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INJECTABLE D-RIBOSE AS A METABOLIC SUPPORT STRATEGY IN PATIENTS UNDERGOING RAPID WEIGHT LOSS INDUCED BY GLP-1 RECEPTOR AGONISTS

D-RIBOSE INJETÁVEL COMO ESTRATÉGIA DE SUPORTE METABÓLICO EM PACIENTES SUBMETIDOS À PERDA DE PESO RÁPIDA INDUZIDA POR AGONISTAS DO RECEPTOR GLP-1

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ABSTRACT

The increasing use of glucagon-like peptide-1 receptor agonists (GLP-1 RAs), such as semaglutide, liraglutide and tirzepatide, has significantly improved weight loss outcomes in patients with obesity and metabolic disorders. However, rapid weight reduction may be associated with loss of lean body mass, fatigue and symptoms related to reduced cellular energy availability.

D-ribose, a naturally occurring pentose involved in the synthesis of adenine nucleotides, plays a key role in the formation of adenosine triphosphate (ATP), the primary cellular energy molecule. In conditions characterized by energetic depletion, D-ribose supplementation has been proposed as a metabolic support strategy to accelerate ATP resynthesis and improve cellular energy balance.

This narrative review aims to analyze the biochemical rationale and potential clinical applications of D-ribose, particularly in injectable form, as an adjunctive strategy in patients undergoing rapid weight loss associated with GLP-1 receptor agonist therapy.

Available evidence suggests that D-ribose may contribute to improved energy metabolism, reduced fatigue and enhanced mitochondrial function in conditions associated with ATP depletion. Although most studies involve oral supplementation, injectable administration may theoretically provide faster systemic availability.

Further clinical studies are required to evaluate the safety, efficacy and therapeutic relevance of injectable D-ribose in patients undergoing rapid pharmacologically induced weight loss.

Objective: he aim of this study is to review the biochemical rationale and current scientific evidence regarding the potential role of D-ribose as a metabolic support strategy for cellular energy recovery in patients undergoing rapid weight loss associated with GLP-1 receptor agonist therapy.

Conclusion: The available evidence suggests that D-ribose presents a consistent biochemical rationale as a metabolic support strategy in conditions associated with cellular energy depletion.
In patients undergoing rapid weight loss induced by GLP-1 receptor agonists, D-ribose may represent a promising adjunctive approach to support mitochondrial function, improve energy metabolism and potentially mitigate symptoms of fatigue and reduced physical performance. However, controlled clinical trials are required to validate the efficacy and safety of injectable D-ribose in this specific clinical context.
Keywords: D-ribose; GLP-1 receptor agonists; rapid weight loss; ATP resynthesis; mitochondrial function; metabolic support.

RESUMO

O uso crescente de agonistas do receptor do peptídeo-1 semelhante ao glucagon (GLP-1 RAs), como semaglutida, liraglutida e tirzepatida, melhorou significativamente os resultados da perda de peso em pacientes com obesidade e distúrbios metabólicos. No entanto, a rápida redução de peso pode estar associada à perda de massa magra, fadiga e sintomas relacionados à redução da disponibilidade de energia celular.
A D-ribose, uma pentose natural envolvida na síntese de nucleotídeos de adenina, desempenha um papel fundamental na formação de adenosina trifosfato (ATP), a principal molécula de energia celular. Em condições caracterizadas por depleção energética, a suplementação com D-ribose tem sido proposta como uma estratégia de suporte metabólico para acelerar a ressíntese de ATP e melhorar o equilíbrio energético celular.
Esta revisão narrativa tem como objetivo analisar a justificativa bioquímica e as potenciais aplicações clínicas da D-ribose, particularmente na forma injetável, como uma estratégia adjuvante

em pacientes submetidos à rápida perda de peso associada à terapia com agonistas do receptor de GLP-1.

As evidências disponíveis sugerem que a D-ribose pode contribuir para a melhora do metabolismo energético, redução da fadiga e aumento da função mitocondrial em condições associadas à depleção de ATP. Embora a maioria dos estudos envolva suplementação oral, a administração injetável pode, teoricamente, proporcionar uma disponibilidade sistêmica mais rápida.

