Pantethine

Introduction

Pantethine is the stable disulfate form of pantetheine, the metabolic substrate that constitutes the active part of coenzyme A molecules (CoA) and acyl carrier proteins (ACP). Oral administration of pantethine has consistently shown an ability to favorably impact a variety of lipid risk factors in persons with hypercholesterolemia, arteriosclerosis, and diabetes. Pantethine administration has also been shown to favorably affect parameters associated with platelet lipid composition and cell membrane fluidity. Due to its role in the formation of CoA, pantethine might assist with detoxification of some xenobiotic compounds. Administration also appears to favorably impact adrenal cortex function. In several animal models, preliminary studies have indicated a protective effect against cataract formation.

Biochemistry

The reactive component of both CoA and ACP is not the pantothenic acid molecule, but the sulfhydryl (SH) group donated from cysteine. Although pantothenic acid is commonly known as vitamin B5, pantethine actually contains the SH molecule required for enzyme activity and provides a more metabolically active form of the vitamin.

Mechanism of Action

The metabolic activity of pantethine is probably due to its role in the synthesis of CoA and ACP. CoA is a cofactor in over 70 enzymatic pathways, including fatty acid oxidation, carbohydrate metabolism, pyruvate degradation, amino acid catabolism, heme synthesis, acetylcholine synthesis, and hepatic phase II detoxification acetylations. ACP is an essential component of the fatty acid synthase complex required for fatty acid elongation.
While the exact mechanism of action of pantethine in normalizing parameters associated with dyslipidemia is unknown, several explanations have been proposed. Some authors have suggested pantethine might be capable of directly modulating the action of several enzymes involved in cholesterol synthesis.1-3 The efficacy of pantethine in normalizing parameters of dyslipidemia might also be due to its ability to increase CoA levels. Theoretically, if pantethine enhances the formation of CoA, the additional CoA might then combine with free acetyl groups to form acetyl-CoA. The acetyl-CoA could then be directed into the TCA cycle or beta-oxidation at the expense of cholesterol formation.

Table 1. Pantethine’s reported impact on lipid parameters in patients with Frederickson’s type IIa, IIb, and IV dyslipidemia

<table>
<thead>
<tr>
<th>Type</th>
<th>Clinical Definition</th>
<th>Pantethine’s Impact</th>
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<tbody>
<tr>
<td>IIa</td>
<td>total cholesterol elevated&lt;br&gt;LDL elevated&lt;br&gt;triglyceride normal</td>
<td>decrease total cholesterol&lt;br&gt;decrease LDL-cholesterol&lt;br&gt;decrease VLDL-cholesterol&lt;br&gt;decrease triglyceride&lt;br&gt;decrease Apo-A&lt;br&gt;increase HDL-cholesterol&lt;br&gt;increase Apo-A</td>
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<tr>
<td>IIb</td>
<td>total cholesterol elevated&lt;br&gt;LDL elevated&lt;br&gt;VLDL elevated&lt;br&gt;triglyceride elevated</td>
<td>decrease total cholesterol&lt;br&gt;decrease LDL-cholesterol&lt;br&gt;decrease VLDL-cholesterol&lt;br&gt;decrease triglyceride&lt;br&gt;decrease Apo-B</td>
</tr>
<tr>
<td>IV</td>
<td>total cholesterol normal&lt;br&gt;VLDL elevated&lt;br&gt;triglyceride elevated</td>
<td>mixed results with total cholesterol&lt;br&gt;mixed results with LDL-cholesterol&lt;br&gt;decrease VLDL-cholesterol&lt;br&gt;decrease triglyceride&lt;br&gt;decrease Apo-B&lt;br&gt;mixed results with HDL-cholesterol&lt;br&gt;increase HDL-cholesterol&lt;br&gt;increase Apo-A</td>
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**Deficiency States and Symptoms**

A deficiency of pantethine is virtually unknown because of its widespread distribution in food.

**Clinical Applications**

*Hyperlipidemia*

Oral supplementation with pantethine typically results in a progressive decrease in total cholesterol, triglycerides, low density lipoprotein (LDL) cholesterol, and apolipoprotein B (Apo-B), and an increase in high density lipoprotein (HDL) cholesterol and apolipoprotein A (Apo-A); however, depending on the type of lipidemia, results might vary (Table 1).4-9

*Platelet Lipid Composition and Fluidity*

Pantethine administration has been shown to favorably affect parameters associated with platelet lipid composition and cell membrane fluidity.10,11 In diabetic patients, composition of platelets is characterized by a derangement in a wide variety of lipid concentrations and a higher microviscosity than in healthy platelets. Administration of pantethine to diabetics is reported to normalize these values to control levels, and result in a concomitant reduction in hyperaggregation.12,13

*Cataract Protection*

Pantethine administration has inhibited cataract formation in several animal models.14-16

*Detoxification*

Acetylation reactions utilizing acetyl-CoA are an important component of the phase II detoxification system. The compounds typically metabolized by acetylation reactions include aliphatic amines (such as histamine and mescaline), aromatic amines (such as sulfonamide), hydrazine and hydrazide, and certain amino acid metabolites (such as phenylethylamine). Because of its biochemical position as the most stable supplemental form of an immediate precursor to CoA, pantethine might be able to play an important role in the metabolism of some xenobiotic compounds.

*Adrenal Function*

Pantethine appears to exert a positive influence on some indicators of adrenal function. Administration of pantethine to 20 individuals with a variety of clinical conditions was reported to buffer the increase in 24-hour urinary 17-hydroxycorticosteroids and plasma 11-hydroxy-corticosteroids stimulated by a loading dose of adrenocorticotropic hormone.17
**Side Effects and Toxicity**

Although digestive disturbances have occasionally been reported in the literature, the majority of researchers have commented on the complete freedom from side effects and subjective complaints experienced by individuals taking pantethine. Doses as high as 10 grams per day in humans produced no toxic manifestations other than occasional diarrhea and minor gastrointestinal disturbances.\(^\text{18}\)

**Dosage**

The most common oral dosage used in the treatment of dyslipidemia has been 300 mg three times per day.

**References**