Evaluation of the beneficial effects of D-Ribose on cardiovascular disease patients: A literature review

By

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D-ribose (DR, also known as α-D-ribofuranose) 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. 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. 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. 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.

According to these facts there were many studies done for the evaluation of the efficacy of the DR supplements in improving the quality of life of cardiovascular disease patients and others to evaluate the presence of any toxic effects after DR treatment. In this literature review we will consider some of these studies that are published between 2000 and 2010.

Patients with chronic coronary heart disease often suffer from congestive heart failure (CHF) despite multiple drug therapies. So here it come a study from US to assess the effect of oral D-ribose supplementation on cardiac hemodynamics and quality of life in 15 patients with chronic coronary artery disease and CHF [(1)]. The study consisted of two treatment periods of 3 weeks, during which either oral D-ribose or placebo was administered followed by a 1-week wash out period, and then administration of the other supplement. Assessment of myocardial functional parameters by echocardiography, quality of life using the SF-36 questionnaire and functional capacity using cycle ergometer testing was performed. The administration of D-ribose resulted in an enhancement of atrial contribution to left ventricular filling, a smaller left atrial dimension and a shortened E wave deceleration by echocardiography. D-ribose also demonstrated a significant improvement of the patient's quality of life. In comparison, placebo did not result in any significant echocardiographic changes or in quality of life.

Another study from US was made on patients with advanced heart failure [(2)]. These patients are exercise intolerance as the cellular energy level decrease in the heart. This study was designed to investigate the role of ribose on ventilation at

anaerobic threshold in congestive heart failure patients. D-ribose (5gms/dose, tid) was assessed in 16 NYHA class III–IV, heart failure patients with VO2, tidal volume/VCO2, heart rate/tidal volume evaluated at 8 weeks. All patients had a significant improvement in ventilatory parameters at anaerobic threshold, along with a 44% Weber class improvement. Ribose improved the ventilatory exercise status in advanced heart failure patients.

One of the tests to evaluate heart function is dobutamine stress test, were the patient is injected with dobutamine & carefully monitored. Dobutamine is a sympathomimetic drug which will stimulate the heart in similar way in exercise. A study from India investigated the ability of D-Ribose with low dose dobutamine to improve the contractile response of viable myocardium to dobutamine and to assess the efficacy of D-ribose in reducing stress-induced ischemia [(3)]. Twenty-six patients with ischemic cardiomyopathy completed a two-day, randomized, double blind crossover trial comparing the effects of D-Ribose and placebo on regional wall motion. In segments with discordant responses, there were more ischemic segments with placebo compared to D-Ribose (36 vs. 26, p = 0.253). Nineteen patients developed ischemia during the dobutamine and placebo infusion and 13 patients had ischemia during dobutamine and D-ribose infusion (p = 0.109). DRibose improved contractile responses to dobutamine in viable myocardium with resting dysfunction but had no significant effect in reducing the frequency of stress-induced wall motion abnormalities.

Other studies rather than considering the improvement effects after using DR, they looked for using it as a pretreatment for protection masseurs. Using animal model (rats) a study showed that in normal hearts, ribose pretreatment significantly elevated anaerobic energy reserve in the heart and delayed the onset of irreversible ischemic injury by 25%. While in hypertrophied hearts, ribose pretreatment significantly improved ventricular function (maximum rate of pressure rise, 25%; normalize contractility, 13%) [(4)]. Another study on animal model concluded that DR not only improves hemodynamic parameters, cardiac contractility but also prevents the activation of pro-apoptotic c-*f*os which is a regulating factor of apoptotic genes causing the activation of neuronal cell death, demonstrating a neuroprotective effect of DR during slow ventricular tachycardia [(5)].

As being a drug with beneficial effects, it's important to do toxicological studies to evaluate its safety and side effects on human being. A study evaluated the toxicity from sub-chronic administration of DR to male and female albino Wistar rats [(6)]. Groups of 20 male and 20 female rats were exposed via the diet to 0%, 5%, 10%, or 20% DR, seven days per week, for 13 consecutive weeks. Absolute cecal weights were increased in the mid- and highdose animals, and the relative weights were increased in all treated animals. Analysis of microscopic histopathology revealed no evidence of changes that could be attributed to the DR treatment. This study supports a concentration of 5% DR in the diet, corresponding to an average daily intake of DR of 3.6 and 4.4 g/kg body weight/day in male and female rats, respectively, as being the absolute no observed adverse effect level (NOAEL) for this substance. Another study to evaluate oral embryotoxicity/teratogenicity of D-Ribose (DR) was conducted in female rats [(7)]. 28 rats/group were exposed via the diet to 0, 5, 10, or 20% DR (0.0, 4.25, 7.94, 9.91 g/kg body weight/day), from day 0 of gestation until Caesarian section and maternal sacrifice on day 21. All animals survived to the end of the study.

Administration of DR to pregnant rats at concentrations up to 20% of the diet resulted in no significant adverse effects on the developing embryo/fetus at doses that were not otherwise a severe metabolic stress on the dam, which conclude NOAEL for teratogenicity could be seen at a concentration of 5% DR in the diet, corresponding to an average daily intake of DR of between 3.64 and 4.61 g/kg body weight/day.

Animal model studies gives important indication for the presence of toxicity, but it's important to be supported by human studies. There is a study assessed the toxicity of extended consumption of D-ribose in healthy adults [8]. Nineteen subjects ingested 20 grams/Day (10 grams, twice a Day) of ribose with serial measurements of biochemical and hematological parameters at Days 0, 7, and 14. No significant toxic changes over the 14-day assessment period occurred in complete blood count, albumin, alkaline phosphatase, gamma glutamyltransferase, alanine amiotransferase, and aspartate aminotransferase. However, D-ribose did produce an asymptomatic, mild hypoglycemia of short duration. Uric acid levels increased at
Day 7, but decreased to baseline values by Day 14. D-ribose consumption for 14 days appears not to produce significant toxic changes in both hematological and biochemical parameters in healthy human volunteers.

We can conclude from previous data:

- DR has beneficial effects by improving diastolic functional parameters and enhancing quality of life in patients with coronary artery disease in CHF.
- Ribose improved the ventilatory exercise status in advanced heart failure patients.
- DR pretreatment improves hemodynamic parameters, cardiac contractility and has a neuroprotective effect during slow ventricular tachycardia.
- DR has NOAEL after sub-chronic administration or for teratogenicity
- DR has no significant toxic changes in both hematological and biochemical parameters in healthy human.

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