

# Vitamins & Cofactors

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## Vitamins & Cofactors

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### Vitamins

- Definition: essential nutrients required in the diet
- Different vitamins for different species
  - e.g., for rats & mice ascorbate is not a vitamin
  - E. coli* do not have any vitamins
- Vitamins are classified as water soluble or fat soluble

### Cofactors/Coenzymes

- Definition: low  $M_r$  molecules that act as carriers or give special functionality to enzymes
- Many coenzymes have vitamin molecules as their basis

Need to know: name, abbreviation, recognize structure, role in chemistry

# Vitamins & Cofactors

## Vitamins and Coenzymes

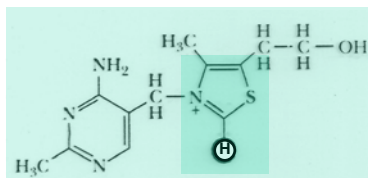
Vitamin	Coenzyme Form	Reaction mediated	Human Deficiency Disease
<b>Water-Soluble</b>			
① Thiamine (vitamin B <sub>1</sub> )	Thiamine pyrophosphate	Acyl-group transfer	Beriberi
② Niacin (nicotinic acid)	Nicotinamide adenine dinucleotide (NAD <sup>+</sup> ) Nicotinamide adenine dinucleotide phosphate (NADP <sup>+</sup> )	Re-dox	Pellagra
③ Riboflavin (vitamin B <sub>2</sub> )	Flavin adenine dinucleotide (FAD) Flavin mononucleotide (FMN)	Re-dox	–
④ Pantothenic acid	Coenzyme A	Acyl-group transfer	–
⑤ Pyridoxal, pyridoxine, pyridoxamine (vitamin B <sub>6</sub> )	Pyridoxal phosphate	Amino-group transfer	dermatitis
⑥ Cobalamin (vitamin B <sub>12</sub> )	5'-Deoxyadenosylcobalamin Methylcobalamin	Alkylation	Pernicious anemia
⑦ Biotin	Biotin-lysine complexes (biocytin)	Carboxylation	–
⑧ Lipoic acid	Lipoyl-lysine complexes (lipoamide)	Acyl-group transfer	–
⑨ Folic acid	Tetrahydrofolate	C1-group transfer	Megaloblastic anemia
⑩ Ascorbic acid (vitamin C)	Ascorbate	Re-dox	Scurvy
<b>Fat-soluble</b>			
① Retinol (vitamin A)	Retinal		Night blindness
② Ergocalciferol (vitamin D <sub>2</sub> )			
③ Cholecalciferol (vitamin D <sub>3</sub> )			Rickets
③ α-Tocopherol (vitamin E)			–
④ Vitamin K			Hemorrhage

# Vitamins & Cofactors

## ① Vitamin B<sub>1</sub>

Acyl-group transfer

Vitamin



Thiamine (vitamin B<sub>1</sub>)

Thiazole ring

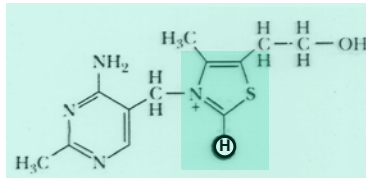
In 1911, Casimir Funk realized that this “amine” was “vital” for life. He coined the term “vital-amine,” which eventually was shortened to the word, “vitamin.”

# Vitamins & Cofactors

## ① Vitamin B<sub>1</sub>

Acyl-group transfer

Vitamin

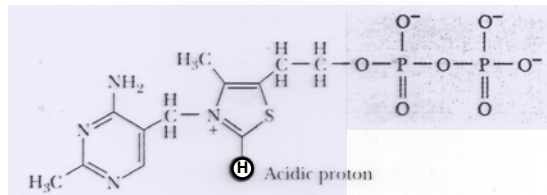


Thiazole ring

Thiamine (vitamin B<sub>1</sub>)

In 1911, Casimir Funk realized that this “amine” was “vital” for life. He coined the term “vital-amine,” which eventually was shortened to the word, “vitamin.”