Mais estudos clínicos são necessários para avaliar a segurança, a eficácia e a relevância terapêutica da D-ribose injetável em pacientes submetidos à perda de peso rápida induzida farmacologicamente.

Objetivo: O objetivo deste estudo é revisar a justificativa bioquímica e as evidências científicas atuais sobre o papel potencial da D-ribose como uma estratégia de suporte metabólico para a recuperação da energia celular em pacientes submetidos à perda de peso rápida associada à terapia com agonistas do receptor GLP-1.

Conclusão: As evidências disponíveis sugerem que a D-ribose apresenta uma justificativa bioquímica consistente como uma estratégia de suporte metabólico em condições associadas à depleção de energia celular. Em pacientes submetidos à perda de peso rápida induzida por agonistas do receptor GLP-1, a D-ribose pode representar uma abordagem adjuvante promissora para apoiar a função mitocondrial, melhorar o metabolismo energético e potencialmente mitigar os sintomas de fadiga e redução do desempenho físico. No entanto, são necessários ensaios clínicos controlados para validar a eficácia e a segurança da D-ribose injetável neste contexto clínico específico.

Palavras-chave: D-ribose; agonistas do receptor GLP-1; perda de peso rápida; ressíntese de ATP; função mitocondrial; suporte metabólico.

1. INTRODUCTION

The increasing use of GLP-1 receptor agonists in the treatment of obesity and type 2 diabetes has promoted significant weight loss and relevant metabolic improvement (1–3). However, accelerated weight loss may be associated with a reduction in lean mass and alterations in cellular energy availability, especially in patients undergoing significant caloric restriction (4).

Clinically, some of these patients present symptoms such as persistent fatigue, reduced muscle strength, and decreased physical performance, possibly related to decreased ATP resynthesis capacity and thermogenic adaptation associated with weight loss (4,8).

Given this scenario, D-ribose, a pentose essential in the formation of adenine nucleotides, has been investigated as a metabolic support under conditions of cellular energy stress (5–7).

This study is characterized as a narrative literature review, conducted based on a survey of the main international scientific databases, including PubMed, Scopus, Web of Science, and Google Scholar, using descriptors related to "D-ribose," "ATP resynthesis," "GLP-1 receptor agonists," "weight loss," "muscle mass loss," and "mitochondrial function."

Clinical trials, systematic reviews, and experimental studies relevant to understanding the role of D-ribose in cellular energy recovery were prioritized.

The justification for this article is based on the need to discuss adjuvant strategies that can assist in managing the energy

deficiency observed in patients undergoing accelerated weight loss induced by incretin therapies.

2. BIOCHEMICAL FUNDAMENTALS OF D-RIBOSE

D-ribose is a structural component of ATP, ADP, and AMP, participating directly in the pentose phosphate pathway and the resynthesis of adenine nucleotides (5).

Under conditions of cellular energy depletion such as hypoxia, ischemia, or intense caloric restriction, currently observed in patients using GLP-1 analogs, endogenous ATP recovery can be slow. Studies demonstrate that D-ribose supplementation can accelerate the replacement of adenine nucleotides in muscle and myocardial tissue, with the potential for energy and functional balance in the individual (6).

3. ACCELERATED WEIGHT LOSS, GLP-1, AND ENERGY DEFICIENCY

Clinical studies with semaglutide show significant weight loss, with a concomitant reduction in lean mass in varying proportions; some studies report a loss of up to 15% of body weight with prolonged use (1).

Muscle mass loss is associated with a decrease in basal metabolism, mitochondrial oxidative capacity, and overall metabolic efficiency (4). Thermogenic adaptation after weight loss can worsen this scenario, further reducing energy expenditure (8).

Clinically, the following is observed:

- Persistent fatigue

- Reduced muscle strength
- Feeling of low energy
- Decreased physical performance
- Drowsiness
- Difficulty concentrating

4. POTENTIAL ROLE OF INJECTABLE D-RIBOSE

The administration of D-ribose may contribute to:

4.1. ATP Resynthesis

Acceleration of ATP recovery after energy depletion (6).

