Tannins: Hormetic Longevity-Triggers or just Energy-Allocators?

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The 3 Cornerstones of our Hormesis Study

- The primary endpoint:

  Lifespan

- The stressors/hormetins:

  Tannins / Tannin building blocks

- The organism:

  Caenorhabditis elegans

Tannins: Contrasty Polyphenols

- Plants synthesize polyphenols (PP) for
  - defense
  - attraction
- PP have antioxidative, anti-inflammatory, and antimicrobial capacities
- PP protect against
  - Cardiovascular and neurodegenerative diseases
  - Cancer
  - Oxidative stress
  - Ageing

Tannins: Contrasty Polyphenols

- Tannins…
  - have protein-binding & precipitating capacities
  - are anti-nutritional substances due to
    - precipitation of digestive enzymes
    - binding of nutritional proteins
    - astringent taste

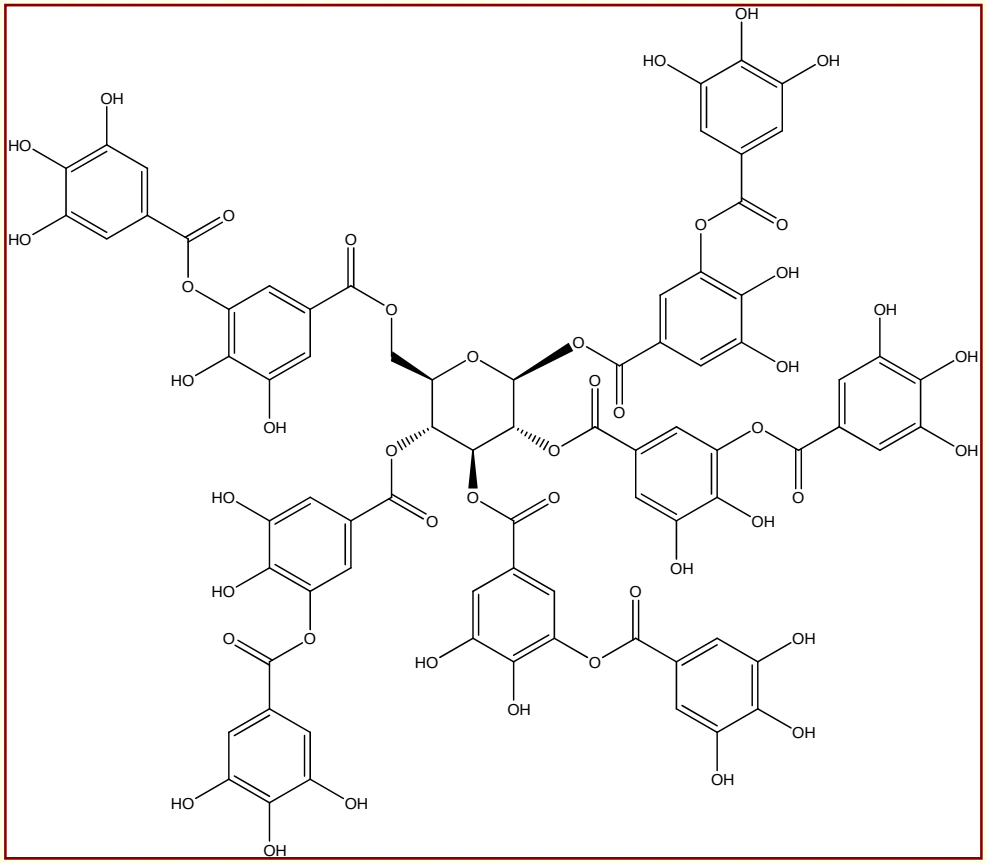
Tannins: Contrasty Polyphenols

- Tannins…
  - showed health-promoting and toxic properties
  - can act antioxidative as well as prooxidative

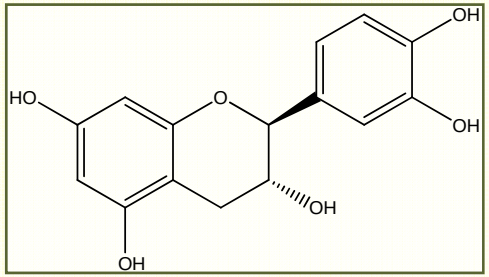
Tannins: Contrasty Polyphenols

Are these contrary findings expression of the distinctive hormetic action of tannins ?

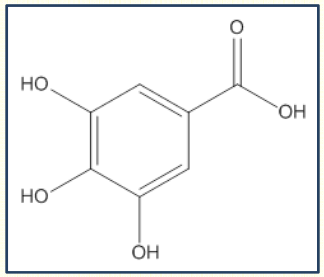
Tannins: Contrasty Polyphenols



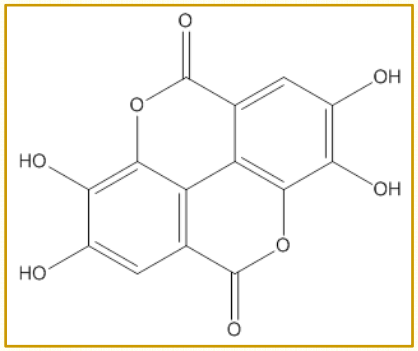
Tannic acid



Catechin



Gallic acid



Ellagic acid

Why do we use the nematode *C. elegans* ?