Coenzyme

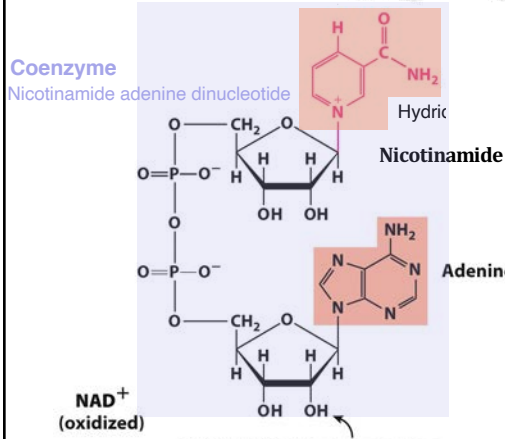
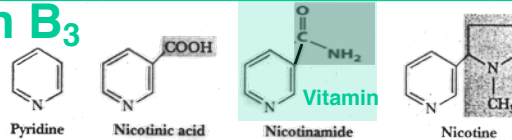


Thiamine pyrophosphate (TPP)

# Vitamins & Cofactors

## ② Vitamin B<sub>3</sub> (aka Niacin)

Re-dox



NAD<sup>+</sup>  
(oxidized)

In NAD<sup>+</sup> this hydroxyl group is esterified with phosphate.

- These are commonly called pyridine nucleotides.
- They **can dissociate** from the enzyme after the reaction.
- In a typical biological oxidation reaction, **hydride** from an alcohol is transferred to NAD<sup>+</sup>, giving NADH.
- Renamed **niacin** for **nicotinic acid** and **vitamin**

# Vitamins & Cofactors

## ② Vitamin B<sub>3</sub> (aka Niacin)

Pyridine      Nicotinic acid      Nicotinamide      Nicotine

Re-dox

Coenzyme  
Nicotinamide adenine dinucleotide

NAD<sup>+</sup> (oxidized)

Nicotinamide

Adenine

In NAD<sup>+</sup> this hydroxyl group is esterified with phosphate.

Hydride (H<sup>-</sup>)

NADH (reduced)

Pro-S

Pro-R

• These are commonly called pyridine nucleotides.

• They can dissociate from the enzyme after the reaction.

• In a typical biological oxidation reaction, hydride from an alcohol is transferred to NAD<sup>+</sup>, giving NADH.

• Renamed **niacin** for **nicotinic acid** and **vitamin**

# Vitamins & Cofactors

## ③ Vitamin B<sub>2</sub> (aka riboflavin)

Coenzymes

Re-dox

• Flavin Cofactors Allow Single Electron Transfers

• Permits the use of molecular oxygen as an ultimate electron acceptor

- flavin-dependent oxidases

• Flavin cofactors are **tightly bound** to proteins.

λ<sub>max</sub> = 570 nm

λ<sub>max</sub> = 450 nm

Vitamin

Riboflavin

D-Ribitol

Isolone Ring

# Vitamins & Cofactors

3

## Vitamin B<sub>2</sub> (aka riboflavin)

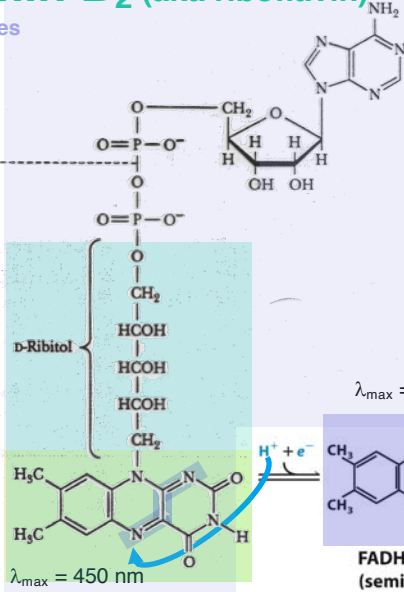
Coenzymes

Flavin adenine dinucleotide, FAD

Flavin mononucleotide, FMN

Riboflavin

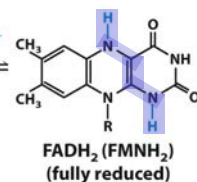
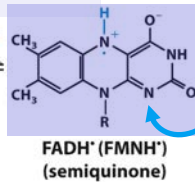
D-Ribitol



Re-dox

- Flavin Cofactors Allow Single Electron Transfers
- Permits the use of molecular oxygen as an ultimate electron acceptor
  - flavin-dependent oxidases
- Flavin cofactors are **tightly bound** to proteins.

