (CBG) or vehicle control initiated at the L4 stage. A total initial population of 100 worms was tested for each treatment condition. For the body bends assay, locomotion was assessed by counting the number of complete body bends within a 30s period on day 3 and day 8.

**Results.** We first evaluated whether CBG enhances resistance to heat stress, we pretreated worms with different concentrations (10, 30, and 100 µM) of CBG for 2 days at 20℃, followed by exposure to heat stress. Worms treated with CBG at 10 µM and 30 µM showed significantly increased survival compared to the control group. In our lifespan assays, age-synchronized worms were treated with CBG starting from L4 stage at concentrations of 10, 30 and 100 µM at 20℃. As a result, only the 10µM CBG treatment resulted in a significant lifespan extension compared to the control, while 30 µM and 100 µM did not show any beneficial effect. Subsequently, we evaluated the effect of 10 µM CBG on *C. elegans* locomotion, a commonly used metric to assess health span. The results demonstrated that the treatment with CBG significantly enhanced the body bending in worms on day 8.

**Conclusion/Discussion.** This study demonstrates that CBG enhances thermotolerance, extends lifespan and improves locomotion at low concentrations in *C. elegans*. There results suggest that CBG possesses geroprotective properties, supporting its potential as a natural compound for promoting healthy ageing.

**References:**

Li, S., Li, W., Malhi, N. K., Huang, J., Li, Q., Zhou, Z., Wang, R., Peng, J., Yin, T., & Wang, H. (2024). Cannabigerol (CBG): A Comprehensive Review of Its Molecular Mechanisms and Therapeutic Potential. Molecules, 29(22). <https://doi.org/10.3390/molecules29225471>