C5720 Biochemie

13-Koenzymy a vitaminy

Obsah

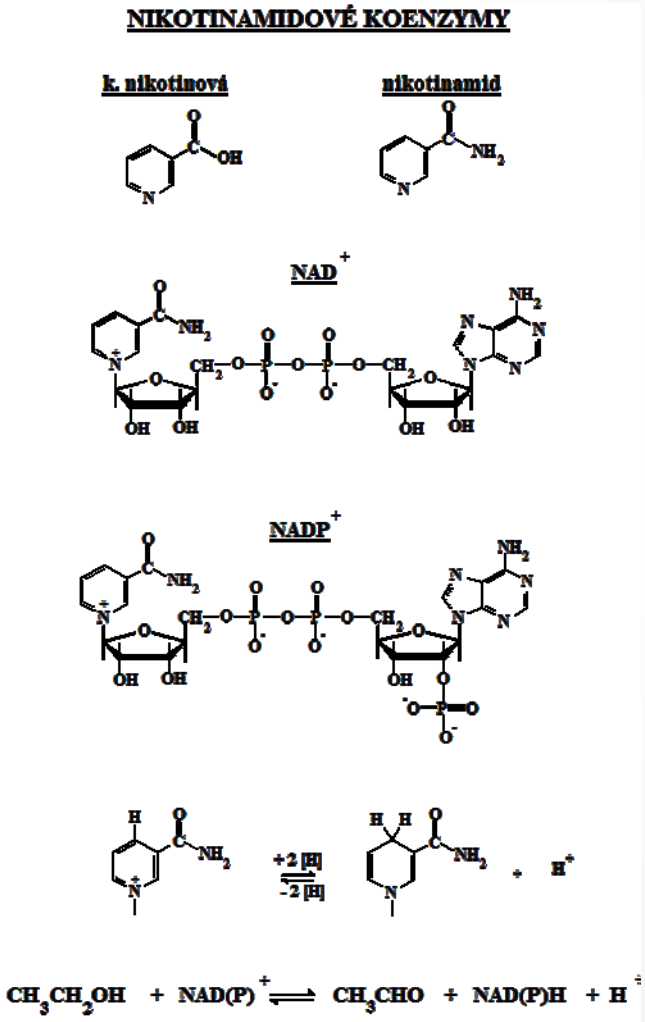
- Koenzymy a vitaminy. Koenzymy oxidoreduktáz (nikotinamid a NAD, flaviny, chinony, hemy, železosirné proteiny, lipoát,) transferáz (ATP, UDP, CDP, biotin, thiamin, koenzym A, THF, pyridoxalfosfát, vit B12) Vitamin C, lipofilní vitaminy (A, D3, K).

Typy kofaktorů

- Rozdělení podle reakcí
  - Někdy spadají do více skupin (THF)
- Jako prekurzory slouží vitaminy
  - Většinou, někdy jiné esenciální složky
  - Možnost syntézy z neesenciálních prekurzorů - hem
- Relativita pojmu
  - Kofaktor x druhý substrát (ATP)
  - Vazba kovů
  - Produkty přeměny aminoacylů