4.2. Fatigue Improvement

Studies in patients with fibromyalgia and chronic fatigue syndrome have demonstrated subjective improvement in energy levels (7).

4.3. Mitochondrial Support

By increasing the availability of substrate for adenine nucleotide synthesis, it may act as metabolic support in states of energy dysfunction (5,6).

Although most evidence involves oral supplementation, the injectable Route may theoretically offer greater bioavailability and a faster metabolic response, a hypothesis that lacks specific clinical trials.

5. CLINICAL APPLICATION

In patients using GLP-1 agonists or after accelerated weight loss, D-ribose can be considered as an adjuvant strategy for:

- Cellular energy support
- Support for muscle recovery
- Optimization of tissue response in regenerative protocols

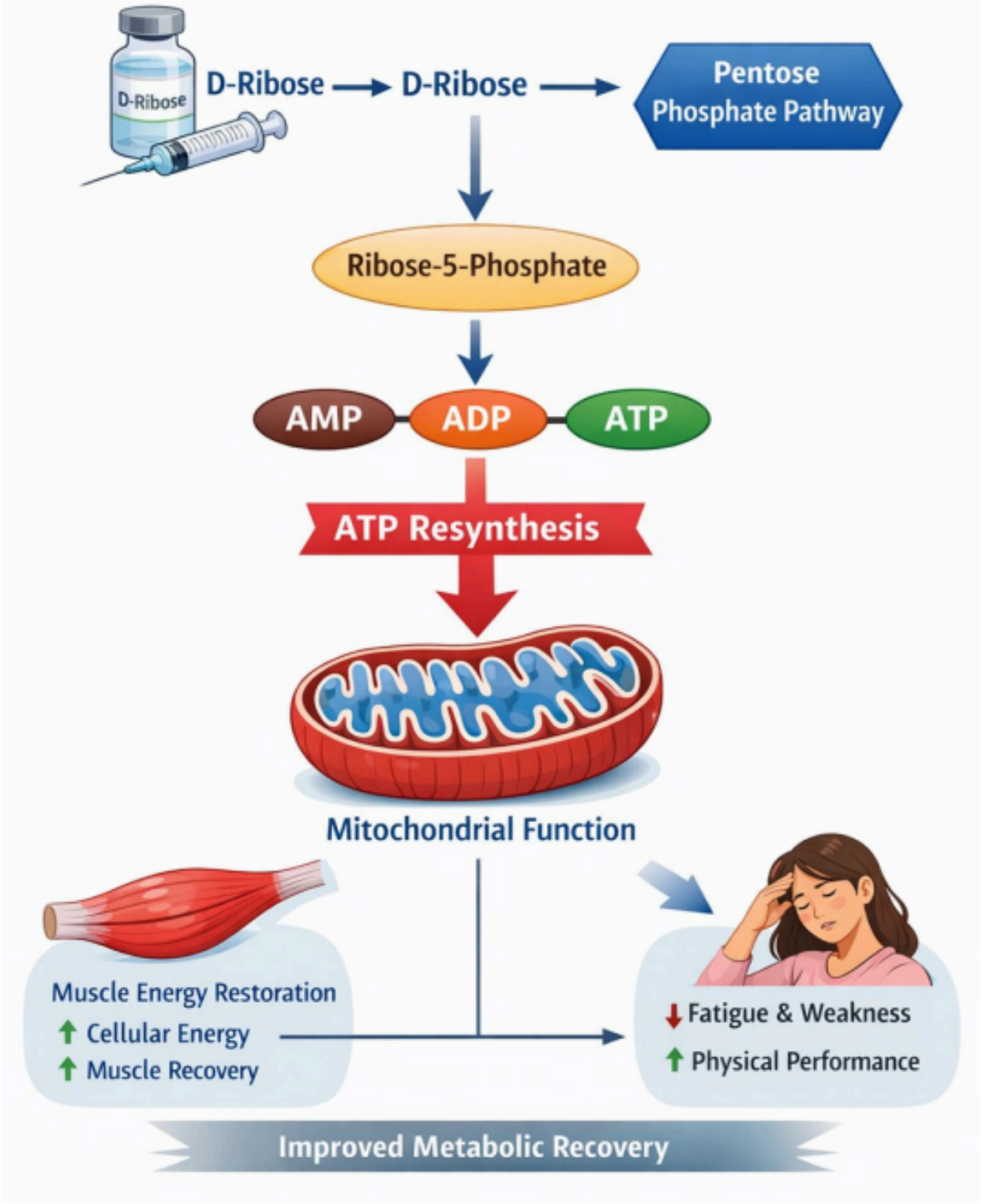
Blood glucose levels should be monitored, as D-ribose can induce a transient reduction in glucose levels (9).

