

## **CoQ10**

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Nutritional pharmacology is expanding into the field of cardiovascular disease by adding safe, heart-protecting options derived from foods such as fatty acids and enzymes into treatment regimens.<sup>i ii iii</sup> In particular, researchers are targeting focus on antioxidants that offset damage caused by free radicals in mitochondria.<sup>iv</sup> A pivotal enzyme from the quinone family known alternately as “Coenzyme Q10”, “CoQ10”, or “ubiquinone” (for its ubiquity in every cell), mitigates oxidation in the mitochondrion by quenching free radicals that accumulate there. The benefits of exogenous supplementation with CoQ10 for human patients with cardiovascular disease have been recognized for over twenty years, but introduction into veterinary cardiology has been slow.

### **Oxidation and the Heart**

Oxidative stress occurs when reactive oxygen species (ROS) overwhelm the organism’s antioxidant defenses. ROS generators within compromised hearts include stressed cardiomyocytes, activated vascular endothelia, activated neutrophils, and perivascular tissue.<sup>v</sup> Oxidants from these sources contribute to necrosis following ischemia.<sup>vi</sup> Failing hearts produce more ROS than do healthy hearts.

Out of all the organelles in heart cells, mitochondria exhibit the highest vulnerability to oxidative damage. Since mitochondria provide the metabolic energy necessary for cellular survival, preventing and/or reversing oxidative damage could provide dramatic medical benefits in disease. Cardiac muscle cells, or cardiomyocytes, rely heavily on ongoing ATP production by mitochondria for support of their contractile mechanical function. Mitochondria are so numerous in cardiomyocytes that they occupy up to 60% of the cell’s volume. Decline of mitochondrial ATP generation leads to contractile compromise and, potentially, heart failure. Estimates indicate that cardiomyocytes use 75% of mitochondrial ATP-derived energy for contraction of the myocardium while 25% goes to maintaining ionic homeostasis.<sup>vii</sup>

### **Antioxidation and the Heart**

CoQ10 promotes cardiomyocyte homeostasis and survival.<sup>viii</sup> It does so at least in part by preserving mitochondrial ATP production, which as noted previously supports contractile function and cardiac output. In a heart facing reperfusion injury, CoQ10 can also limit injury by enhancing SOD and GPx activity.<sup>ix</sup> In its antioxidant capacity, CoQ10 regenerates alpha-tocopherol, the reduced form of vitamin E. Recently, researchers have begun to investigate the pleiotropic effects associated with CoQ10, finding that its actions include regulation and alteration of genomic expression. In so doing, CoQ10 targets multiple genes involved in cell signaling and intermediary metabolism.<sup>x</sup>

The outcome of CoQ10 supplementation include enhanced electron transport and ATP production, improved antioxidant protection and redox signaling, and stabilization of the mitochondrial permeability transition pore that protects against apoptotic cell death.<sup>xi</sup>

### **Specific Applications of CoQ10 in cardiac disease**

Although myocardial infarction is thought to occur rarely in small animals,<sup>xii xiii</sup> heart disease of other types occurs with relative frequency, including breed-related cardiomyopathy in dogs, hypertrophic cardiomyopathy in cats, chronic congestive heart failure in dogs,<sup>xiv</sup> and doxorubicin-induced cardiotoxicity. These conditions increase the risk of oxidative stress, which CoQ10 can help counteract.<sup>xv xvi xvii</sup>

### **CoQ10 and Doxorubicin-Induced Cardiotoxicity**

The anthracycline-based chemotherapeutic, doxorubicin, appears widely in chemotherapy regimens for cancer. However, its main detractor is dose-related cardiotoxicity. CoQ10 prevents or reduces doxorubicin-linked cardiomyopathy. It limits oxidative damage to the inner mitochondrial membrane and the oxidative damage that doxorubicin causes to mitochondrial DNA that leads to apoptosis in cardiomyocytes.<sup>xviii</sup> Three non-randomized clinical trials provide evidence that CoQ10 coadministered with anthracyclines diminishes cardiotoxicity without compromising anti-tumor effects.<sup>xix</sup> However, whether this holds true in veterinary patients await further examination with large, randomized clinical trials.

### **Tissue Penetration of CoQ10 Supplementation**

Whether or not exogenously administered CoQ10 reaches target tissues depends heavily on product bioavailability, dosage, species, and duration of treatment.<sup>xx</sup>

### **Drug Interactions**

CoQ10 carries a strong safety profile,<sup>xxi</sup> but one concern deserves mention, especially when considering CoQ10 supplementation for animals at risk for thromboembolic disease. The structural similarity of CoQ10 to vitamin K has raised questions about pro-coagulant attributes and antagonism of the anticoagulant benefits of warfarin.<sup>xxii</sup> In contrast, a 2007 study reported an increased risk of bleeding in patients taking warfarin and CoQ10.<sup>xxiii</sup> Thus, it is uncertain whether CoQ10 affects coagulation parameters and, if so, in which direction and at what dose.

### **Future Work**

As with most dietary supplements and herbs prescribed for animals, pharmacokinetics and pharmacodynamics of the many CoQ10 preparations remain largely unknown for

veterinary patients.<sup>xxiv</sup> <sup>xxv</sup> Dosing guidelines vary widely, regardless of species. Fortunately, CoQ10 so far appears safe even at intakes of 1200 mg/day in humans.<sup>xxvi</sup>

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