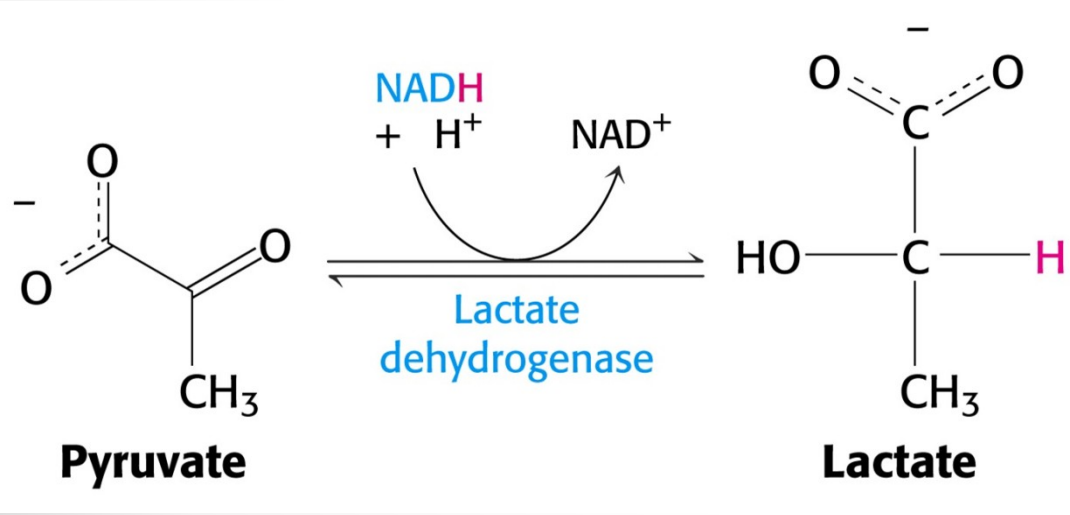
Kofaktory oxidoreduktas

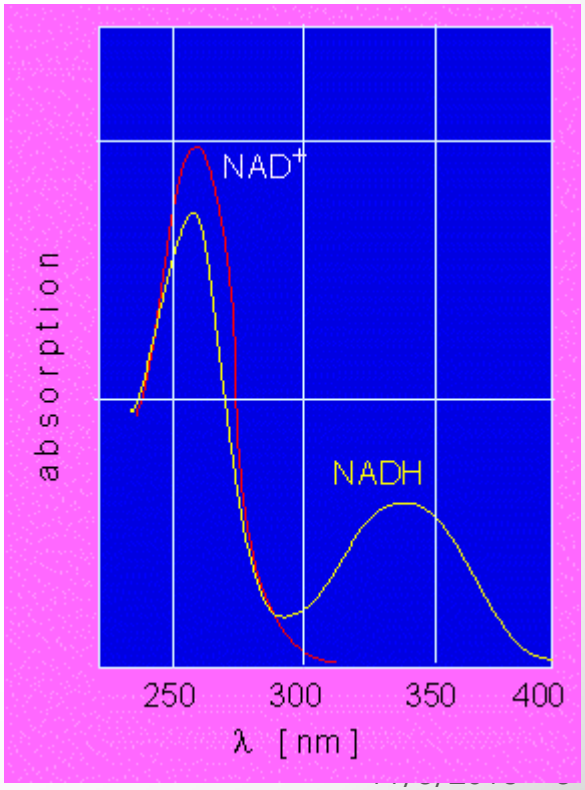
- Nikotinamidové
- Koenzymy
- Prekurzor niacin
- Disociabilní
- 2e$^-$ redukce
- Přenos H$^-$
- NAD$^+$ - respirace
- NADP$^+$ - redukce
- Změna spektra
- A_{340} = f(c)