5.1. Route Of Administration: Intramuscular With Systemic Action

When administered intramuscularly (IM), D-ribose exhibits systemic absorption because:

- Muscle tissue is highly vascularized
- It allows gradual absorption into the systemic circulation
- It partially avoids initial hepatic metabolism (when compared to the oral route)

However, it is important to highlight an essential scientific point: Most of the available literature refers to oral administration (6,7,9). Therefore, when used via IM injection, it is an application with a biochemical rationale extrapolated from the known pharmacodynamics of the molecule.



5.2. Other Clinical Applications Of D-ribose

In addition to the context of metabolic support in patients undergoing accelerated weight loss, D-ribose has been investigated in different medical areas, especially those associated with high levels of Cellular energy supply. The central physiological rationale is based on its structural participation in the synthesis of adenine

nucleotides, fundamental for the production of adenosine triphosphate (ATP), a molecule essential for cellular function (5).

In cardiology, D-ribose presents the most consistent body of evidence.

During ischemic events, significant ATP depletion occurs in the myocardium, whose recovery can be slow due to the limited availability of ribose-5-phosphate, an essential component for the synthesis of adenine nucleotides. Studies demonstrate that D-ribose supplementation can accelerate ATP resynthesis and improve parameters of ventricular function, particularly diastolic function, in patients with coronary artery disease and congestive heart failure (6,10). This effect is related to the optimization of the pentose phosphate pathway and the greater availability of substrate for myocardial energy regeneration. In the field of neurometabolic medicine, D-ribose has been studied primarily in conditions associated with chronic fatigue and fibromyalgia. A pilot study demonstrated significant improvement in energy levels, mental clarity, and quality of life in patients supplemented with D-ribose (7). Although the exact mechanisms are still under investigation, it is believed that the benefit is related to improved cellular bioenergetics and support for mitochondrial function, especially in tissues with high metabolic demand such as the central nervous system.

In sports medicine, D-ribose has been evaluated as a strategy for muscle recovery after intense exercise. ATP depletion during strenuous physical exertion can compromise performance and delay recovery. Evidence suggests that supplementation can accelerate

the replacement of adenine nucleotides in skeletal muscle, contributing to reduced fatigue and improved exercise tolerance (11).

Additionally, in integrative and functional medicine, D-ribose has been employed as support in conditions associated with mitochondrial dysfunction, post-infectious states, chronic metabolic stress, and postoperative recovery, based on the same principle of restoring cellular energy availability (5–7).

Despite the promising findings, it is important to emphasize that most of the available evidence refers to oral administration and that many studies have small sample sizes. Larger randomized clinical trials are still needed to consolidate formal therapeutic indications. However, the consistent biochemical rationale and preliminary results support the growing interest in the clinical application of D-ribose in different medical specialties.

