(–)-Epicatechin enhances fatigue resistance and oxidative capacity in mouse muscle

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Abstract

During exercise, skeletal muscle performance depends in great part on the use of aerobic metabolism to supply the energetic demand of contractions. Endurance training increases the muscle aerobic capacity, which is not only associated with enhanced exercise performance, but also with a decreased risk of cardiovascular and metabolic diseases. Recently, it has been shown that regular use of small doses of dark chocolate may result in similar health benefits to exercise training. We show here that mice fed for 15 days with (–)-epicatechin (present in dark chocolate) had improved exercise performance accompanied by: (1) an increased number of capillaries in the hindlimb muscle; and (2) an increased amount of muscle mitochondria as well as signalling for mitochondrial biogenesis. These results suggest that (–)-epicatechin increases the capacity for muscle aerobic metabolism, thereby delaying the onset of fatigue. These findings may have potential application for clinical populations experiencing muscle fatigue.

Abstract

The flavanol (–)-epicatechin, a component of cacao (cocoa), has been shown to have multiple health benefits in humans. Using 1-year-old male mice, we examined the effects of 15 days of (–)-epicatechin treatment and regular exercise on: (1) exercise performance, (2) muscle fatigue, (3) capillarity, and (4) mitochondrial biogenesis in mouse hindlimb and heart muscles. Twenty-five male mice (C57BL/6N) were randomized into four groups: (1) water, (2) water–exercise (W-Ex), (3) (–)-epicatechin ((–)-Epi), and (4) (–)-epicatechin–exercise ((–)-Epi-Ex). Animals received 1 mg kg−1 of (–)-epicatechin or water (vehicle) via oral gavage (twice daily). Exercise groups underwent 15 days of treadmill exercise. Significant increases in treadmill performance (~50%) and enhanced *in situ* muscle fatigue resistance (~30%) were observed with (–)-epicatechin. Components of oxidative phosphorylation complexes, mitofilin, porin, nNOS, p-nNOS, and Tfam as well as mitochondrial volume and cristae abundance were significantly higher with (–)-epicatechin treatment for hindlimb and cardiac muscles than exercise alone. In addition, there were significant increases in skeletal muscle capillarity. The combination of (–)-epicatechin and exercise resulted in further increases in oxidative phosphorylation-complex proteins, mitofilin, porin and capillarity than (–)-epicatechin alone. These findings indicate that (–)-epicatechin alone or in combination with exercise induces an integrated response that includes structural and metabolic changes in skeletal and cardiac muscles resulting in greater endurance capacity. These results, therefore, warrant the further evaluation of the underlying mechanism of action of (–)-epicatechin and its potential clinical application as an exercise mimetic.