From: J. Berger & R. Sommer, Max-Planck-Institut für Entwicklungsbiologie, Tübingen

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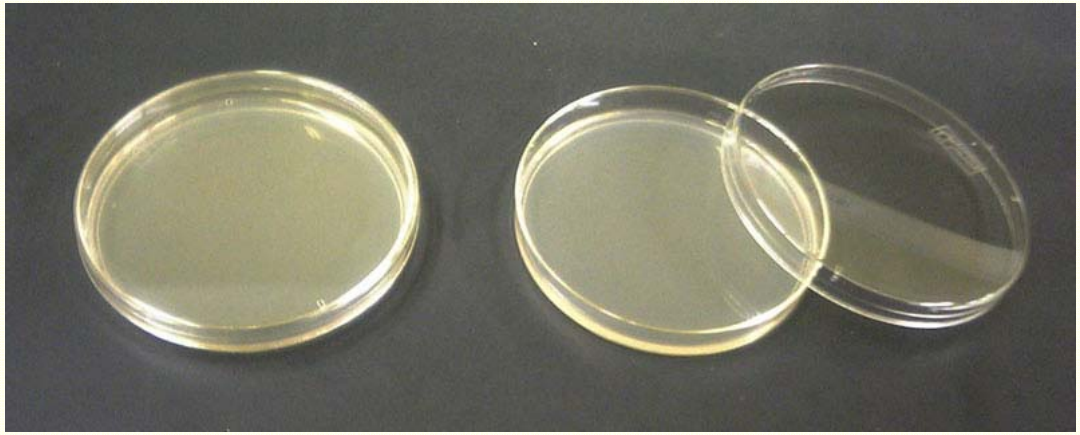
- Easy handling & cultivation



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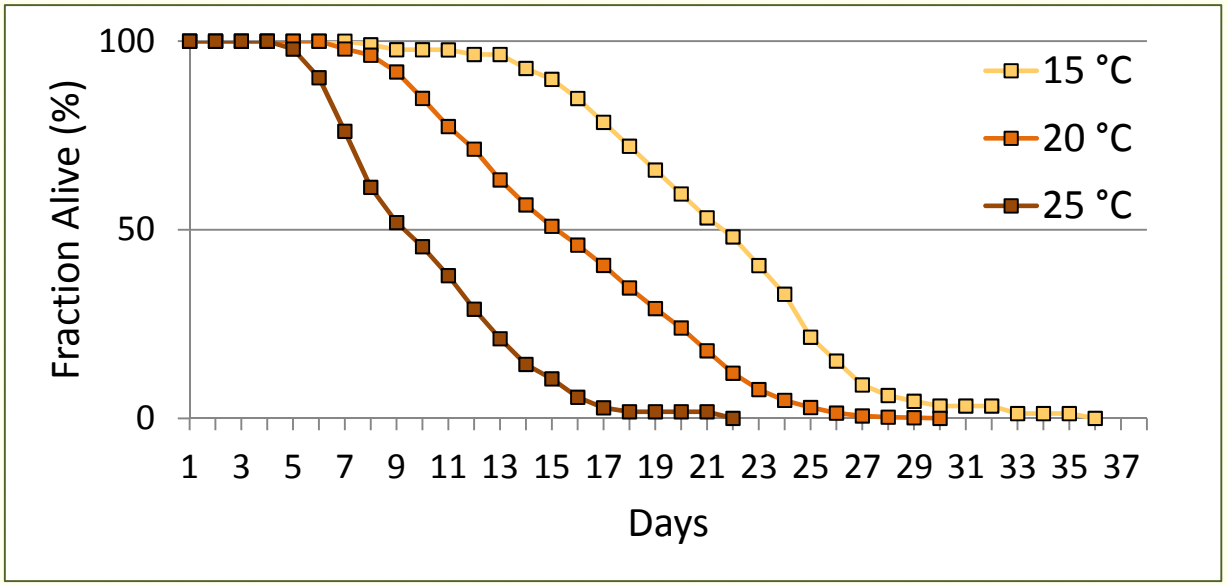

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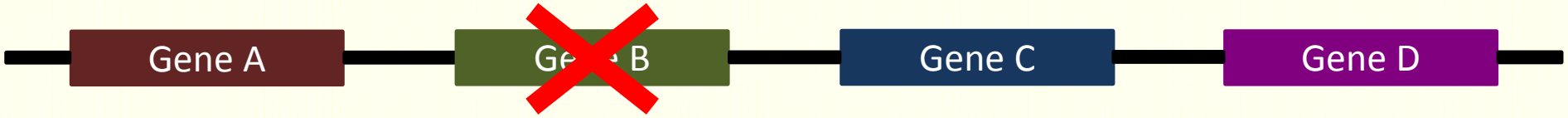

Why do we use the nematode *C. elegans*?