$\lambda_{max} = 570 \text{ nm}$



# Vitamins & Cofactors

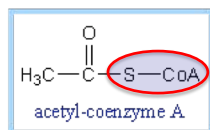
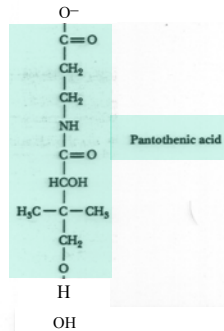
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## Pantothenic acid

Vitamin

Acyl-group transfer

Coenzyme A



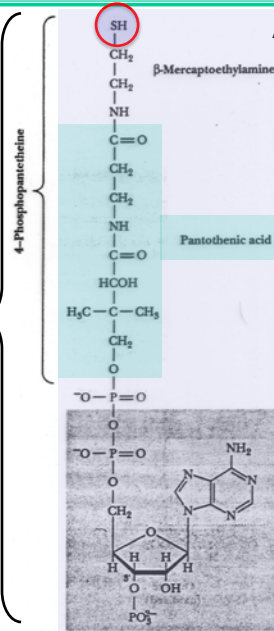
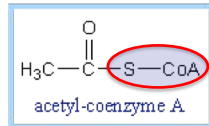
# Vitamins & Cofactors

## ④ Pantothenic acid

Vitamin

Acyl-group transfer

Coenzyme A

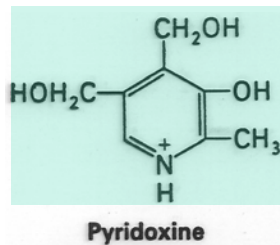


# Vitamins & Cofactors

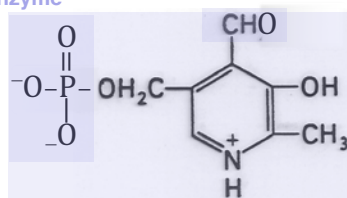
## ⑤ Vitamin B<sub>6</sub>

Vitamin

Amino-group transfer



Coenzyme

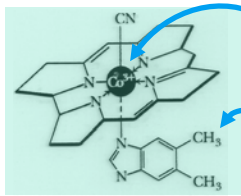


# Vitamins & Cofactors

## ⑥ Vitamin B<sub>12</sub>

Alkylation

Vitamin

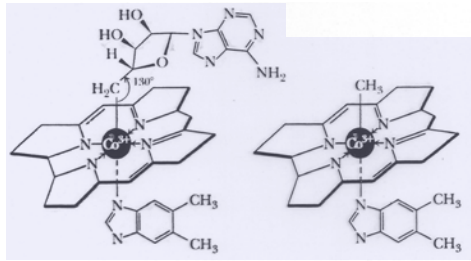


Cobalt ion

Dimethylbenzimidazole

Cyanocobalamin  
Vitamin B<sub>12</sub>

Coenzyme



5'-Deoxyadenosylcobalamin

Methylcobalamin

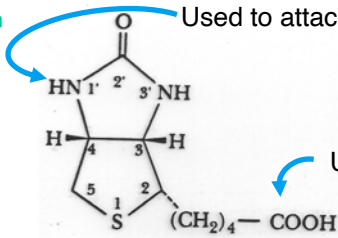
Coenzyme Forms

# Vitamins & Cofactors

## ⑦ Biotin

Carboxylations

Vitamin

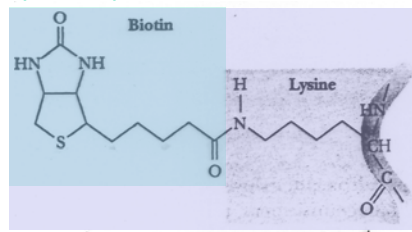


Used to attach carboxyl group (-CO<sub>2</sub><sup>-</sup>)

Tightly binds Avidin and streptavidin ( $K_d \sim 10^{-15}$ ); used in biotechnology

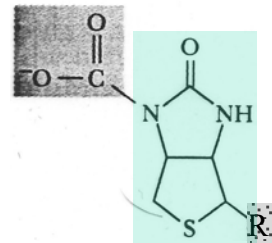
Used to attach to enzyme (Lys)

