by approximately 15%. Supplementation of resveratrol at either concentration did not extend the lifespan of males fed with a high-fat diet. Similarly, supplementation of resveratrol at 400 μM increased the mean lifespan of females fed with a high-fat diet by about 10% without changes in daily food intake.[30] These reports suggest that the composition of dietary nutrients should be considered when testing the longevity effects of nutraceuticals like resveratrol.

In addition to *C. elegans* and *D. melanogaster*, the effect of resveratrol on longevity was tested in other lower organisms. Supplementation of 30 and 130 μM resveratrol extended the median and maximum lifespan of honey bees (*Apis melllifera*) by 38% and 33%, respectively, under normal oxygen condition, but not in hyperoxic conditions.[31] However, resveratrol failed to extend the lifespan in mosquitoes (*Anopheles stephensi*) and the crustacean *Daphnia*.[32,33]

13.2.2 Lifespan-Extending Effects of Resveratrol in Vertebrate: Fishes and Rodents

The longevity benefits of resveratrol were also investigated in higher model organisms. Three independent studies documented the effects of lifespan extension by resveratrol in the annual fish *Nothobranchius*. In 2006, Valenzano *et al.* reported that the lifespan of the Gonarezhous strain of *Nothobranchius furzeri* was increased by food supplementation of 24–600 μg g^{-1} resveratrol in a dose-dependent manner without any loss of fertility.[20] The maximum lifespan of this seasonal fish was extended by 59% with 600 μg g^{-1} resveratrol supplementation. In 2012, another *Nothobranchius* strain was also tested for the effects of resveratrol.[34] Supplementation of 200 μg g^{-1} resveratrol in food extended the maximum lifespan by 28%, from 64 to 82 weeks in *Nothobranchius guentheri*.[34] Similarly, in 2013, Genade *et al.* reported that 12 μg per fish per day of resveratrol extended the median and maximum lifespan of *Nothobranchius guentheri* by 42.9% and 17%, respectively.[35]

Resveratrol also has been shown to have a prolongevity effect in mammals. In 2006, Baur *et al.* fed 1 year-old male C57BL/6NIA mice with a high-calorie diet containing 22.4 mg kg^{-1} day^{-1} of resveratrol for 110 weeks.[19] Supplementation of resveratrol changed the physiology of mice fed with the high-fat diet towards those with a standard diet, reducing the risk of death in mice fed with the high-fat diet by 31%.[19] Unlike the prolongevity effect of resveratrol on lifespan in those with a high-fat diet, resveratrol failed to extend the lifespan of healthy mice supplemented with a standard diet. In 2008, Pearson *et al.* supplemented 1 year-old C57BL/6NIA mice with 100 or 400 mg kg^{-1} resveratrol.[36] In this study, they showed that resveratrol had no effect on the lifespan of mice.[36] In 2010 and 2013, the National Institute on Aging's Intervention Testing Program also reported that supplementation of 300 or 1200 mg kg^{-1} resveratrol to 1 year-old or 4 month-old genetically heterogeneous mice did not extend their lifespan, both in males and females.[37,38] Similarly, supplementation of 4 mg kg^{-1} resveratrol did not extend the lifespan of 12 month-old Wistar rats.[39]