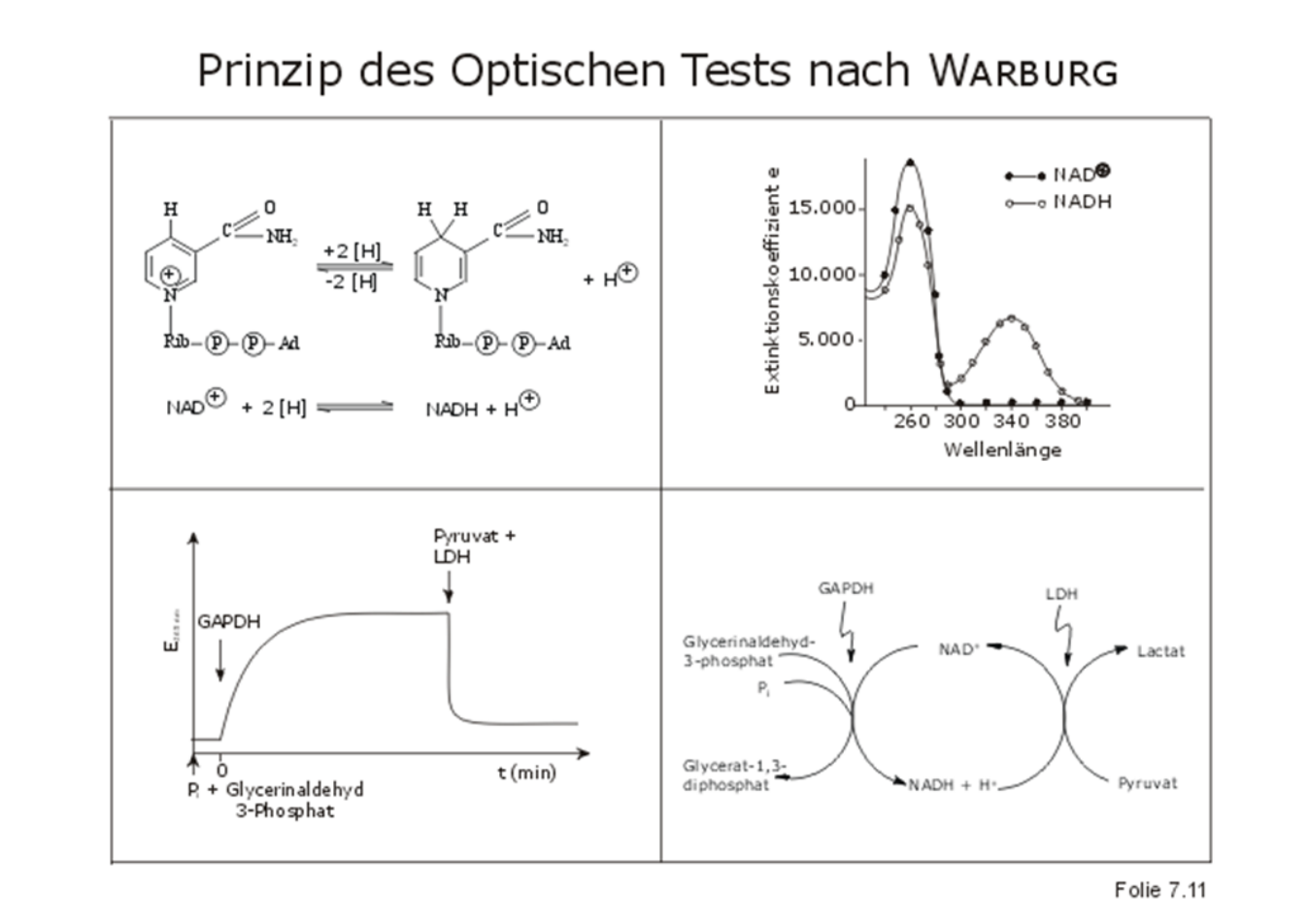
Kofaktory oxidoreduktas

- Warburgův optický test



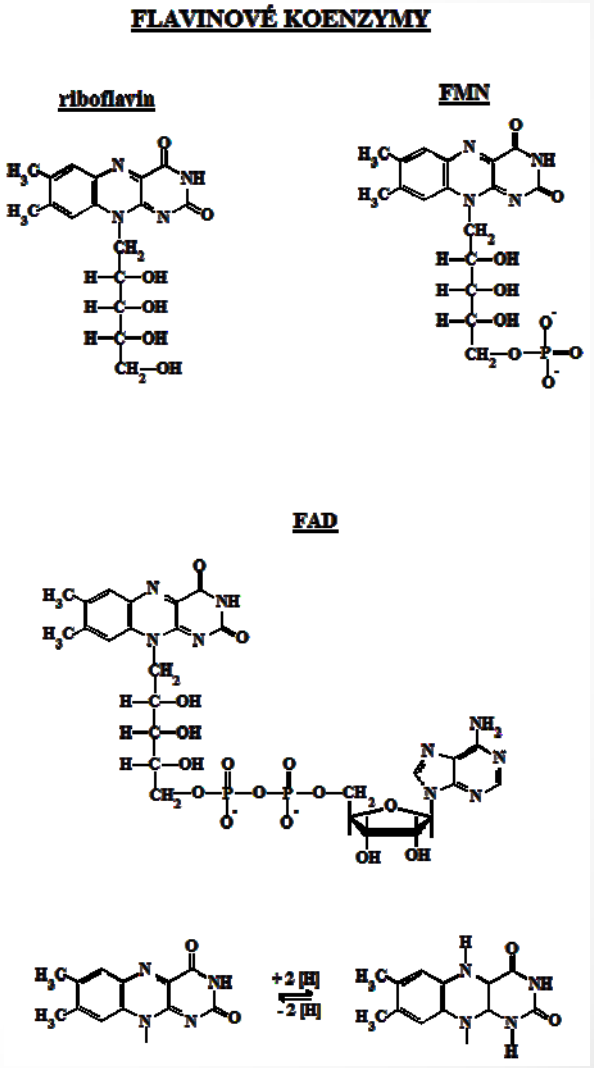


Warburgův optický test



Kofaktory oxidoreduktas

- Flavinové kofaktory
- Prekurzor riboflavin
- Prostetické skupiny
- 2 $1e^-$ kroky
- Semichinony, radikály
- Změna A nevýrazná
- Žlutá (ox) x leukoforma (red)



