Chem 109 C
Bioorganic Compounds

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Overview and Introduction:

• enzymes are biological catalysts
• many enzymes are inactive without cofactors
• cofactors are 1) metal ions or 2) coenzymes
• coenzymes - organic molecules, derived from vitamins
## Chapter 23: Coenzymes

<table>
<thead>
<tr>
<th>Coenzyme</th>
<th>Vitamin</th>
<th>Reaction catalyzed</th>
</tr>
</thead>
<tbody>
<tr>
<td>NAD(^+), NADP(^+) / NADH, NADPH</td>
<td>niacin, nicotinamide</td>
<td>oxidation/reduction of alcohols</td>
</tr>
<tr>
<td>FAD / FADH(_2)</td>
<td>riboflavin (B2)</td>
<td>oxidation/reduction, other</td>
</tr>
<tr>
<td>Thiamine pyrophosphate TPP</td>
<td>thiamine (B1)</td>
<td>acyl group transfer</td>
</tr>
<tr>
<td>Lipoic acid /dihydropipoic acid</td>
<td>lipoic acid</td>
<td>oxidation/reduction</td>
</tr>
<tr>
<td>Coenzyme A, CoASH</td>
<td>pantothenic acid (B5)</td>
<td>acyl group transfer</td>
</tr>
<tr>
<td>Biotin</td>
<td>biotin (B7)</td>
<td>carboxylation</td>
</tr>
<tr>
<td>Pyridoxal phosphate PLP</td>
<td>pyridoxin (B6)</td>
<td>6 amino acid reactions</td>
</tr>
<tr>
<td>Coenzyme B(_{12})</td>
<td>vitamin B12</td>
<td>isomerization</td>
</tr>
<tr>
<td>Tetrahydrofolic acid, THF</td>
<td>folic acid</td>
<td>one-carbon transfer</td>
</tr>
<tr>
<td>Vitamin KH(_2)</td>
<td>vitamin K</td>
<td>carboxylation</td>
</tr>
</tbody>
</table>

Vitamin KH\(_2\) is not soluble in water

see Table 23.1 in Chapter 23
Chapter 23: Coenzymes

Factors characterizing a coenzyme:

- Chemical structure
- Associated vitamin
- Type of reaction catalyzed
- Reaction mechanism
- Dietary source
- Associated disease
NAD$^+$ is a catabolic enzyme

- [NAD$^+$]/[NADH] $\sim$ 1000 : 1 (cytosol)
  - [0.3 mM]

- catalyze redox (oxidation-reduction) reactions
- source of nicotinamide: meats, vegetables, peanuts etc.
- deficiency disease: pellagra (skin lesions, sensitivity to light etc.)
NAD$^+$-NADH, NADP$^+$-NADPH

- NADP$^+$ is an anabolic enzyme
- $[\text{NADP}^+] / [\text{NADPH}] \sim 1 : 100$

- catalyze redox (oxidation-reduction) reactions
- source of nicotinamidem: meats, vegetables, peanuts etc.
- deficiency disease: pellagra (skin lesions, sensitivity to light etc.)
Oxidation with NAD$^+$ (or NADP$^+$):

$$
\begin{align*}
\text{OH} & \\
R & \quad R' & + & \text{NAD}^+ & + & :B^- & \xrightarrow{\text{dehydrogenase}} & \text{R} - \text{R}' & + & \text{NADH} & + & H-B
\end{align*}
$$

General mechanism of oxidation:
**Oxidation with NAD\(^+\) (or NADP\(^+\)), examples:**

\[
\begin{align*}
\text{malate} & \quad + \quad \text{NAD}^+ \quad + \quad :\text{B}^- \\
\rightarrow & \quad \text{oxaloacetate} \quad + \quad \text{NADH} \quad + \quad \text{H-B}
\end{align*}
\]

- important reaction in the citric acid cycle
Reduction with NADH (or NADPH), a reverse process:

\[ \text{R}R' + \text{NADH} + \text{H-B} \xrightarrow{\text{dehydrogenase}} \text{R}R' + \text{NAD}^+ + :\text{B}^- \]

General mechanism of reduction:

- NADH and NADPH are $\text{H}^-$ donors
Reduction with NADPH (or NADH), examples:

\[
\text{\begin{align*}
\text{O} \quad \text{NH}_3^+ & \quad + \quad \text{NADPH} & \quad + \quad \text{H-B} & \quad \overset{\text{homoserine dehydrogenase}}{\underset{}{\rightarrow}} \quad \text{HO} \quad \text{NH}_3^+ \\
\text{C} \quad \text{O} \quad \text{O} & \quad + \quad \text{NADP}^+ & \quad + \quad :B^- & \quad \text{C} \quad \text{O} \quad \text{O} \quad \text{N} \quad \text{H}_3^+ \\
\end{align*}}
\]

$\beta$-aspartate semialdehyde

homoserine

- important reaction in an anabolic pathway
Oxidation - a more complex example:

D-glyceraldehyde-3-phosphate + NAD^+ + H^+ \rightarrow \text{glyceraldehyde-3-phosphate dehydrogenase} \rightarrow \text{D-1,3-diphosphoglycerate} + \text{NADH} + \text{H}^+
D-glyceraldehyde-3-phosphate + NAD⁺ → D-1,3-diphosphoglycerate + NADH + H⁺
\[
\text{glyceraldehyde-3-phosphate dehydrogenase}
\]

\[
\begin{align*}
\text{D-glyceraldehyde-3-phosphate} & \quad \text{+ NAD}^+ & \quad \text{+ O}\text{O}_3^{2-} \quad \text{+ NADH} & \quad \text{+ H}^+ \\
\rightarrow & & \phantom{\text{D-glyceraldehyde-3-phosphate} & \quad \text{+ NAD}^+ & \quad \text{+ O}\text{O}_3^{2-} \quad \text{+ NADH} & \quad \text{+ H}^+ }
\end{align*}
\]

D-1,3-diphosphoglycerate
D-glyceraldehyde-3-phosphate + NAD+ \xrightarrow{\text{dehydrogenase}} \text{D-1,3-diphosphoglycerate} + NADH + H^+
\[
\text{glyceraldehyde-3-phosphate dehydrogenase}
\]

D-glyceraldehyde-3-phosphate ➔ D-1,3-diphosphoglycerate

\[
\text{substrate} \quad \text{GAP} \quad \text{NAD}^+ \quad \text{NADH} \quad H^+
\]

\[
\text{NAD}^+ \quad \text{NADP}^+
\]
\[
\text{glyceraldehyde-3-phosphate dehydrogenase}
\]

\[
\begin{align*}
D\text{-glyceraldehyde-3-phosphate} & \rightarrow \text{D-1,3-diphosphoglycerate} \\
\text{(substrate)} & \rightarrow \text{(GAP)} \\
\end{align*}
\]
The reaction is catalyzed by the enzyme glyceraldehyde-3-phosphate dehydrogenase. It involves the conversion of D-glyceraldehyde-3-phosphate to D-1,3-diphosphoglycerate.

D-glyceraldehyde-3-phosphate + NAD⁺ → D-1,3-diphosphoglycerate + NADH + H⁺
Stereochemistry of enzymatic reactions: enzyme reactions are stereospecific

$\text{CH}_3\text{CH(OH)} + \text{NAD}^+ \rightarrow \text{CH}_3\text{CO} + \text{NADH}_a + \text{H}^+$

$\text{alcohol dehydrogenase}$

Reduction of carbonyl group

$R'\text{R} \rightarrow R'\text{O}H$