- Easy handling & cultivation
- Hermaphroditic reproduction & high number of progeny
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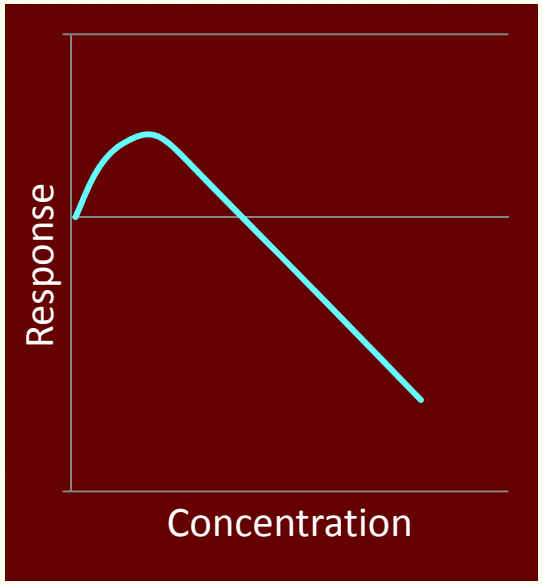
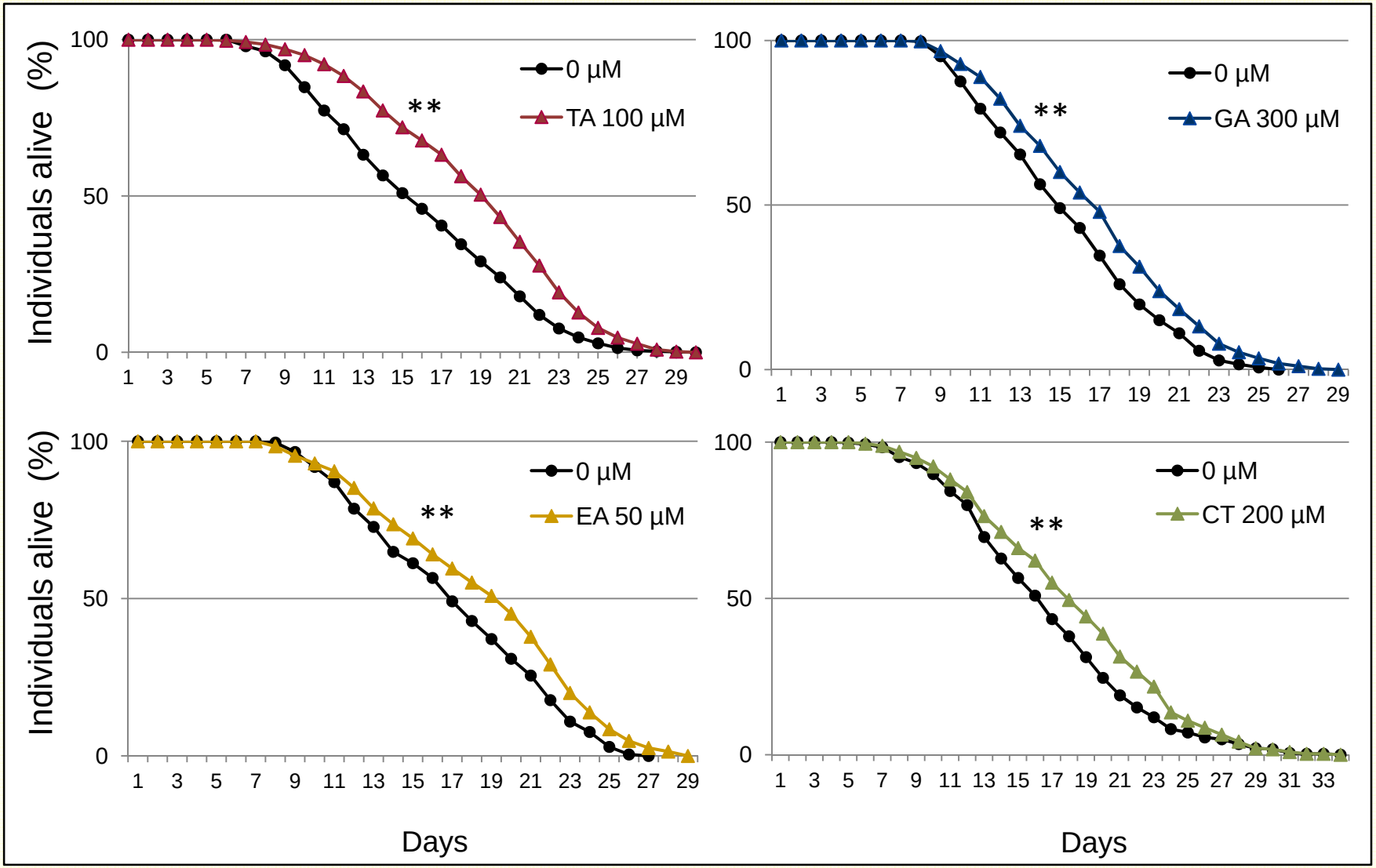
- Complete sequenced genome
- Diverse mutant strains
- Observation of numerous hormetic effects



Do the tannins offer a lifespan extension in *C. elegans* ?

Longevity via Tannin Exposure



What is the background for tannin mediated longevity ?

Possible Background Mechanisms

- Hormesis
- Calorie Restriction
- Targeted molecular modulation
- Antimicrobial capacities
- Antioxidative capacities

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Calorie Restriction

Calorie Restriction=

Longevity and ageing deceleration by reducing the amount of food to about 30-50 % of the *ad libitum* amount

Plausible, because:

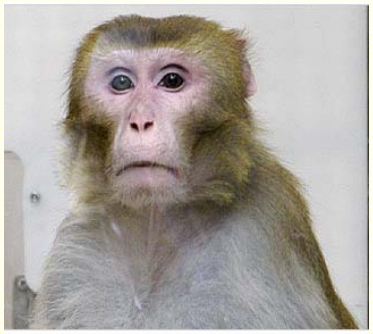
Tannins possess antinutritional capacities

Calorie Restriction

- 1989: Start of a Calorie Restriction rhesus monkey experiment
- They get only 30% of the *ad libitum* food amount
- So far:
  - Less age related diseases like cancer, heart disease or diabetes
  - Better brain function
  - Extension of the median lifespan

