

Course 2851 Principles of Metabolism
Metabolism and endocrinology programme, Karolinska Institutet

Lecture 8
Cofactors & vitamins

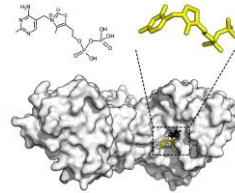
Roland Nilsson, Ph.D

Department of Medicine, Solna
Center for Molecular Medicine
Karolinska Institutet



Cofactors, "traditional" view

Cofactor: a molecule required by an enzyme



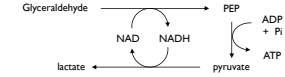
Thiamine phosphate bound to transketolase. PDB: 4KXV



Cofactors for a pathway / process

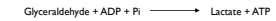
Carriers or mediators required for a process but *not* consumed by it

Example:



Here NAD and NADH are cofactors, since they are not consumed.

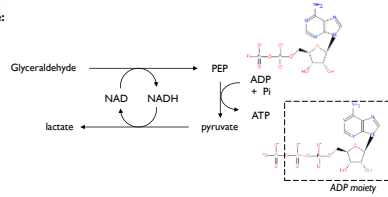
Sum formula for pathway:



Moieties as cofactors

Part of a molecule can be unchanged in a process

Example:

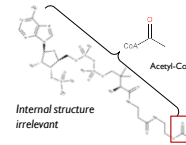


Viewed this way, the ADP moiety is a cofactor, not consumed by the process.



Cofactors as carriers

Transporting "building blocks" of metabolism



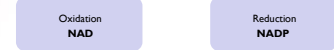
| Cofactor | Carried group |
|----------------------------|---|
| Coenzyme A | Acyl groups |
| Tetrahydrofolate (THF) | One-carbon groups (-CH ₃ , -CH ₂ , -CH ⁺ , -CHO) |
| S-adenosylmethionine (SAM) | Methyl group (-CH ₃) |
| NAD, NADP | Electrons / hydride ions (H ⁻) |
| Heme | Oxygen |
| ATP, GTP | High-energy phosphate |
| UDP | Sugars, aminosugars |
| CTP | Lipids (glycerol, choline, ethanolamine) |

Differs from enzyme-bound cofactors!

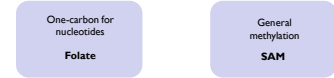


Carriers "compartmentalize" metabolism

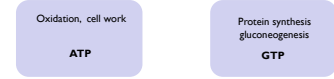
NAD and NADP both carry H- groups, but specialize in oxidative and reductive metabolism



Tetrahydrofolate generally donates -CH₃ to SAM, but not the other way around. *



ATP is the main energy carrier in oxidative metabolism; GTP in certain anabolic processes



* Rudiger and Janicke, FEBS Letters 4:316-318, 1969.



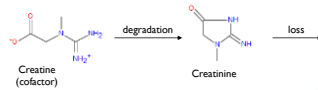
Cofactors are only needed in trace amounts

- Theoretically, demand is zero for nondividing cells
- Higher demand during cell growth / proliferation, but much lower than nutrients
- Plasma and culture medium contain tiny amounts of cofactors



Amino acids 10—500 μ M **Cofactors** 1—100 nM

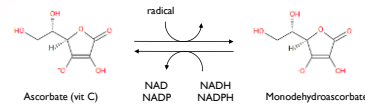
- Some loss due to degradation



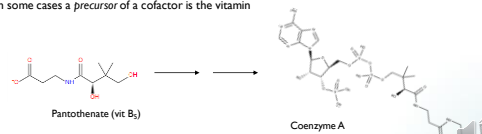
Cofactors are often vitamins

- Since the diet contains plenty, synthesis is not needed and has been lost in evolution

Ascorbate (vitamin C)

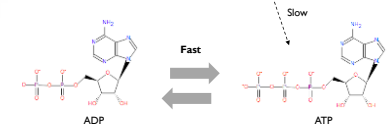


- In some cases a precursor of a cofactor is the vitamin



"Activated" cofactors cannot be provided to cells (?)

Turnover rate much higher than uptake / synthesis



Is it possible to provide antioxidants?