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 / FADH₂</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 B₁₂</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 KH₂</td>
<td>vitamin K</td>
<td>carboxylation</td>
</tr>
</tbody>
</table>

Vitamin KH₂ 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⁺-NADH, NADP⁺-NADPH

- NAD⁺ is a catabolic enzyme
- [NAD⁺]/[NADH] ~ 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
- [NADP$^+$]/[NADPH] ~ 1 : 100

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

$$R'\, R' + NAD^+ + :B^- \xrightarrow{dehydrogenase} R'\, R' + NADH + H-B$$

General mechanism of oxidation:

[Diagram depicting the reaction steps involving NAD$^+$, showing the oxidation of an alcohol to a carbonyl group and the involvement of a dehydrogenase enzyme.]
Oxidation with NAD$^+$ (or NADP$^+$), examples:

$$\text{malate} + \text{NAD}^+ + \text{H}^+ \rightarrow \text{oxaloacetate} + \text{NADH} + \text{H}^+$$

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

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

General mechanism of reduction:

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

\[
\begin{align*}
\text{O} & \quad \text{NH}_3^+ \\
\text{COO}^- & \quad + \quad \text{NADPH} & \quad + \quad \text{H-B} \quad \xrightarrow{\text{homoserine dehydrogenase}} \quad \text{HO} & \quad \text{NH}_3^+ \\
\beta\text{-aspartate semialdehyde} & \quad \rightarrow & \quad \text{COO}^- & \quad + \quad \text{NADP}^+ & \quad + \quad :B^-
\end{align*}
\]

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

\[
\begin{align*}
\text{D-glyceraldehyde-3-phosphate} & \quad \text{glyceraldehyde-3-phosphate dehydrogenase} \quad \text{D-1,3-diphosphoglycerate} \\
\text{D-glyceraldehyde-3-phosphate} & \quad + \quad \text{NAD}^+ \quad + \quad \text{NAD}^+ \quad + \quad \text{H}^+ \\
\end{align*}
\]
\[
\text{D-glyceraldehyde-3-phosphate} + \text{NAD}^+ \rightarrow \text{D-1,3-diphosphoglycerate} + \text{NADH} + \text{H}^+
\]
D-glyceraldehyde-3-phosphate + NAD$^+$ + HPO$_4^{2-}$ → glyceraldehyde-3-phosphate dehydrogenase → D-1,3-diphosphoglycerate + NADH + H$^+$
$\text{glyceraldehyde-3-phosphate dehydrogenase}$

$\text{D-glyceraldehyde-3-phosphate} + \text{NAD}^+ \rightarrow \text{D-1,3-diphosphoglycerate} + \text{NADH} + \text{H}^+$
NAD$^+$, NADP$^+$

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

\[
\text{glyceraldehyde-3-phosphate dehydrogenase}
\]
\[
\text{glyceraldehyde-3-phosphate dehydrogenase}
\]

\[
\begin{align*}
\text{D-glyceraldehyde-3-phosphate} & \quad \quad + \quad \quad \text{NAD}^+ \quad + \quad \quad \text{O}-\text{P} \quad \quad \rightarrow \\
\text{D-1,3-diphosphoglycerate} & \quad \quad + \quad \quad \text{NADH} \quad + \quad \quad \text{H}^+
\end{align*}
\]
Stereochemistry of enzymatic reactions: enzyme reactions are stereospecific

\[
\begin{align*}
\text{alcohol dehydrogenase} & \quad \text{H-B} \\
\text{reduction of carbonyl group} & \quad \text{:B}^- \\
\end{align*}
\]