Calorie Restriction

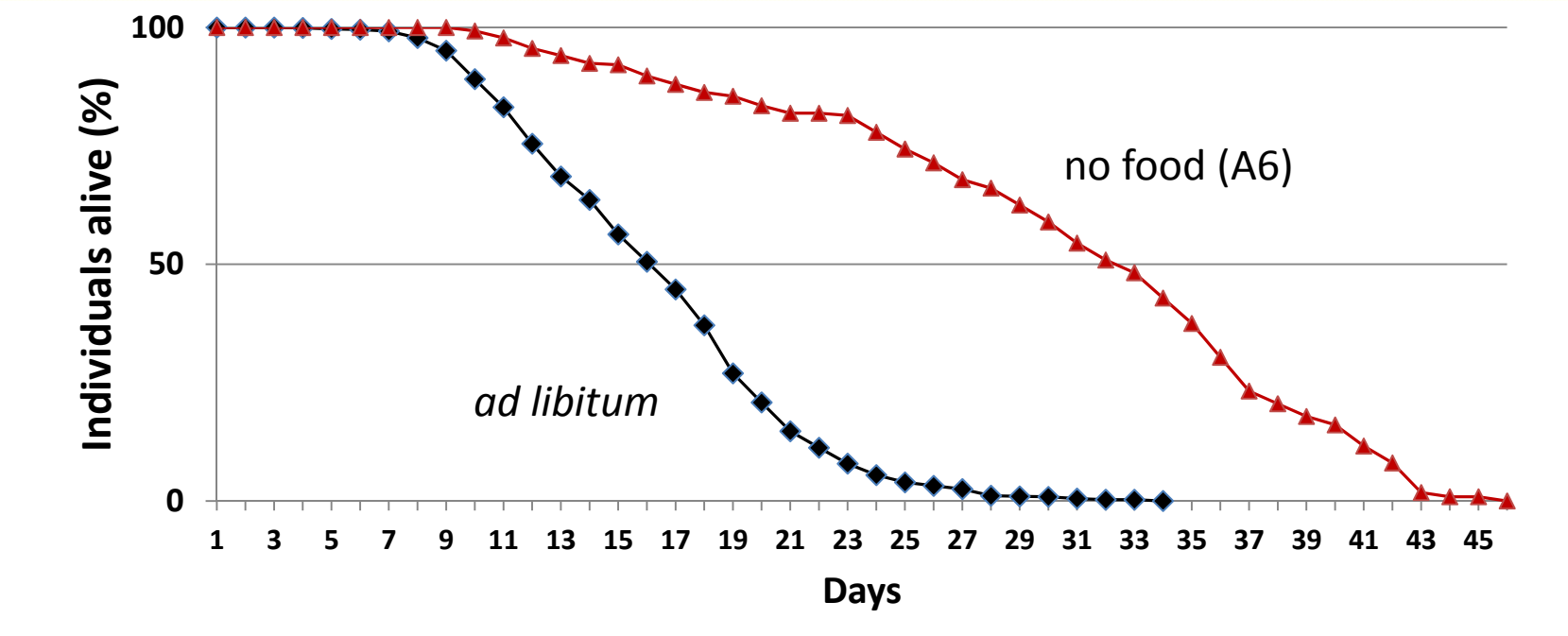
ad libitum



Healthy,
but hungry

Calorie Restriction

Calorie Restriction in C. elegans



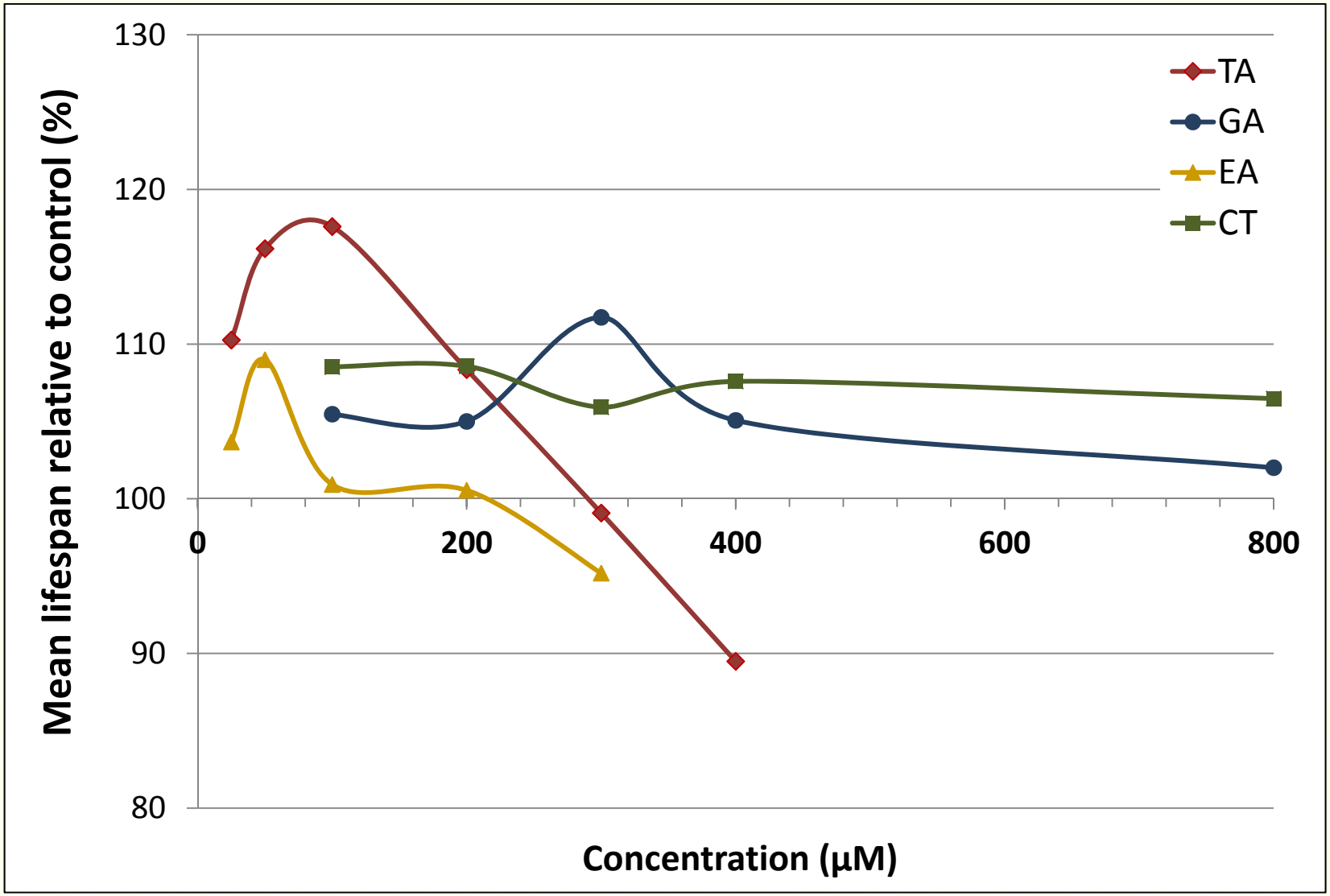
Possible Background Mechanisms

- Hormesis
- Calorie Restriction
- Targeted molecular modulation
- Antimicrobial capacities
- Antioxidative capacities

Proofs for Hormesis

- Dose or concentration dependent response
- Stimulatory effects in low concentrations
- Reversal of effects in high concentrations

Are Tannins Hormetic ?