Kofaktory oxidoreduktas

- Redukce FAD

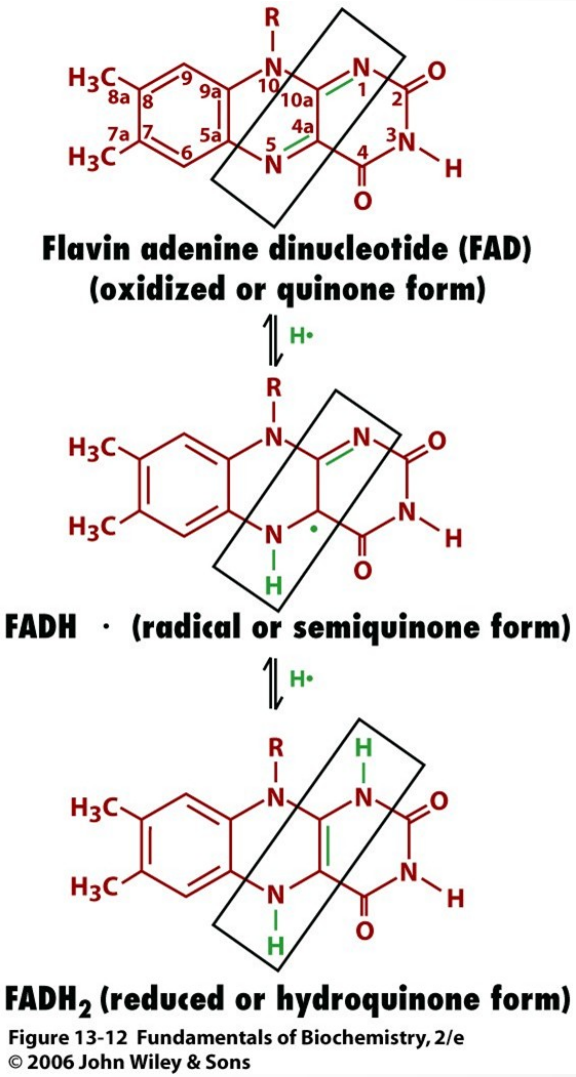
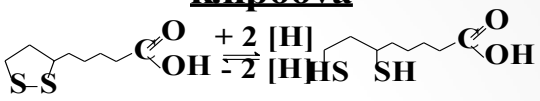


Figure 13-12 Fundamentals of Biochemistry, 2/e
© 2006 John Wiley & Sons

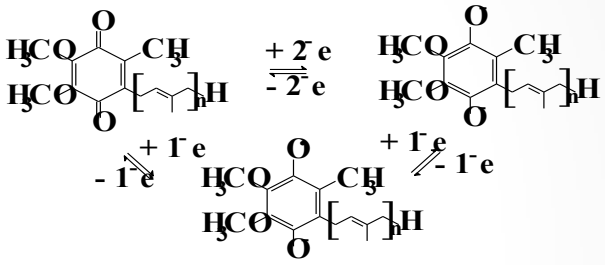
Kofaktory oxidoreduktas

- Kys. lipoová (thioktová)
  - Vitamin
  - Vázán amidicky na apoprotein
  - Odtud lipoamid
- Ubichinon, CoQ
  - Volná interakce
  - UQ-5n, CoQ_n, n = 6 – 10
  - Semichinony, radikály, ROS
- Ferredoxinové typy
  - Nehemově vázané Fe, FeS proteiny
  - Klastry Fe-S různé struktury
- Hemově vázané Fe
  - Různé substituenty, též lipofilní
  - Různý způsob vazeb
- GSH
  - Detoxikace, GSH peroxidasa x reduktasa
  - Též přenos skupin, xenobiotika

