BCMB 3100 -
Introduction to Coenzymes & Vitamins

- Cofactors
- Essential ions
- Coenzymes
- Cosubstrates
- Prosthetic groups
- Coenzymes structure/function/active group
- Vitamins

Coenzymes

Some enzymes require ________ for activity
(1) _______________ (mostly metal ions)
(2) _______________ (organic compounds)

Apoenzyme + Cofactor → Holoenzyme
(protein only) (active)
(inactive)

Coenzymes

- Coenzymes act as group-transfer reagents
- Hydrogen, electrons, or other groups can be transferred
- Two types of coenzymes:
  - ____________________
  - ____________________

Metal ions have diverse functions in enzymes

- Participate in ______________, generally tightly bound to enzyme, function e.g. as electrophilic catalysts or aid in generating a nucleophile

- Participate in ______________ at the active site
Types of cofactors

Coenzymes

**Ca**
**K**
**Mg**
**Mn**
*ATP*
*SAM*
*UDP-sugar*
*NAD*/NADP*
*tetrahydrofolate*
*CoA*
*ubiquinone*
*protein coenzymes*

See:
* pg. 126 for info on metal ions in catalysis
* Table 13.2 (page 261) as summary table for coenzymes

The pyruvate dehydrogenase complex requires 4 coenzymes

<table>
<thead>
<tr>
<th>Coenzyme Classification</th>
</tr>
</thead>
<tbody>
<tr>
<td>* There are two classes of coenzymes</td>
</tr>
<tr>
<td>(1) ____________ are altered during the reaction and regenerated by another enzyme</td>
</tr>
<tr>
<td>(2) ____________ remain bound to the enzyme during the reaction, and may be covalently or tightly bound to enzyme</td>
</tr>
</tbody>
</table>

Table 6.2 Enzyme cofactors

<table>
<thead>
<tr>
<th>Coenzyme*</th>
<th>Enzyme†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thiamine pyrophosphate (TPP)</td>
<td>Pyruvate dehydrogenase</td>
</tr>
<tr>
<td>Flavin adenine dinucleotide (FAD)</td>
<td>Lactate dehydrogenase</td>
</tr>
<tr>
<td>Nicotinamide adenine dinucleotide (NAD)</td>
<td>Glucose-6-phosphate dehydrogenase</td>
</tr>
<tr>
<td>Pyridoxal phosphate (PLP)</td>
<td>Methylmalonyl-CoA mutase</td>
</tr>
<tr>
<td>Coenzyme A (CoA)</td>
<td>Acetyl-CoA carboxylase</td>
</tr>
<tr>
<td>Biotin</td>
<td>Pyruvate carboxylase</td>
</tr>
<tr>
<td>Lipoic acid/lipoamide</td>
<td>Thioredoxin reductase</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Metal</th>
<th>Enzyme†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zn††</td>
<td>Carbonic anhydrase</td>
</tr>
<tr>
<td>Mg‖</td>
<td>Leucine aminopeptidase</td>
</tr>
<tr>
<td>Mo</td>
<td>Nitrosomonas</td>
</tr>
<tr>
<td>Se</td>
<td>Glutathione peroxidase</td>
</tr>
<tr>
<td>B&lt;sup&gt;12&lt;/sup&gt;</td>
<td>Spermidine synthase</td>
</tr>
<tr>
<td>K&lt;sup&gt;+&lt;/sup&gt;</td>
<td>Acetyl-CoA thiolase</td>
</tr>
</tbody>
</table>

*The enzymes listed are examples of enzymes that employ the indicated cofactors.
†When derived from vitamins, coenzymes are either tightly or loosely bound to the enzyme.
‡Omitting the suffixes, the molecules are referred to as thiamine, FAD, NAD, PLP, and CoA, respectively.

See: http://www.nd.edu/~aseriann/pyrde.html
**S-Adenosylmethionine (SAM)**

SAM is the donor of methyl groups for most biosynthetic reactions.

\[
\text{S-Adenosylmethionine} + X \rightarrow \text{S-Adenosylhomocysteine} + X-\text{CH}_3
\]

Example: SAM donates the methyl group for the synthesis of the hormone epinephrine from norepinephrine.

