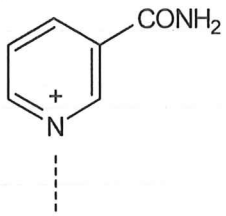
Cofactors of Enzymes 4

Names and structures of basic heterocycles. Coenzymes, cofactors, their functions, structures, examples of reactions, relation of cofactors to vitamins.

Cofactors of Oxidoreductases

Nicotinamide Adenine Dinucleotide (NAD^+)



1. Complete the remaining parts of the structure. What is the difference between $NADP^+$ and NAD^+?
2. NAD^+ is composed of two nucleotides. Give their names and structures and describe how they are connected.
3. What is the function of both coenzymes?
4. Draw the structure of reduced form of NAD^+. Why the reduced form of NAD^+ has no positive charge?
5. What vitamin is a part of this coenzyme, what are its sources?
6. Write the equations of reactions of NAD^+ with: a) lactate (catalyzed by lactate dehydrogenase)
   b) ethanol (catalyzed by alcohol dehydrogenase).

NAD^+-dependent enzymes e.g. (citric acid cycle): ....

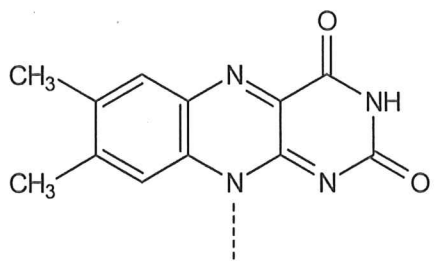
(complete) (glycolysis): ....

(detoxification of ethanol): ....

$NADP^+$-dependent enzymes: e.g. (synthesis of fatty acids): oxoacyl reductase

(synthesis of cholesterol): HMG-CoA reductase

Flavine Nucleotides (FMN, FAD)



7. Describe the structure of both nucleotides.
8. Which heterocycles are contained in flavine part of this cofactor?
9. What is the name of structure depicted?
10. What is the function of FAD?
11. Which vitamin is a part of flavine cofactors?

12. Write the structure of reduced form of FAD.

.....

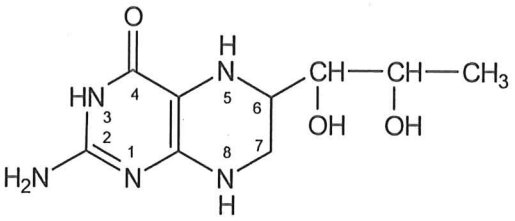
13. Write the equation of the reaction of $FADH_2$ with fumarate.

FMN-dependent enzymes: e.g. (respiratory chain): NADH dehydrogenase

FAD-dependent enzymes: e.g. (citric acid cycle): *(complete)* .....

(oxidative decarboxylation of 2-oxoacids): pyruvate dehydrogenase

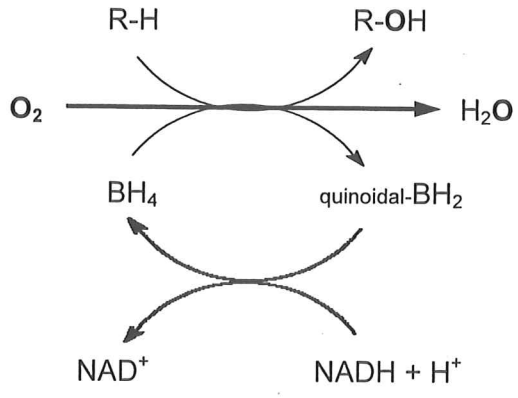
Tetrahydrobiopterin (BH_4)



5,6,7,8-tetrahydrobiopterin

14. Which heterocycles are comprised in the structure of tetrahydrobiopterin?

Function of BH_4 in some reactions catalyzed by monooxygenases:



Enzymes utilizing BH_4, e.g. (hydroxylases of aromatic acids): .....