Coenzyme (covalent)



The biotin-lysine (biocytin) complex

Carboxylbiotin



# Vitamins & Cofactors

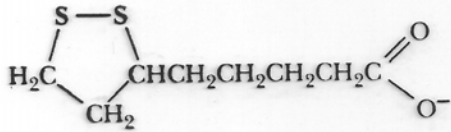
## ⑧ Lipoic Acid

Acyl-group transfer

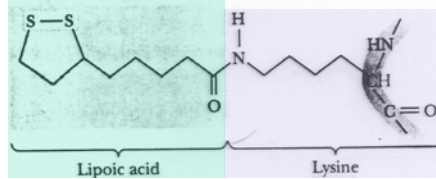
Vitamin

Coenzyme (covalent)

Lipoic acid, oxidized form



Lipoamide complex



# Vitamins & Cofactors

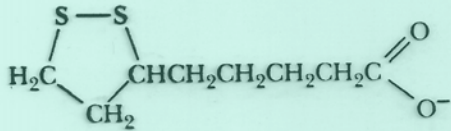
## ⑧ Lipoic Acid

Acyl-group transfer

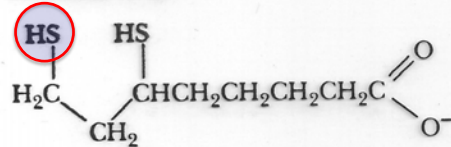
Vitamin

Coenzyme (covalent)

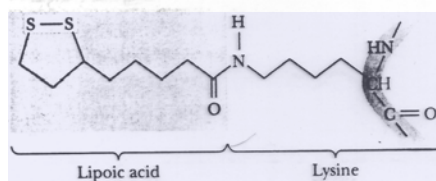
Lipoic acid, oxidized form



Reduced form



Lipoamide complex





# Vitamins & Cofactors

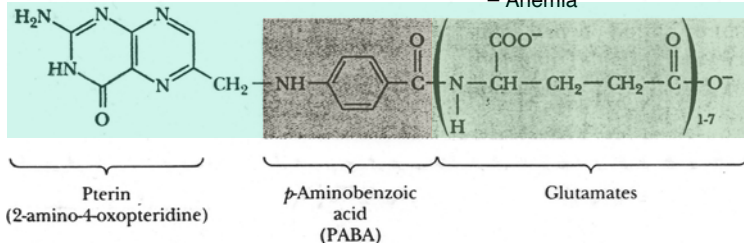
## 9 Folic Acid (aka Vitamin B<sub>9</sub>)

One-carbon transfer

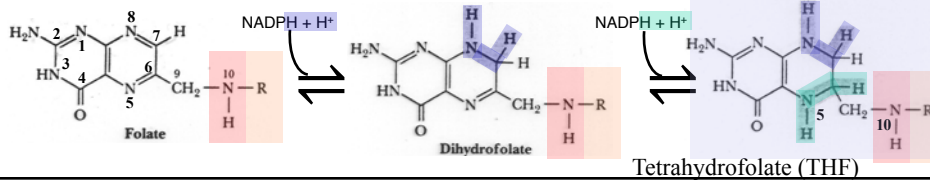
Vitamin

Folic acid

- Folate deficiency:
  - Diarrhea
  - Depression
  - Confusion
  - Anemia
- During pregnancy: fetal neural tube defects



Coenzyme



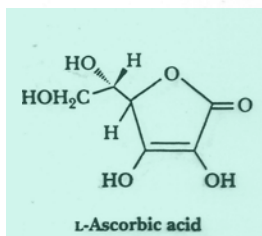
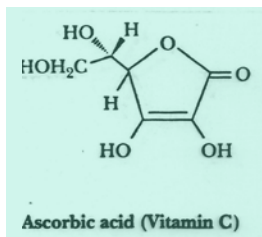
# Vitamins & Cofactors

## 10 Ascorbic Acid (aka Vitamin C)

Re-dox

Vitamin

Coenzyme



# Vitamins & Cofactors

## ⑩ Ascorbic Acid (aka Vitamin C)

Re-dox

Vitamin  
Coenzyme

