Chapter 12

PANTOTHENIC ACID (VITAMIN B₅), COENZYME A AND RELATED COMPOUNDS

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1 INTRODUCTION

Pantothenic acid (R- or D-(+)-N-(2,4-dihydroxy-3,3-dimethyl-1-oxobutyl)-β-alanine; for chemical formula, see Table 1) was first isolated in the 1930s from liver and found to be an essential growth factor for yeasts (Williams and co-workers, 1943). During this same period, it was also identified independently with the chick anti-dermatitis factor, the filtrate factor, the chick anti-pellagra factor and an essential growth factor for lactic acid bacteria. Later these activities were shown to be identical with pantothenic acid. Since the factor could be obtained from a variety of plants and animal tissues, it was designated pantothenic acid, meaning ‘from everywhere’ by Williams. The compound is also referred to as vitamin B₅. It was independently synthesized by two groups in 1940.

Pantothenic acid occurs in all types of living organisms in a free form and in conjugated forms such as coenzyme A, pantetheine (Lactobacillus bulgaricus factor) and 4'-phosphopantetheine (Acetobacter suboxydans factor) (see Table 1). The coenzyme form of the vitamin is coenzyme A. It was discovered as an essential cofactor for the acetylation of sulfonamide in the liver and the acetylation of choline in the brain by Lipmann and co-workers (1953). Since that time, it has been identified with ‘active acetate’ and has been found to be essential for a variety of biochemical transacylation reactions. 4'-Phosphopantetheine is also a coenzyme form of pantothenic acid. It functions as a prosthetic group of the acyl carrier protein of fatty acid synthetase, citrate cleaving enzyme and enzymes involved in the synthesis of peptide antibiotics.

These early studies have been reviewed by several authors (Williams, 1943; Lipmann, 1953; Wagner & Folkers, 1964; Vagelos 1973; Vandamme, 1981; Kleinkauf & von Döhren, 1983).

2 CHEMISTRY

Pantothenic acid can be obtained as a colorless, viscous oil by drying under high vacuum in P₂O₅. It is an acid and has a marked tendency to absorb water.
### Table 1

Pantothenic Acid and its Naturally-Occurring Derivatives

<table>
<thead>
<tr>
<th>Derivative</th>
<th>Structure</th>
<th>Properties</th>
<th>Reference</th>
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| **d-Pantothenic acid**                          | \[
CH_3OH
\]
\[
\text{HOCH}_2\text{C--CHCONH(CH}_2\text{)}_2\text{COOH}
\]
\[
\text{CH}_3
\]
\[
\text{C}_9\text{H}_{17}\text{NO}_5 \quad \text{MW: 219.23}
\] | Unstable, viscous oil. Extremely hydroscopic, easily decomposed by acids, bases, heat. Soluble in water, ethyl acetate, dioxane, glacial acetic acid; moderately soluble in ether, amyl alcohol; insoluble in benzene, chloroform. Solutions are stable between pH 5 and 7. $\left[\alpha\right]_{D}^{25} + 37.5^\circ$. Stiller et al. (1940). |                        |
| **Calcium d-pantothenate**                      | \[
\left(\begin{array}{c}
\text{CH}_3\text{OH} \\
\text{HOCH}_2\text{C--CHCONH(CH}_2\text{)}_2\text{COO} \\
\text{CH}_3
\end{array}\right)\text{Ca}
\]
\[
\text{C}_{16}\text{H}_{32}\text{CaN}_2\text{O}_{10} \quad \text{MW: 476.53}
\] | White needles. Moderately hygroscopic. Soluble in water, glycerol; slightly soluble in alcohol, acetone; insoluble in ether, benzene, chloroform. Decomposed by bases. Solutions are stable between pH 5 and 7. mp 195–196°C (dec); $\left[\alpha\right]_{D}^{25} + 28.2^\circ (c = 5)$. |                        |
| **Sodium d-pantothenate**                       | \[
\text{CH}_3\text{OH}
\]
\[
\text{HOCH}_2\text{C--CHCONH(CH}_2\text{)}_2\text{COONa}
\]
\[
\text{CH}_3
\]
\[
\text{C}_6\text{H}_{16}\text{NaNO}_3 \quad \text{MW: 241.21}
\] | White, hygroscopic crystals. Decomposed by acids and bases. Solutions are stable between pH 5 and 7. mp 122–124°C; $\left[\alpha\right]_{D}^{25} + 27.1^\circ (c = 2)$. For solubility, see calcium pantothenate |                        |
| **4'-Phosphopantothenic acid (Ba salt)**        | \[
\text{O}
\]
\[
\text{CH}_3\text{OH}
\]
\[
\text{HO--P--OCH}_2\text{C--CHCONH(CH}_2\text{)}_2\text{COOH}
\]
\[
\text{OH}
\]
\[
\text{CH}_3
\]
\[
\text{C}_6\text{H}_{16}\text{NO}_{8}\text{P} \quad \text{MW: 313.27}
\] | Soluble in water; insoluble in ethanol. Unstable to bases. Free acid is unstable. $\left[\alpha\right]_{D}^{25} + 9.0^\circ (c = 3.3)$. King & Strong (1951); Okada et al. (1967). |                        |