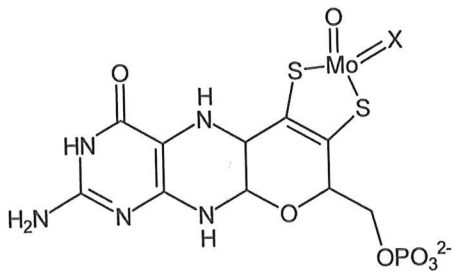
(complete) .....

.....

(synthesis of NO, see page 43): NO-synthase

Coenzyme Q, Fe-S Proteins, Haem – see the chapter Respiratory chain, page 75.

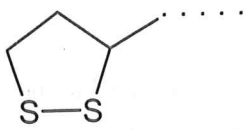
Molybdopterin (Molybdenum Cofactor)



X = O, S

Enzymes utilizing molybdopterin, e.g.: xanthine oxidase, sulfite oxidase

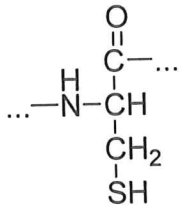
Lipoic Acid



15. Complete the missing part of the structure
16. In which way is lipoic acid bonded to enzyme?
17. In which type of reaction is lipoic acid involved?
18. Draw the structure of dihydrolipoate.

Lipoate-dependent enzymes: (oxidative decarboxylation of 2-oxoacids): (*complete*) . . . .

Glutathione (GSH)

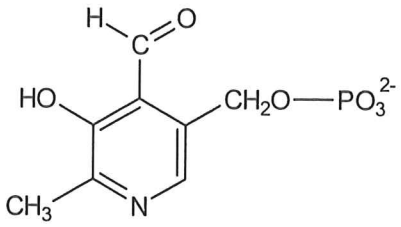


19. Complete the missing parts of the structure and their names.
20. GSH is involved in removal of H_2O_2 and organic peroxides in the cell. Write the common equation of such reaction.
21. How is reduced form of glutathione regenerated? Which coenzyme is necessary for it?

GSH dependent enzymes, e.g. (not only oxidoreductases)
(selenoprotein): glutathione peroxidase
(conjugation of antibiotics): glutathione-*S*-transferase
(membrane transport AA): γ-glutamyl transpeptidase

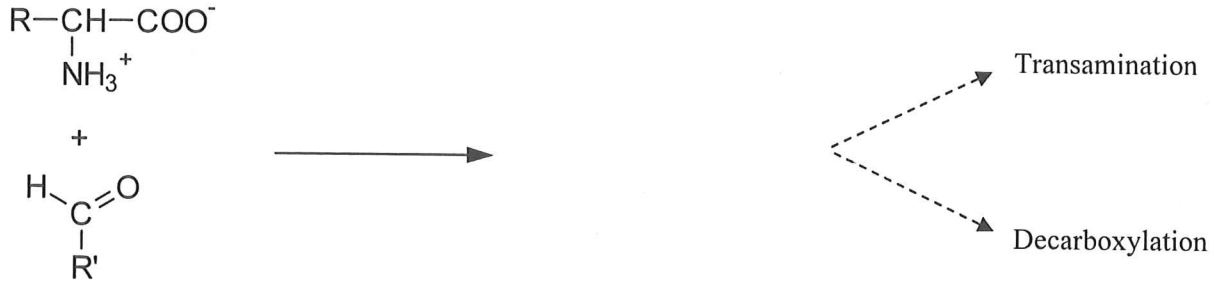
Cofactors of Transferases

Pyridoxal Phosphate



22. Which vitamin is related to pyridoxal phosphate?
23. Name the heterocycle that is contained in the pyridoxal phosphate structure.
24. What other forms of cofactor can be formed in the reaction with amino acids? Draw the partial structures.