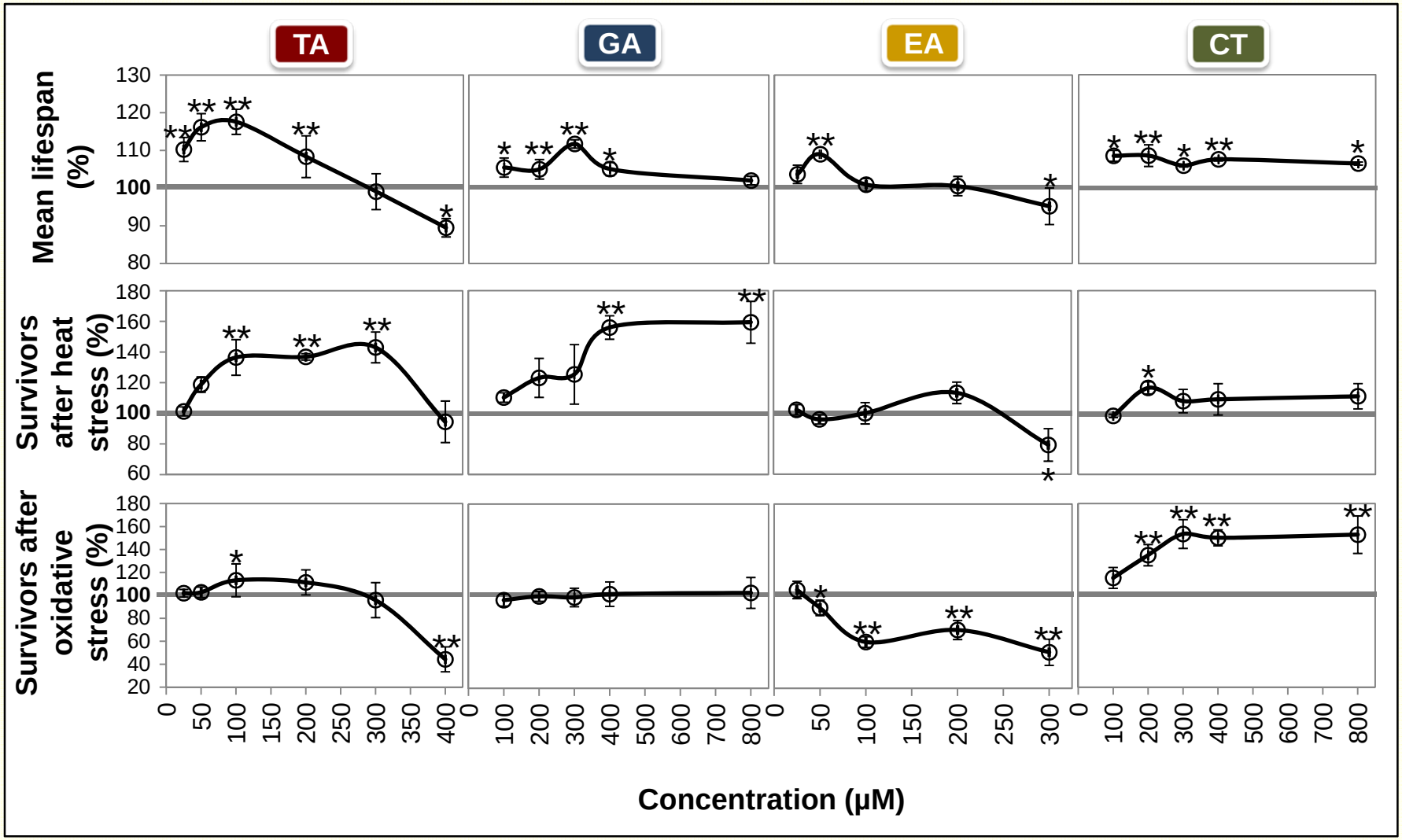


- Only TA & EA are hormetic
- Only TA & EA have enough molecular mass to precipitate and bind proteins efficiently

