Nutraceutical approach to increase healthy aging using *Caenorhabditis elegans* as a model organism

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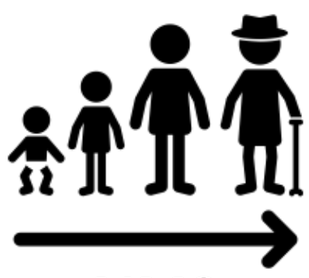
Introduction

Humans are gradually moving towards an aging society: by 2050, one in four people in Europe will be aged 65 or over[1]. Aging is a process of gradual physiological decline[2]. Understanding the mechanisms underlying aging is fundamental to promote healthy aging, but it is complicated by its multifactorial nature, in which environmental factors (e.g. nutrition) play an important role[3,4]. *C. elegans* is a validated model for aging research, with its short life cycle, ease manipulation and conserved signaling pathways[5].



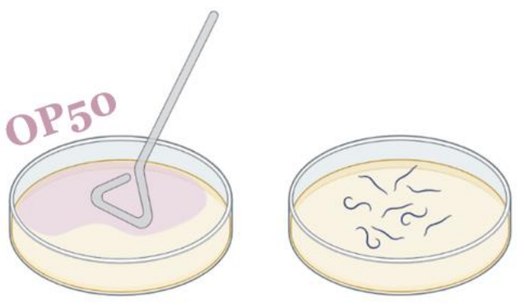
AGING

Characterization of *C. elegans* aging from a phenotypic and molecular point of view, in order to correlate the main lifespan-healthspan physiological parameters to the major aging pathways.

NUTRITION

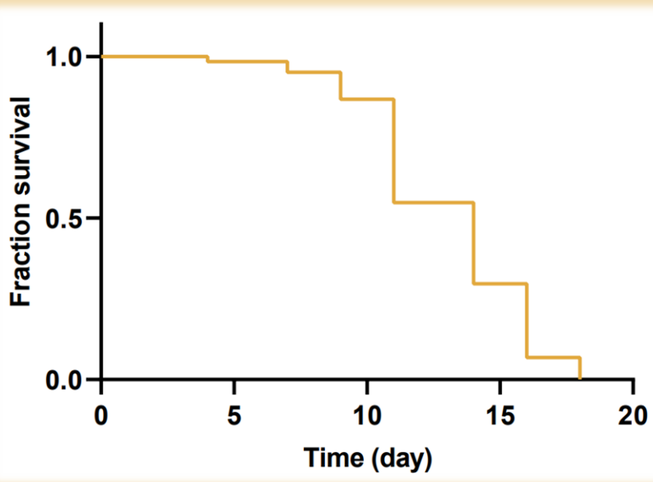
Evaluation of the effect of the *Cinnamomum cassia* buds extract on *C. elegans* aging.

C. elegans mantainment



N2 *wild type C. elegans* strain is mantained at 20°C on plates containing solid nematode growth medium seeded with alive *E. coli* OP50 strain for food[6]. Experiments are carried out using a synchronous population, obtained as follows: ten adult worms are allowed to lay eggs for 12 h; after their removal, newly laid eggs are grown for 3 days. All the experiments are performed adding 5-Fluoro-2-deoxyruridine (FuDR) during the first week, in order to avoid egg hatching. Day 0= 1st day of adulthood.

