Primary hemochromatosis and secondary iron overload conditions, such as thalassemia and sickle cell anemia, result in iron overload and are among the most frequently inherited disorders at an international scale. The prevalence and global clinical burden of iron overload is high resulting in heart and liver diseases. Iron-overload cardiomyopathy is a common cause of mortality in patients with secondary iron overload and is a major comorbidity in patients with primary hemochromatosis. Elucidating the basis pathophysiology of iron-overload mediated injury has provided new insights into potential new therapies for patients with iron overload. We will discuss the potential use of calcium channel blockade and resveratrol therapy for iron overload conditions.