**UDP-sugar**: activated form of sugars used as substrate in many biosynthetic reactions.

**Nucleotide-sugars are cosubstrates in many glycosylation reactions**

**A third example of a cosubstrate coenzyme**

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*Fig. 15.3*
Some coenzymes require vitamins as part of their structure

__________: organic substance required in trace amounts for a number of essential biochemical reactions

Not all vitamins are part of coenzymes; only some are

Some vitamins are ____________

• Four lipid vitamins: A, D, E, K
• All contain rings and long, aliphatic side chains
• All are highly hydrophobic
• The lipid vitamins differ widely in their functions

Vitamin-Derived Coenzymes

• **Vitamins**: required for synthesis of some coenzymes, must be obtained from nutrients
• Animals rely on plants, meat, & microorganisms for vitamin sources
• Most vitamins must be enzymatically transformed to make the coenzyme (e.g. some water soluble vitamins)
• BE SURE TO LEARN WHICH VITAMINS ARE PART OF WHICH COENZYMES (Tables 15.2 & 15.3)
### Vitamins, nutritional deficiency diseases
(see Table 15.3 and Appendix D)

<table>
<thead>
<tr>
<th>Vitamin</th>
<th>Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ascorbate (C)</td>
<td>Scurvy</td>
</tr>
<tr>
<td>Nicotinic acid (B₃)</td>
<td>Pellagra</td>
</tr>
<tr>
<td>Riboflavin (B₂)</td>
<td>Growth retardation</td>
</tr>
<tr>
<td>Pantothenate (B₅)</td>
<td>Dermatitis in chickens</td>
</tr>
<tr>
<td>Thiamine (B₁)</td>
<td>Beriberi</td>
</tr>
<tr>
<td>Pyridoxal (B₆)</td>
<td>Dermatitis in rats</td>
</tr>
<tr>
<td>Biotin</td>
<td>Dermatitis in humans</td>
</tr>
<tr>
<td>Folate</td>
<td>Anemia, spina bifida</td>
</tr>
<tr>
<td>Cobalamin (B₁₂)</td>
<td>Pernicious anemia</td>
</tr>
</tbody>
</table>

### Vitamin C: a vitamin but not a coenzyme

- A reducing reagent for hydroxylation of collagen
- Deficiency leads to the disease scurvy
- Most animals (not primates) can synthesize Vit C

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**Group Activity on Coenzymes**

Be sure to read through “Hints for learning coenzymes” as you prepare and teach your coenzymes to your group.

Be sure to work in your groups to learn the co-enzymes over the next week.
Types of cofactors

<table>
<thead>
<tr>
<th>Coenzymes</th>
<th>Metal ions of metalloenzymes (tightly bound)</th>
<th>Covalent groups (tightly bound)</th>
<th>Prosthetic groups (tightly bound)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ATP</td>
<td>Ca++</td>
<td>*ATP</td>
<td>*FMN/FAD</td>
</tr>
<tr>
<td>SAM</td>
<td>K+</td>
<td>*SAM</td>
<td>*TPP</td>
</tr>
<tr>
<td>NAD+/NADP+</td>
<td>Mg++</td>
<td><em>NAD/NADP</em></td>
<td>*PLP</td>
</tr>
<tr>
<td>tetrahydrofolate</td>
<td>Fe-S center</td>
<td><em>tetrahydrofolate</em></td>
<td><em>Biotin</em></td>
</tr>
<tr>
<td>CoA</td>
<td>Mn++</td>
<td>*CoA</td>
<td>*adenosyl/methyl-cobalamin</td>
</tr>
<tr>
<td>ubiquinone</td>
<td>copper</td>
<td>*ubiquinone</td>
<td>*Lipoic acid/</td>
</tr>
<tr>
<td>protein coenzymes</td>
<td>zinc</td>
<td>*protein coenzymes</td>
<td>lipamide</td>
</tr>
</tbody>
</table>

See: *pg. 126 for info on metal ions in catalysis
*Table 15.2 as summary table for coenzymes

**ATP may also donate pyrophosphoryl and adenosyl groups**

**Fig. 15-12a**

**NOTE:** Electron carrier in many oxidation reduction reactions; used for reactions in pathways that lead to generation of ATP
Nicotinamide adenine dinucleotide phosphate

NOTE: Electron donor in most reductive biosynthesis reactions

Fig. 15.15

Flavine adenine dinucleotide

Example of reduced substrate

Example of oxidized product

Fig. 15.13

 Pg. 258
Fig. 15.17

Coenzyme A (carrying an acetyl group during a reaction)

Fig. 15.18

Pyridoxal phosphate

See pg. 545
Group Activity on Coenzymes

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