people. Briefly, CR individuals had decreased body weight and fat,[75–77] triglycerides,[75,78] basal insulin and glucose levels,[75,78,79] and blood pressure.[75] Increased insulin sensitivity[80] and high density lipoprotein (HDL) levels[75,81] were observed under CR. Finally we have to agree that the capacity of CR to extend life span in humans is still unknown. However, similarities between CR effects on animal models and in humans suggest that CR may be useful to extend healthspan.

10.3 Beneficial Effects of CR

Many studies have shown that CR induces various beneficial changes both in short and long term perspectives for the extension of the life span and prolongation of healthspan. These changes can be used as early markers during the studies of chemicals or drugs with suggested action mechanisms similar to CR. The biological effects of CR include, but are not limited to: modification of important regulatory pathways *via* the expression and activity of key enzymes involved in metabolism; reduction of damage to macromolecules like proteins and nucleic acids and intensification of their clearance if damaged and cannot be repaired; reduction of chronic inflammation and decreasing of inflammatory markers; modulation of apoptosis and action of chaperone molecules; prevention of glucose and insulin intolerance; specific alteration of processes controlling cell repair or death.

10.3.1 Cardiovascular System

A body of evidence predominantly from animal studies and from some limited human trials indicates that CR has beneficial effects on the cardiovascular system. It reduces blood pressure and improves vascular function by decreasing oxidative stress[82] and increasing the availability of nitric oxide (NO) by activation of endothelial nitric oxide synthase (eNOS) and affecting the histone deacetylase Sirt1.[82–85] Increased levels of adiponectin and activation of AMP-activated protein kinase (AMPK) by CR prevented hypertension and cardiac hypertrophy in spontaneously hypertensive rats.[86] Reduced atherosclerosis and improved insulin sensitivity, as well as prevention of oxidative damage in cells of arterial walls, are achieved by decreased blood lipids (triglycerides, cholesterol) and glucose.[58,67,75,87,88] Additionally, CR decreases inflammation markers like TNF-α and IL-6.[75,89,90] Increased myocardial oxidation and ATP production,[91] Sirt1 activity,[92] mitochondrial function and biogenesis[93–95] as well as activation of pro-survival kinases Akt and extracellular signal-regulated kinases (ERKs) under CR conditions reduce the myocardial injury caused by ischemia-reperfusion.[91] Reduction of ventricular hypertrophy and improved diastolic function are possible by reduction of blood pressure, oxidative stress and myocardial fibrosis in parallel with activation of AMPK[86] and increased expression of sarco/endoplasmic reticulum calcium ATPase, SERCA2.[96]