

benefit of α -tocopherol in both *C. elegans* and *D. melanogaster*.¹⁶⁰ Bahadorani *et al.* also showed that supplementation of 0.005–25 IU ml⁻¹ α -tocopherol did not extend the lifespan of *rosy*⁺⁵ wild type flies in normoxic conditions.¹⁶¹ In rodents, several studies have shown that supplementation of α -tocopherol with a concentration range of 20–4000 $\mu\text{g g}^{-1}$ did not extend the mean and maximum lifespan of rats.^{162–166} Moreover, supplementation of vitamin E on short-tailed field voles (*Microtus agrestis*) was reported to significantly shorten the lifespan.¹⁶⁷ However, 250–500 mg g⁻¹ α -tocopherol was recently reported to extend the lifespan of C57BL/6, CD1/UCadiz, and MRL/lymproliferative mice.^{168–170} The reports regarding the longevity effect of α -tocopherol in various model organisms are well summarized in a review by Ernst *et al.*¹⁵⁸

Carotenoids—lipid-soluble pigments synthesized by plants, bacteria, and algae—are also well established to be potent antioxidants and immunostimulants.¹⁷¹ Carotenoids, including β -carotene, lutein, zeaxanthin, and fucoxanthin, contain pigments responsible for yellow, red, and orange colors in food. Although the beneficial effects of carotenoids, like antioxidant, anti-mutagenic, anti-inflammatory, and anti-tumor properties, have been well investigated, studies on the longevity effect of carotenoids have only recently begun. Beta-carotene, an oxygen-lacking form of carotenoid, extended the lifespan of Canton-S wild type *D. melanogaster* at 0.3–1 μM ,¹⁷² and extended the lifespan and ameliorated the damage by γ -ray irradiation in Wistar rats.¹⁷³ In addition, supplementation of lutein, an oxycarotenoid was reported to extend the mean lifespan of Oregon-R wild type *D. melanogaster* at a concentration of 0.1 mg ml⁻¹ by 11.35%.¹⁷⁴ Furthermore, fucoxanthin—a marine carotenoid—showed a beneficial effect on cancer, improvement of the plasma lipid profile,^{175,176} and a lifespan-extending effect on flies.¹⁷² Supplementation of 1 μM fucoxanthin increased the median lifespan of Canton-S wild type *D. melanogaster* by 33%.

Lipoic acid is a potent antioxidant found in spinach, broccoli, tomatoes, and rice. Lipoic acid is known to have beneficial effects for several diseases, including diabetes, cardiovascular disease, cognitive decline, and dementia. Supplementation of 24 μM α -lipoic acid was reported to extend the mean and maximum lifespan of *C. elegans* by 24% and 14%, respectively.¹⁷⁷ However, supplementation of 600 mg kg⁻¹ α -lipoic acid had no effect on the lifespan of C57BL/6C3F1 mice,¹⁷⁸ and administration of 100 mg kg⁻¹ α -lipoic acid decreased the median lifespan of SAMP8 mice.¹⁷⁹

Morphine—an analgesic extracted from the opium poppy (*Papaver somniferum*)—is also reported to possess longevity benefits in mice and flies. Supplementation of 10 mg kg⁻¹ morphine hydrochloride once a week extended the residual lifespan of 28 month-old CBA mice, and 0.25 mg ml⁻¹ morphine hydrochloride extended the residual lifespan of Oregon-R wild type flies when supplied once a week since 5 days or 54 days.¹⁸⁰ Nolinospinoside F—a steroidal saponin extracted from *Ophiopogon japonicas*—was reported to increase the replicative lifespan of K6001 *S. cerevisiae* at concentrations of 1, 3, and 10 μM .¹⁸¹ Caffeic acid (300 μM) and rosmarinic acid (200 μM) extended the lifespan of N2 *C. elegans* fed with heat-killed *E. coli*.¹⁸² There is