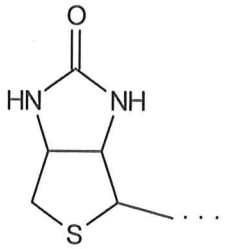
Scheme of aldimine formation in reaction with amino acids



PLP **Aldimine**
(Schiff's base)

Pyridoxal phosphate dependent enzymes, e.g. (transamination): (*complete*) . . . .
(synthesis of haem): δ-aminolevulinate synthase

Biotin

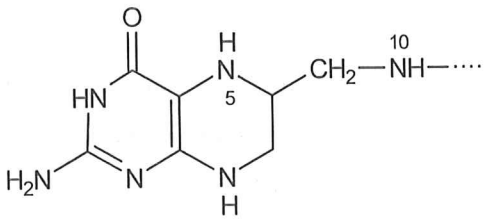


25. Which two heterocycles are contained in the molecule of biotin?
26. Which particular reaction is biotin involved in? Which group is transferred?
27. Which atom binds the group transferred?

Biotin-dependent enzymes, e.g. (anaplerotic reactions of citric acid cycle: . . . . .
(*complete*) (synthesis of fatty acids): acetyl-CoA carboxylase

28. Which of the stated cofactors belongs among the coenzymes: FAD, NAD^+, lipoate, biotin?

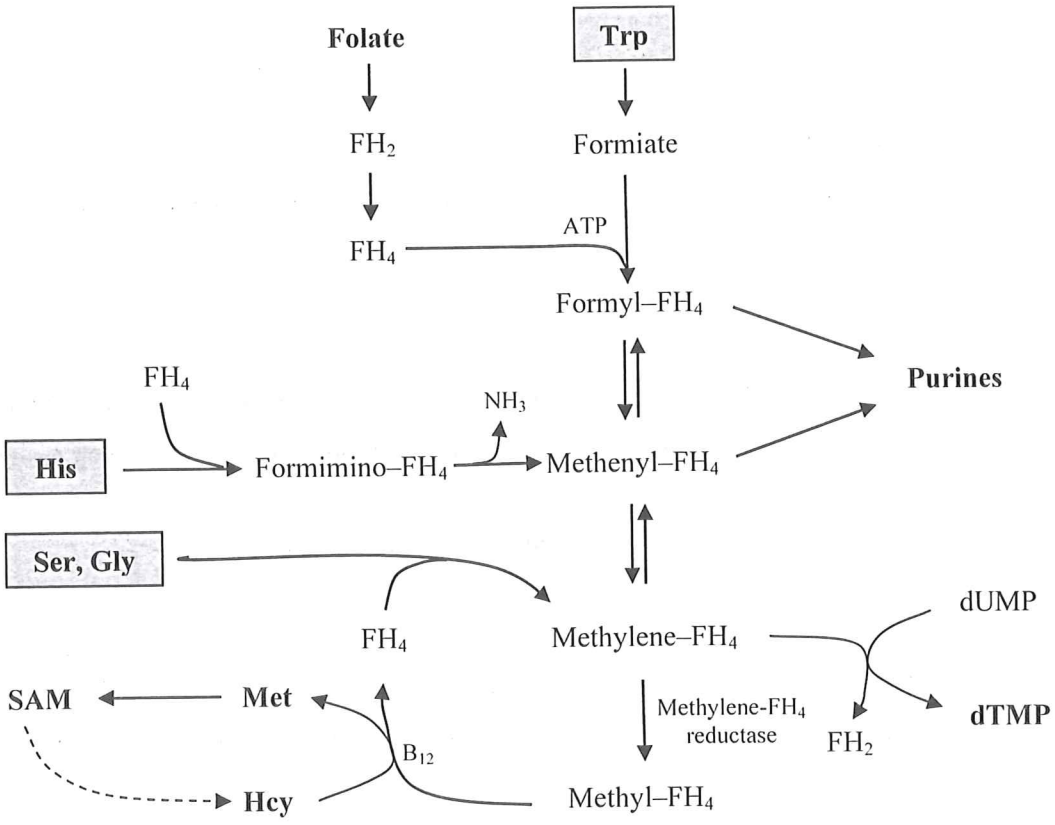
Tetrahydrofolate (H_4folate, FH_4)



29. Describe the structure and complete the formula.

H_4folate carries one-carbon fragments (*complete*):		attached to FH_4 at
Methyl	.....	N^5
Methylene	.....	N^5, N^{10}
Methenyl	–CH=	N^5, N^{10}
Formyl	.....	N^{10}
Formimine	.....	N^5

