The metabolic and molecular mechanisms of α-mangostin in cardiometabolic disorders (Review)

ABSTRACT

α-mangostin is a xanthone predominantly encountered in Garcinia mangostana. Extensive research has been carried out concerning the effects of this compound on various diseases, including obesity, cancer and metabolic disorders. The present review suggests that α-mangostin exerts promising anti-obesity, hepatoprotective, antidiabetic, cardioprotective, antioxidant and anti-inflammatory effects on various pathways in cardiometabolic diseases. The anti-obesity effects of α-mangostin include the reduction of body weight and adipose tissue size, the increase in fatty acid oxidation, the activation of hepatic AMP-activated protein kinase and Sirtuin-1, and the reduction of peroxisome proliferator-activated receptor γ expression. Hepatoprotective effects have been revealed, due to reduced fibrosis through transforming growth factor-β 1 pathways, reduced apoptosis and steatosis through reduced sterol regulatory-element binding proteins expression. The antidiabetic effects include decreased fasting blood glucose levels, improved insulin sensitivity and the increased expression of GLUT transporters in various tissues. Cardioprotection is exhibited through the restoration of cardiac functions and structure, improved mitochondrial functions, the promotion of M2 macrophage populations, reduced endothelial and cardiomyocyte apoptosis and fibrosis, and reduced acid sphingomyelinase activity and ceramide depositions. The antioxidant effects of α-mangostin are mainly related to the modulation of antioxidant enzymes, the reduction of oxidative stress markers, the reduction of oxidative damage through a reduction in Sirtuin 3 expression mediated by phosphoinositide 3-kinase/protein kinase B/peroxisome proliferator-activated receptor-γ coactivator-1α signaling pathways, and to the increase in Nuclear factor-erythroid factor 2-related factor 2 and heme oxygenase-1 expression levels. The anti-inflammatory effects of α-mangostin include its modulation of nuclear factor-κB related pathways, the suppression of mitogen-activated protein kinase activation, increased macrophage polarization to M2, reduced inflammasome occurrence, increased Sirtuin 1 and 3 expression, the reduced expression of inducible nitric oxide synthase, the production of nitric oxide and prostaglandin E2, the reduced expression of Toll-like receptors and reduced proinflammatory cytokine levels. These effects demonstrate that α-mangostin may possess the properties required for a suitable candidate compound for the management of cardiometabolic diseases.