

## D-ribose in Chronic Fatigue Syndrome, Fibromyalgia, and Cardiac Disease

By Tori Hudson, ND

D-ribose is a naturally occurring 5-carbon sugar found in all living cells. It is the D-isomer of D-ribose that has been shown to possess biological activity. The body naturally converts glucose into D-ribose, which is then used to drive the pathways of energy metabolism. One of the problems faced when the body's D-ribose stores have been depleted is that tissues such as heart and muscle are unable to produce it quickly enough to restore this depleted energy store. It is this delay that slows cellular and tissue energy recovery.

The body rebuilds energy supplies that have been depleted through de novo synthesis and it also attempts to conserve energy substrates through salvage pathways during periods of metabolic stress. Both the new synthesis of energy supplies and the salvage pathway of energy preservation are regulated by D-ribose and rate limited by the availability of D-ribose, and only D-ribose performs this metabolic function. If the body doesn't have a sufficient supply of D-ribose when the energy pools are under demand, these pathways driving de novo synthesis and salvage do not function. This is why D-ribose is so critical as an energy component and forms the basic building block of adenosine triphosphate (ATP) synthesis. Simple sugars or complex carbohydrates, fats, and proteins are the main fuel sources for the cell. All of these are burned to provide fuel for cellular energy.

D-ribose is a component of ATP, Ribonucleic acid (RNA), nicotinamide adenine dinucleotide (NADH), and coenzyme-A, all needed by the mitochondria to maintain cellular energy homeostasis. In the body, we form D-ribose through the pentose phosphate pathway (PPP) or through the hexose monophosphate shunt. In heart and muscle tissue, the PPP is fairly slow because these tissues lack the enzymes needed to shunt the glucose in the pathway of D-ribose synthesis. These tissues instead prefer to use glucose to fuel ATP. The enzymes glucose-6-phosphate dehydrogenase and 6-phosphogluconate dehydrogenase preserve glucose metabolism, at a cost to D-ribose synthesis. When D-ribose is needed to rebuild the ATP pools, the process is slow and is itself a poor fuel when compared to simple sugars. It is, however, essential for the synthesis of ATP. Providing supplemental D-ribose for heart and muscle tissue speeds up the rebuilding of depleted ATP pools, thereby promoting a quicker, more efficient tissue recovery.<sup>1,2,3</sup> This is the theoretical basis for D-ribose supplementation.

Most body tissues cannot make enough D-ribose to restore energy levels to normal once they have been depleted. When cells suffer metabolic stress or mitochondrial dysfunction, ATP is catabolized and metabolic recovery is compromised. It is possible that these mechanisms may be similar to what occurs in individuals with chronic fatigue syndrome (CFS). Under these conditions, adenosine diphosphate (ADP) accumulates and the cells try to balance the ratios of ATP with ADP to maintain energy. These reactions lead to catabolic end products that are washed out of the cell with a subsequent loss in purines and adenine nucleotides, but there is a potential that these catabolites can be salvaged and recycled, by as much as 90%.<sup>4,5,6</sup> One therapeutic

option is to try to restore these energy substrates in order to recover the function of the cell, including muscle cells. By providing supplementation in the form of D-ribose, it is possible to enhance the nucleotide recovery and preserve or even rebuild cellular energy stores.<sup>7,8,9</sup>

### Chronic Fatigue Syndrome And Fibromyalgia

D-ribose research in CFS and fibromyalgia was initiated with a case study in 2004 of a veterinary surgeon with fibromyalgia.<sup>10</sup> After 3 weeks of D-ribose, this individual was back to full-time work, with the fatigue and muscle pain having disappeared. This level of clinical result is surprisingly quick and complete, but it does show us with this case result, that positive outcomes do exist. Another important study was conducted involving high-intensity athletes.<sup>11</sup> While it did not include patients with CFS, it still demonstrates the impact of D-ribose on muscle energy. Post exercise, muscle energy levels in the athletes were reduced by almost 30%. The study demonstrated that supplementing with 10 g of D-ribose per day for 3 days following the exercise restored muscle levels to normal while those treated with placebo received no effect.

