

understood why it can enter a very resistant Dauer larval stage to wait for 2 months for better times, before resuming its normal life cycle,²⁸ and why mutations of the insulin-IGF1-like signalling pathway regulating metabolism, responses to food shortage and Dauer formation strongly increase longevity in the laboratory.²⁹

Another consequence of the features of this worm is that its only way to survive various threats could be to live longer, even if not entering the Dauer (duration in German) larval stage, because the lifespan in the soil is less than 2 days, *i.e.* 7-fold less than in the laboratory.³⁰ When subjected to a toxic chemical product in the soil, and because the worm cannot escape, an appropriate response could be to live longer, waiting for dilution (rain?) or destruction (bacteria?) of the product in the soil. It is thus not unexpected that many toxic molecules can increase lifespan in worms, even if some (too toxic or concentrated) also decrease lifespan. For instance, longevity is increased by the toxic products juglone (+6–29%),³¹ hyperbaric oxygen (+22%),³² hydrogen sulfide (+74%),³³ carbon dioxide (+26–44%),³⁴ plumbagin (+12%),³⁵ and dimethyl formamide (+30%).³⁶ These results are probably hormetic effects (beneficial effects of a low dose of a toxic product: see below), but other molecules not considered to be toxic also increase lifespan in worms. These increases could be explained by a real positive effect because worms are offered essential molecules (*e.g.* vitamin E: +22%³⁷), but molecules *a priori* considered by the experimenter as beneficial (*e.g.* antioxidants, like trolox: +31%³⁸) could indeed have a hormetic effect. Whatever the mechanism of the increased lifespan could be, this increase probably better reflects the life-history strategy of the worm, *i.e.* a very plastic lifespan when confronted with a threat rather than a real effect on the aging process.

Therefore, any experiment showing that a chemical product increases lifespan in *C. elegans* should be interpreted with caution because this beneficial effect is maybe only linked to the life-history strategy of this worm and thus could not have any beneficial effect on lifespan in other species with different life-history strategies. Thus, it is not certain that such studies set “the stage for future studies to investigate whether compounds that increase lifespan in the nematode may also have a beneficial effect on aging in mammals”.³⁹ One could agree with the conclusion that “while *C. elegans* remains a valuable organism for the study of ageing, it is critical to consider its natural history when interpreting results from such studies”.³⁰

3.3 Toxic and Essential Molecules May Have the Same Effects at Low Doses

The effect on lifespan of many molecules has been tested in past decades, particularly in *Drosophila melanogaster*.⁴⁰ On the one hand, essential molecules such as vitamins may have positive effects at low doses, because deficiency is deleterious, but they can be toxic at a high dose (*e.g.* vitamin A on lifespan of *D. melanogaster* flies⁴¹). On the other hand, low doses of toxic molecules can