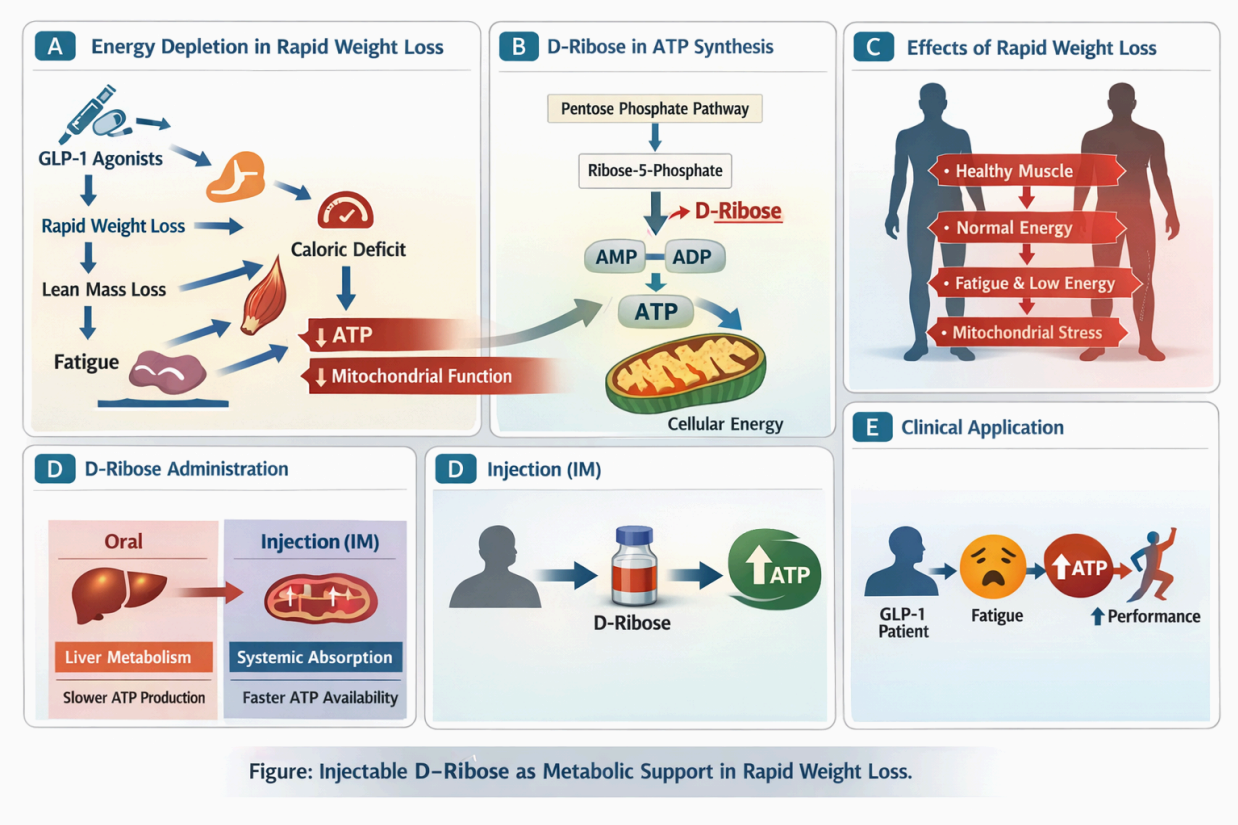


Figure: Injectable D-Ribose as Metabolic Support in Rapid Weight Loss.

A — Energy depletion with GLP-1; B — D-Ribose in ATP synthesis; C — Effects of rapid weight loss; D — Oral vs IM D-ribose; E — Clinical application model

6. DISCUSSION

The increasing use of GLP-1 receptor agonists in the treatment of obesity has transformed the clinical management of excess weight, promoting significant weight reductions and improvements in various metabolic markers. However, recent studies demonstrate that accelerated weight loss may be associated with a proportional reduction in lean mass, alterations in mitochondrial function, and metabolic adaptation characterized by decreased basal energy expenditure (1–4).

Muscle mass loss represents a relevant factor in this context, since muscle tissue constitutes an important metabolic reservoir and plays a fundamental role in energy homeostasis. Decreased lean mass can contribute to symptoms frequently reported by patients using incretin therapies, such as persistent fatigue, reduced muscle strength, and decreased physical performance.

In this scenario, strategies focused on cellular bioenergetic support have aroused increasing scientific interest. D-ribose presents a particularly relevant biochemical rationale, as it constitutes an essential structural component in the synthesis of adenine nucleotides, including ATP, ADP, and AMP. Under conditions of metabolic stress or energy depletion, the availability of ribose-5-phosphate can become a limiting factor for ATP resynthesis, prolonging the state of cellular energy deficit (5,6).