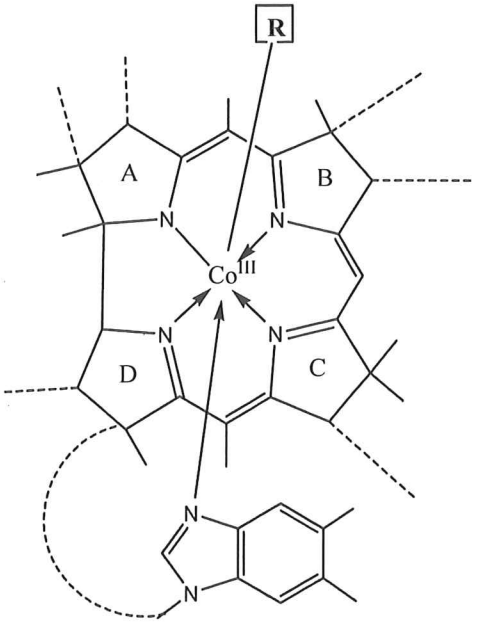
Formation, interconversion and utilization of FH_4 derivatives



Hcy . . . homocysteine, SAM . . . *S*-adenosylmethionine

30. Write the partial equation of the transformation of methenyl-FH_4 to methylene FH_4 (NADH acts as cofactor).
31. Give the main sources of one-carbon units in the body.
32. State an example of a methylation reaction at which the methyl group is donated by FH_4.
33. What is the principle of antibacterial action of sulfonamides?

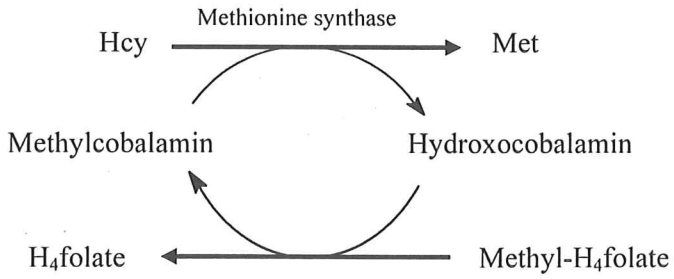
Cobalamins (Vitamin B_{12})



R ... 5'-deoxyadenosine (mitochondria)
–OH (cytosol)
$–CH_3$ (cytosol)

34. Describe the cofactor structure.
35. Draw the structure of 5'-deoxyadenosine.

Significance of methylcobalamin

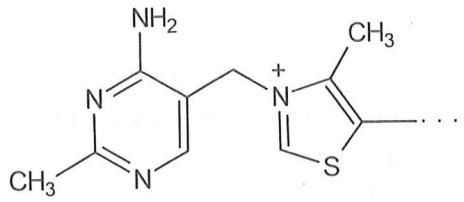


Vitamin B_{12} dependent enzymes, e.g. (methionine resynthesis): methionine synthase
(propionate utilization): methylmalonyl-CoA mutase

36. Vitamin B_{12} deficiency may lead to inactivation of FH_4 ("folate trap"). Explain it.

37. A lack of vitamin B_{12} may result in disturbances in DNA synthesis preventing cell division, especially the formation of new erythrocytes. Consequently anaemia (megaloblastic or pernicious) is developed. Explain it.

Thiamine Diphosphate (TDP)



TDP dependent enzymes, e.g. (citric acid cycle): .....

(oxidative decarboxylation of 2-oxo acids): ....

transketolase reaction in pentose cycle

38. Give the names of both heterocycles in the molecule. Complete the formula.

39. What group is transferred and in which form?

40. Which atom of the cofactor binds the group transferred?

41. What vitamin is a part of cofactor structure?

42. What types of reactions TDP takes part in?

43. One of the symptoms of beriberi (in Sinhalese = *I am not able to*) is that blood pyruvate is markedly increased. Explain it. In which way the symptoms of this disease can be eliminated?