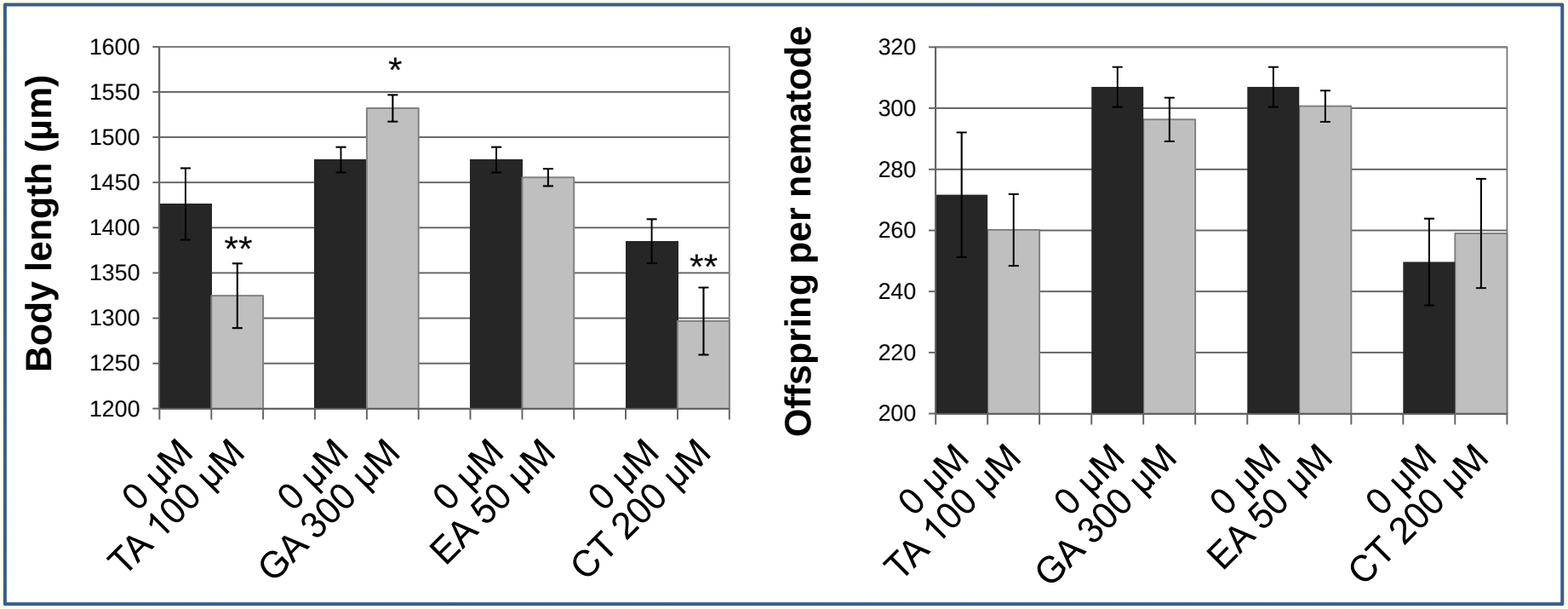
➔ The protein precipitating and binding capacities might be the key for tannin mediated hormesis

Are there any side effects ?