Experimental and clinical studies demonstrate that D-ribose supplementation can accelerate the replacement of adenine nucleotides in tissues with high energy demands, such as skeletal muscle and myocardium. This mechanism has been described

mainly in contexts of cardiac ischemia, chronic fatigue, and muscle recovery after intense exertion (6,7,11).

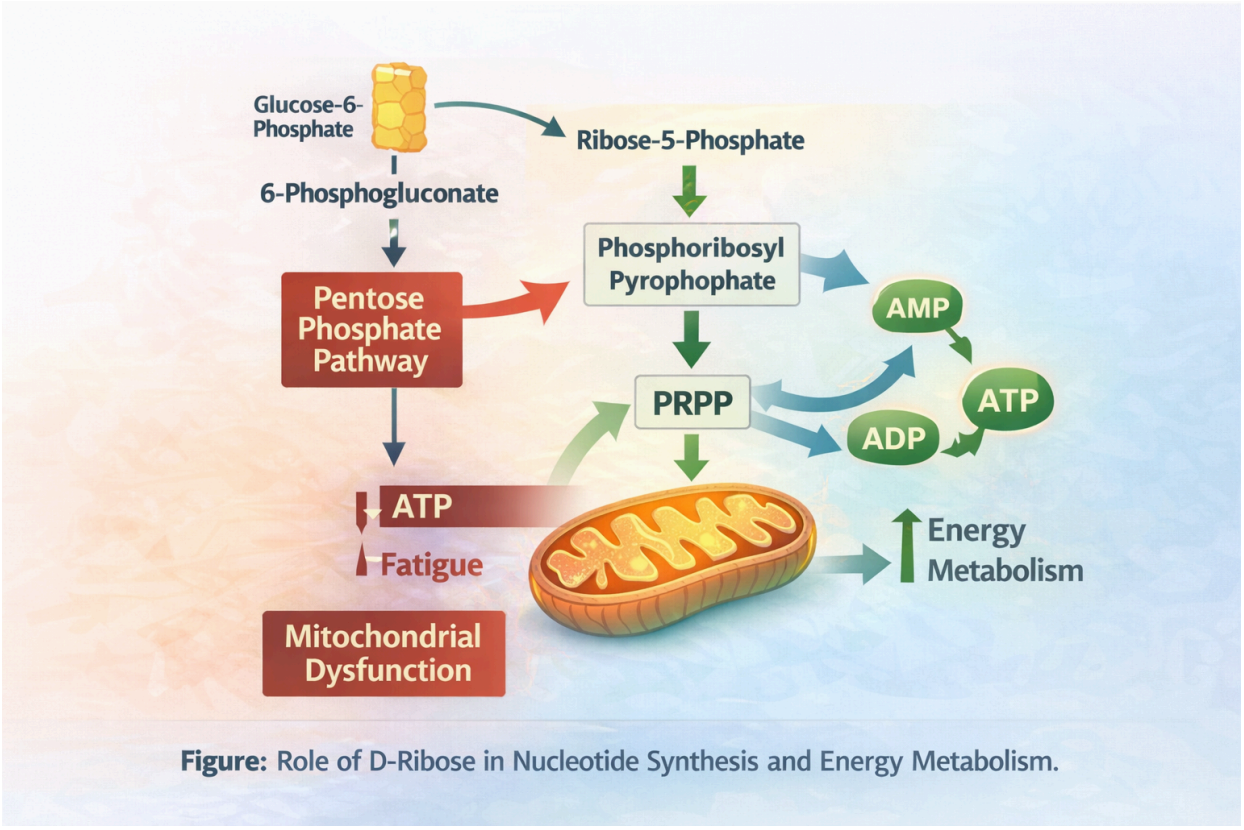


Figure: Role of D-Ribose in Nucleotide Synthesis and Energy Metabolism.

Although most of the available evidence involves oral supplementation, the hypothesis of using injectable D-ribose is based on the possibility of greater systemic bioavailability and a potentially faster metabolic response. From a pharmacokinetic point of view, intramuscular administration allows progressive absorption through highly vascularized muscle tissue, potentially favoring systemic distribution of the molecule.