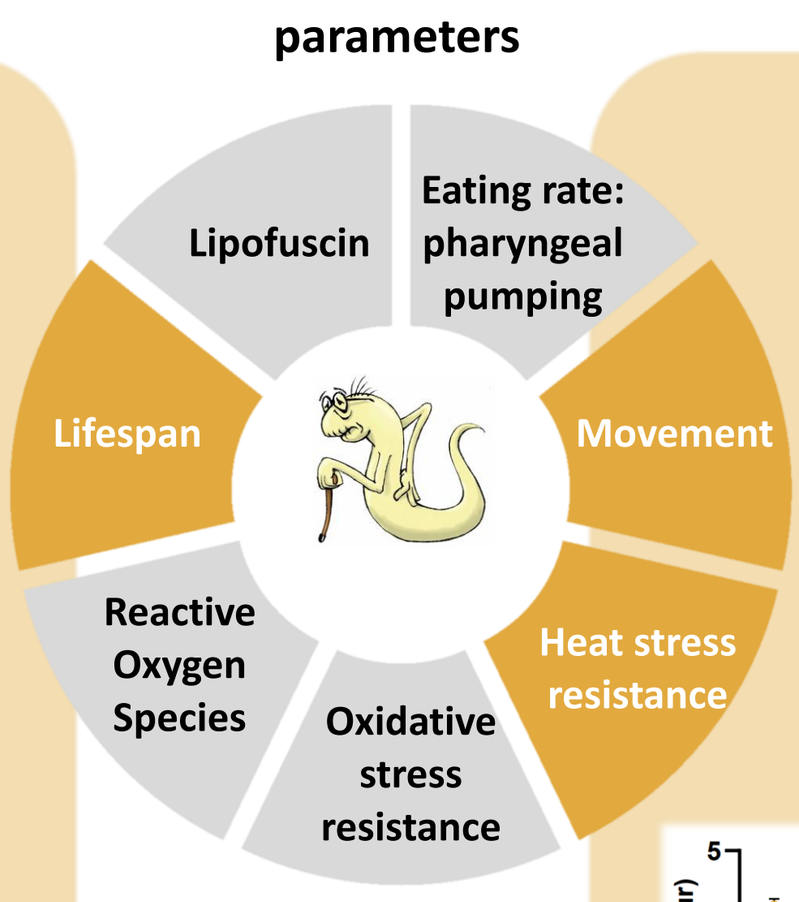
Results

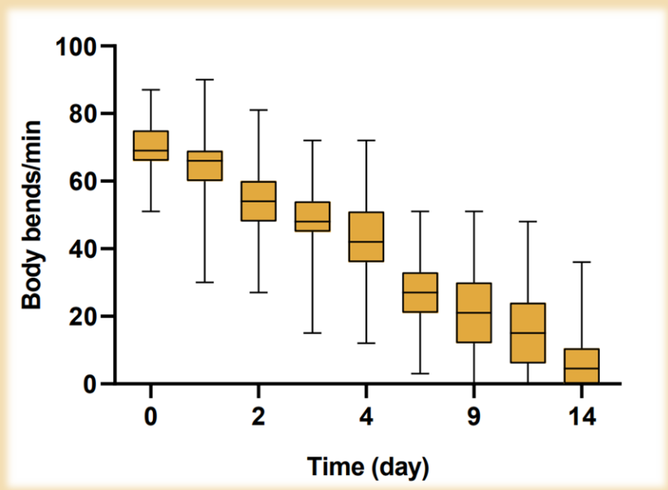


	Number of worms	Median lifespan[1]	Maximum lifespan[2]
N2	60	13,2 ± 0,83	18,8 ± 0,49

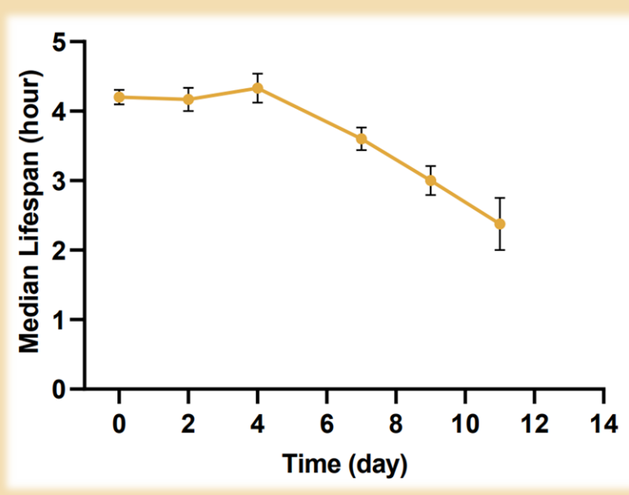
[1]Day when 50% of worms survived.
[2]Oldest age reached by the last surviving worm.
Mean ± SEM is reported.

Worms were counted and transferred every other day until all animals were dead.



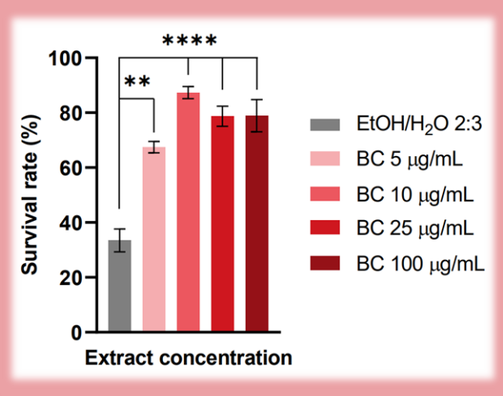


The count of the worm body bends clearly shows a progressive decline of movement during *C. elegans* lifespan since the early adulthood…



… Otherwise, *C. elegans* resistance to heat stress at 37°C decreases only in old age.

***Cinnamomum cassia* buds extract (BC):** hydroalcoholic extract (water 70%, EtOH 30%) containing mainly cinnamaldehyde and procyanidins[7].



The effective dose to assess cinnamon bud anti-aging properties was defined by heat stress test (37°C), pre-treating 1-day adult worms with a single dose for 48 hours. Median lifespan (h) of non-treated worms was chosen as the time point to assess possible survival differences.

THINGS TO DO:

1. Oxidative stress resistance
2. ROS accumulation
3. Pharyngeal pumping rate
4. Lipofuscin content
5. Aging pathways

THINGS TO DO:

1. Lifespan
2. Healthspan parameters detection
3. Aging pathways (mutant strains)

Conclusions

- ✓ As expected, both the physiological parameters decrease during *C. elegans* lifespan, but the decline starts at different time points of life cycle. Therefore, we can assume that they may be regulated by different pathways.
- ✓ Cinnamon buds extract induces an increase in the heat stress resistance at low concentrations (5-10 µg/ml), reaching a plateau at higher concentrations (25-100 µg/ml).

1. UNDESA Population Division (2015).
2. Huang et al., *Proceedings of the National Academy of Sciences* 101.21 (2004).
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4. Okoro et al., *Molecules* 26.23 (2021).
5. Zhang et al., *Frontiers in Endocrinology* 11 (2020).
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7. Ciaramelli et al.,, *Frontiers in chemistry* (2022).

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