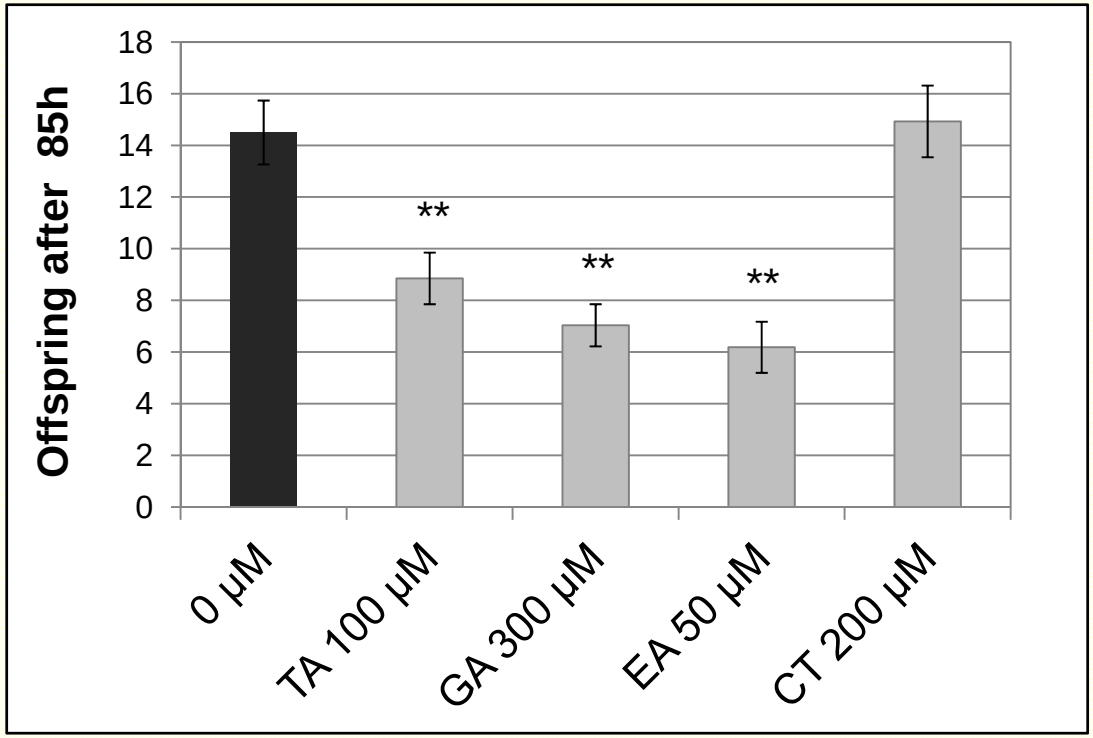
Stress Resistance



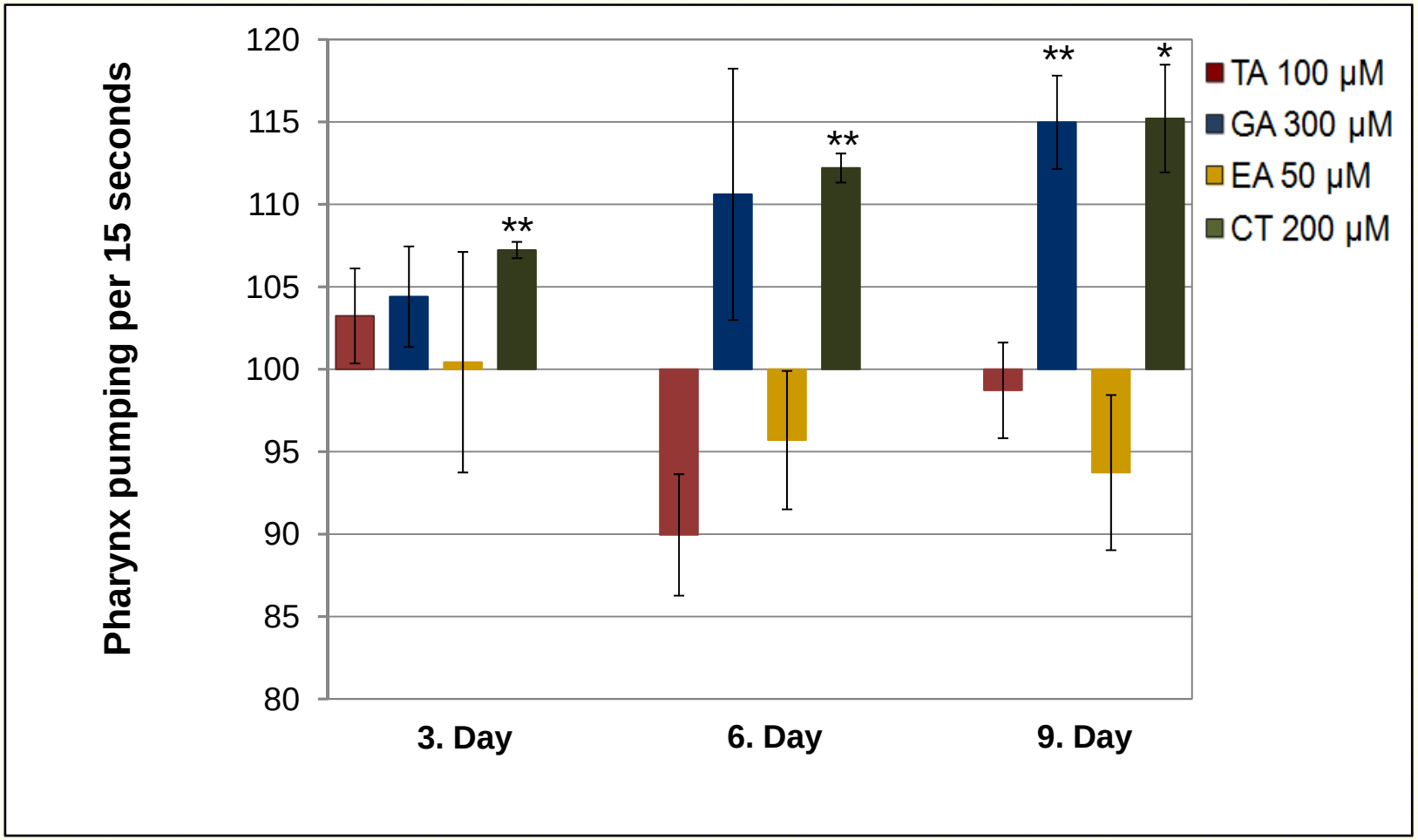
Growth & Reproduction



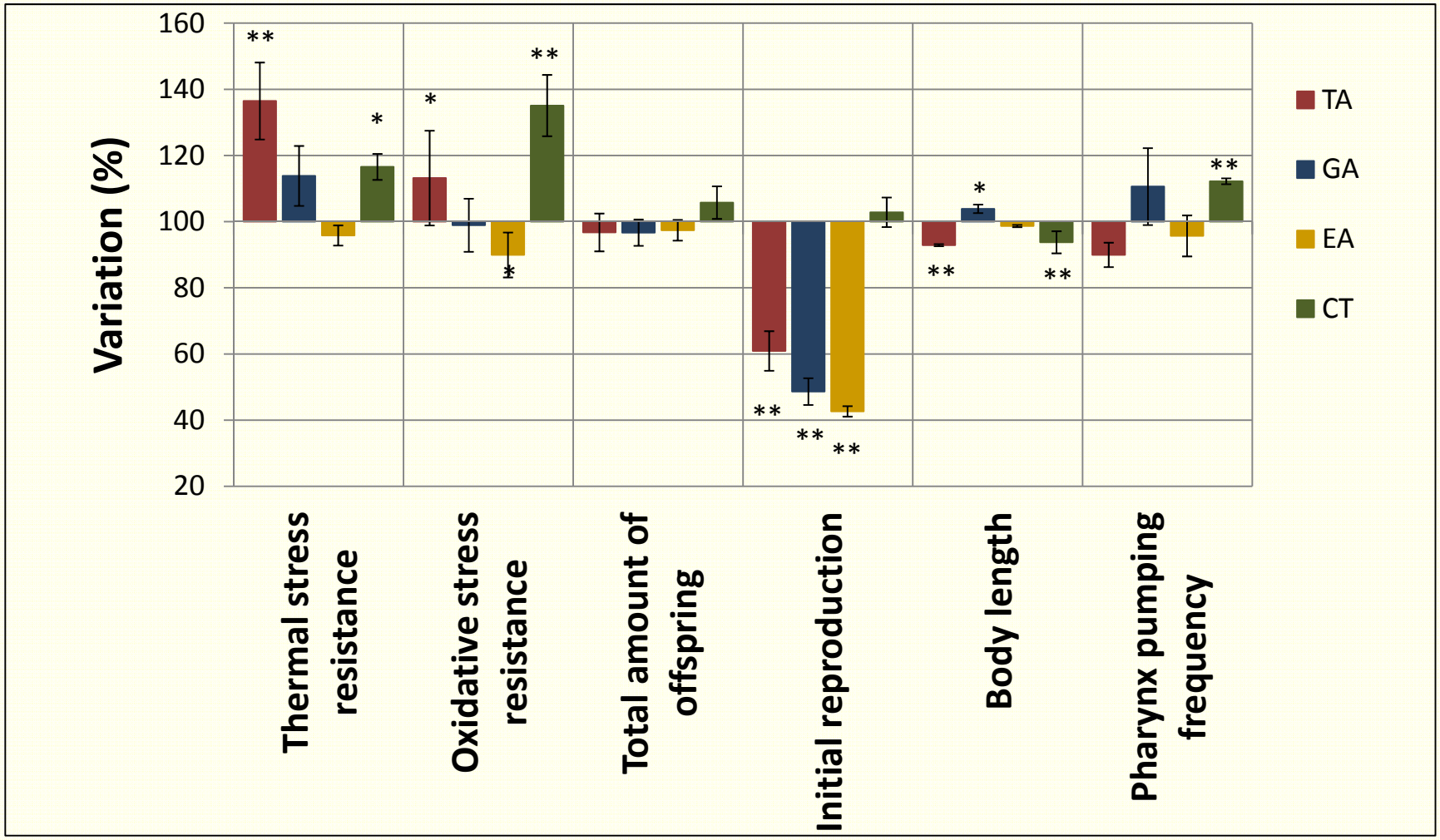
Start of Reproduction



Pharynx Pumping Frequency



There are side effects !



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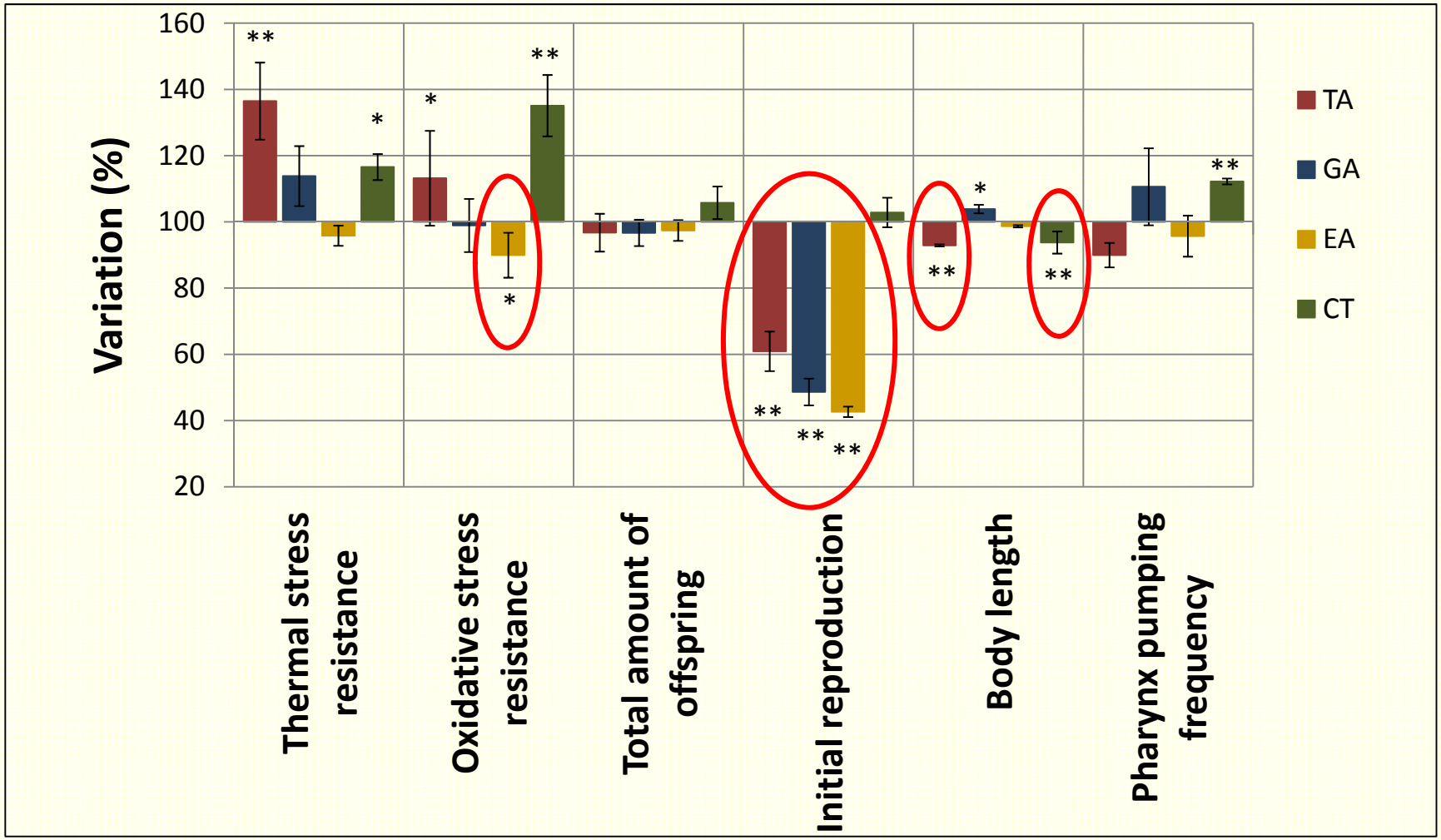

The Disposable Soma Theory
(Thomas Kirkwood, 1977)

Organisms distribute their energy to repair, maintenance, growth, and reproduction

Additional energy consumption for one sector

→ → →

Energy imbalance

→ → →

Reduced growth or reproduction

Conclusion

- Tannin building blocks offer longevity
- Hormesis not always detectable
- Longevity-concentrations also lead to side-effects in
  - Growth
  - Reproduction
  - Stress resistance

Conclusion

- Hormesis seems not to be free of charge!
- Hormesis might be the result of a reallocation of energy/resources

- In future studies several endpoints should be examined in parallel, to detect possible "costs" of hormesis

Thank You!

Saul et al. (2011)
Diversity of Polyphenol Action in *Caenorhabditis elegans:* Between Toxicity and Longevity.
J. Nat. Prod. 74, 1713-1720