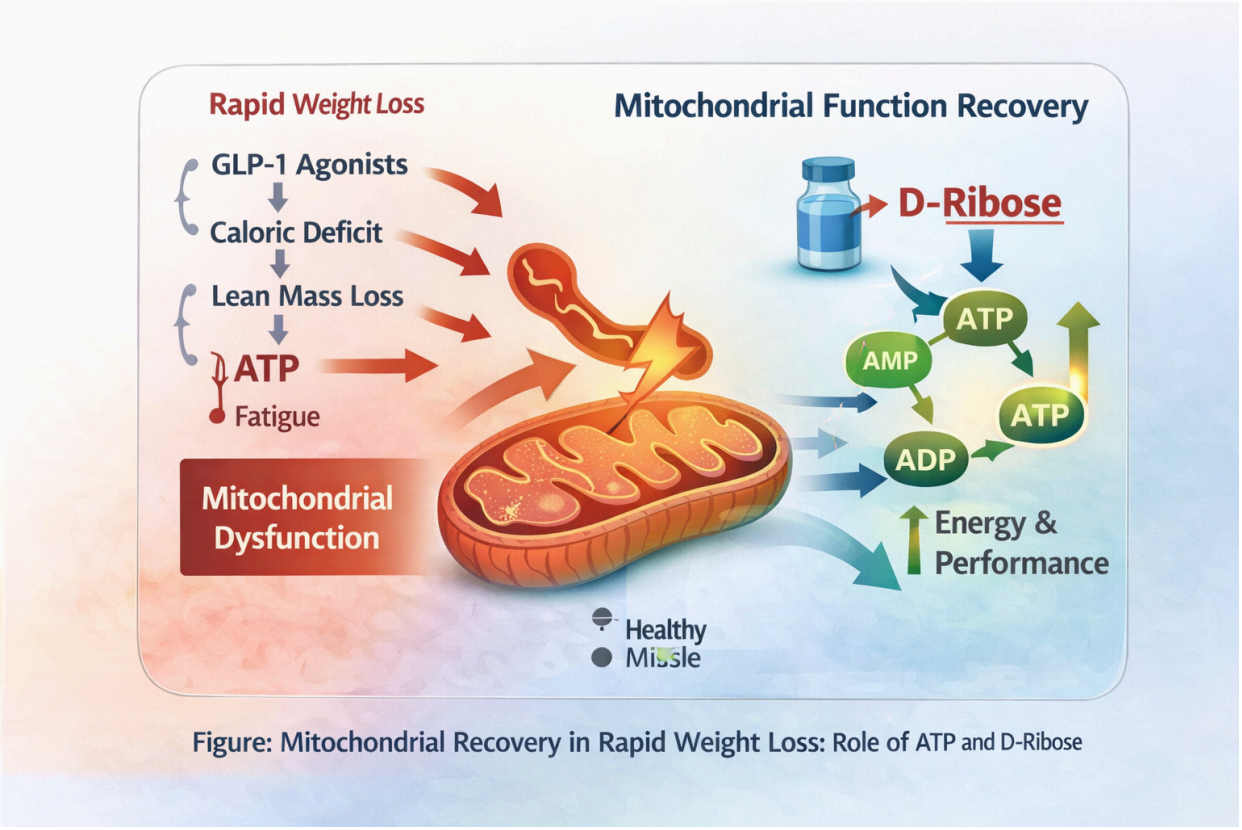


Figure: Mitochondrial Recovery in Rapid Weight Loss: Role of ATP and D-Ribose

7. CONCLUSION

The available evidence suggests that D-ribose presents a consistent biochemical rationale as a metabolic support strategy in conditions associated with cellular energy depletion.

In patients undergoing rapid weight loss induced by GLP-1 receptor agonists, D-ribose may represent a promising adjunctive approach to support mitochondrial function, improve energy metabolism and potentially mitigate symptoms of fatigue and reduced physical performance. However, controlled clinical trials are required to validate the efficacy and safety of injectable D-ribose in this specific clinical context.

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