Other studies have shown no benefit of D-ribose supplementation on muscle energy. For example, a double-blind randomized study using 4 g doses of D-ribose 4 times daily did not find a beneficial impact on post-exercise muscle ATP recovery and maximal exercise performance.<sup>12</sup>

An open-label non-controlled pilot study was conducted to evaluate the effect of D-ribose on symptoms in 41 CFS and fibromyalgia patients.<sup>13</sup> D-ribose was given at a dose of 5 g 3 times per day for an average of 3 weeks. Questionnaires before and after D-ribose intervention were compared and showed a significant improvement in 5 categories: energy, sleep, mental clarity, pain intensity, and well-being. At the end of the study, approximately 66% of patients experienced significant improvement while using D-ribose. These patients had a 45% average increase in energy and a 30% overall improvement in well-being.

Individuals with CFS/fibromyalgia are found to have 20% less energy in their muscles defective or inefficient mitochondria, nutrient deficiencies in cells and tissues needed to process food into energy, and thickened capillary walls slowing the rate of energy synthesis.<sup>14,15,16,17,18,19,20,21</sup>

Patients with fibromyalgia and/or CFS may therefore have alterations in their muscle energy use, metabolism, and anaerobic thresholds. As cellular energy is depleted, fatigue and muscle pain become more and more severe and the muscles require additional energy in their recovery efforts. Energy is used faster than fuel becomes made available to renew it and the fatigue, soreness, pain, and stiffness continue to progress. Some researchers propose that energy depletion reaches a critical point and CFS/fibromyalgia becomes a state in which the mechanisms for recovery are overwhelmed.

D-ribose research in the area of fibromyalgia and/or CFS is in its infancy. Randomized controlled trials are necessary to confirm the benefits of theories, pilot studies, and clinical observation. However,

the data presented here, including that of the pilot study, and in patients with enzyme deficiencies, confirms many clinicians' observations that D-ribose supplementation is a viable therapeutic option to reducing pain and fatigue and helping to restore health to those who suffer from CFS and fibromyalgia.<sup>22,23,24,25</sup>

## Cardiac Function

While it is generally understood that cardiovascular disease is the most prevalent health problem in adults in the United States and the number one cause of death, it is a lesser-known fact that 20% of men and women over age 40 are at risk for developing congestive heart failure (CHF) during their lifetime.<sup>26</sup> Diastolic dysfunction has been identified as a major predictor of CHF risk, and D-ribose directly maintains adenine nucleotide pools that are necessary to maintain cardiac diastolic function and increase the energy reserve of the heart.<sup>27,28</sup> During the diastolic phase of the heartbeat, the ability of the heart to relax is dependent on calcium ions being pumped out of the cell. In order for the ventricle to fill completely, complete relaxation is necessary so that adequate filling of the ventricle can occur. In order to achieve this ventricular relaxation, a fully charged ATP pool is required. D-ribose is directly related to ATP concentration and recovery and diastolic cardiac function. Animal studies show that when D-ribose is given to hearts after a period of ischemia, cardiac ATP levels increase and diastolic function increases.<sup>29</sup> Numerous clinical and laboratory studies that have shown that supplementing with D-ribose will enhance the recovery of adenine nucleotide pools as well as enhancing diastolic function in heart pathology.<sup>30,31,32,33,34</sup>

As a result of the research to day, clinicians are commonly using D-ribose supplementation to improve cardiac function, exercise tolerance, and quality of life in patients with CHF in particular, but also in ischemic heart disease, angina pectoris, and cardiomyopathy. Additional research demonstrates the benefit of D-ribose supplementation in protecting healthy hearts, improving anaerobic energy reserves, and raising the cardiac tissue hypoxic threshold such that during periods of intense exercise and endurance sports, cardiac stress is reduced because of greater cardiac muscle energy stores.<sup>35,36,37</sup> Preliminary research suggests that cardiac patients, especially those with CHF, athletes, and even adults over the age of 40 with clear risk factors for heart disease could benefit from the cardioprotective benefits of D-ribose supplementation. More research is needed to confirm this.

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