

have anti-oxidative and anti-inflammatory characteristics, which contribute to the improvement of health and prevention of age-related diseases, such as cancer, diabetes, cardiovascular disease, and neurodegenerative disorders.³ The beneficial effects of phytochemicals on the prevention and treatment of age-related diseases are well-documented in the literature.⁴⁻⁷ In addition to these benefits, some phytochemicals have attracted attention from the general public due to their potential in retarding the aging process and for their previous results associated with extending the lifespan of various organisms including yeast, worms, flies, fishes, and rodents.^{1,2} The most representative phytochemical associated with the extension of lifespan is resveratrol, a compound rich in red wine with a lot of biological and physiological activities.⁸ In this chapter, we summarize and review the longevity benefits and the putative underlying mechanisms of these phytochemicals, with particular attention to resveratrol.

13.2 Resveratrol

Resveratrol (3,4',5-trihydroxy stilbene) is the most extensively investigated phytochemical to retard aging, extend lifespan, and improve health. Resveratrol is a phytoalexin and polyphenolic compound found in various plants, including berries and peanuts, especially in the skin of red grapes, produced in response to stresses such as fungal infection and ultraviolet irradiation.⁸ Although resveratrol has been shown to exist naturally in both isomeric *trans* and *cis* forms, *trans*-resveratrol has been the focus of past investigations, mostly for its beneficial effects. Resveratrol was first isolated from white hellebore (*Veratrum grandiflorum*) in 1940, and was identified to have cancer-chemopreventive activity in mice.⁹ Since then, resveratrol has been well established to have various biological effects, such as anti-oxidant and anti-inflammation effects.^{10,11} Moreover, it has been shown to be beneficial against various age-related diseases, such as cardiovascular disease, cancer, neural disease, and metabolic disease, including diabetes.^{2,12-16}

13.2.1 Lifespan-Extending Effect of Resveratrol in Invertebrates: Yeasts, Worms and Flies

The longevity benefit of resveratrol has been highlighted since the study by Howitz and his colleagues in 2003. They screened for activators of sirtuin and showed the lifespan extension in *Saccharomyces cerevisiae* by resveratrol.¹⁸ In this initial screening, resveratrol was found to be the most potent Sirt1 activator mimicking the effects of calorie restriction; resveratrol administration increased the lifespan of yeasts by 70%.¹⁷ After this finding, several studies showed that resveratrol increased the lifespan of evolutionarily distant species, including worms, flies, fishes, and rodents.¹⁷⁻²¹

Several studies tested the lifespan-extending effect of resveratrol in various concentrations and in several mutant strains using worms. Wood *et al.*