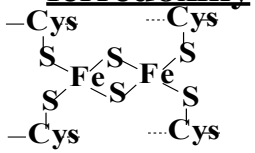
k.lipoová



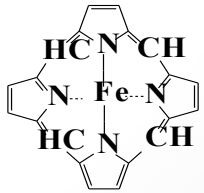
ubichinon



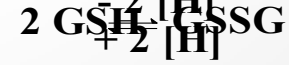
ferredoxiny



hem



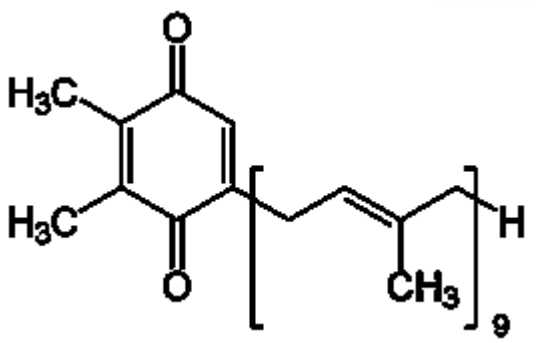
glutathion

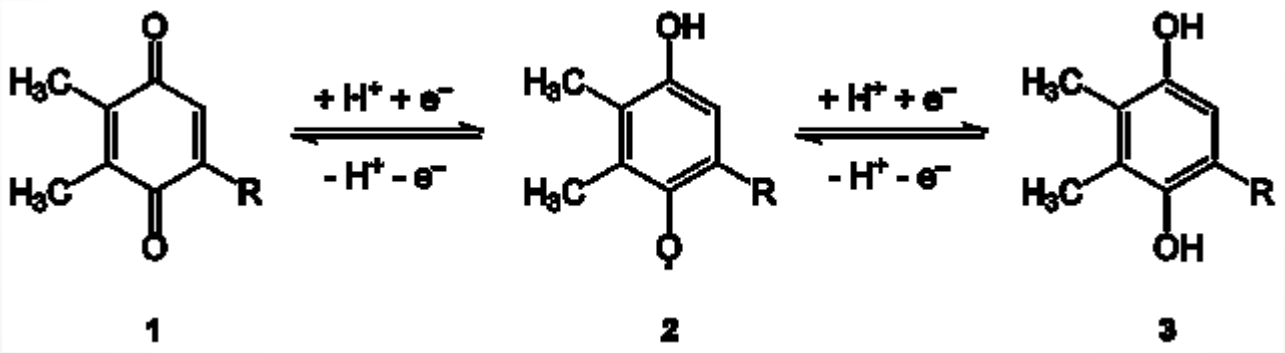


Kofaktory oxidoreduktas

- Plastochinon
  - Obdoba UQ

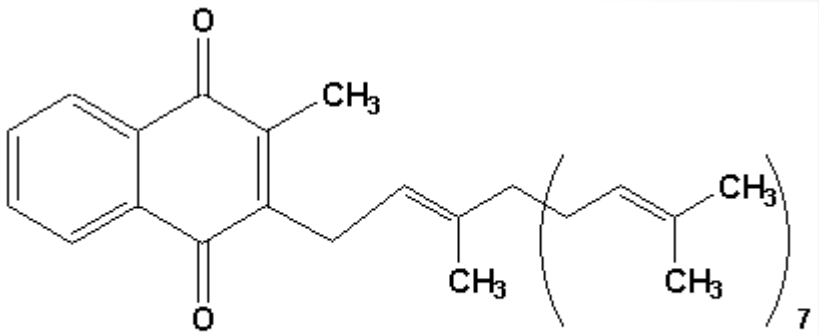
  u fotosyntézy
  - Redukce 2 x $1e^-$





Kofaktory oxidoreduktas

- Naftochinony
  - Vitaminy K
  - Speciální funkce
  - Tvroba karboxyGlu
  - Srážení krve



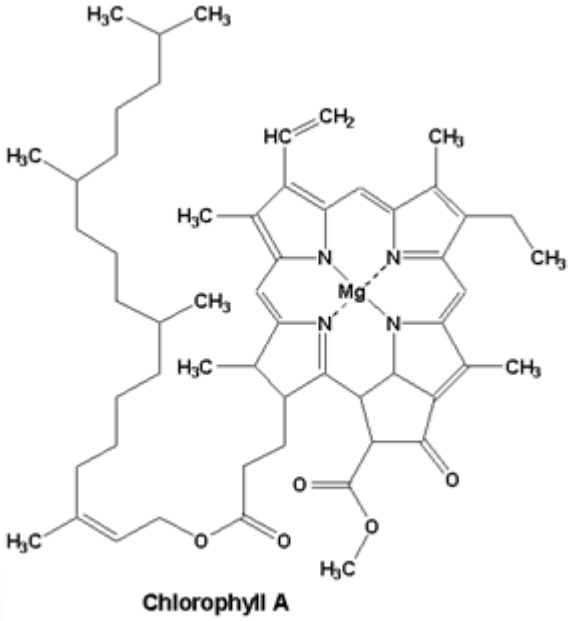
Menaquinone (vitamin K2)

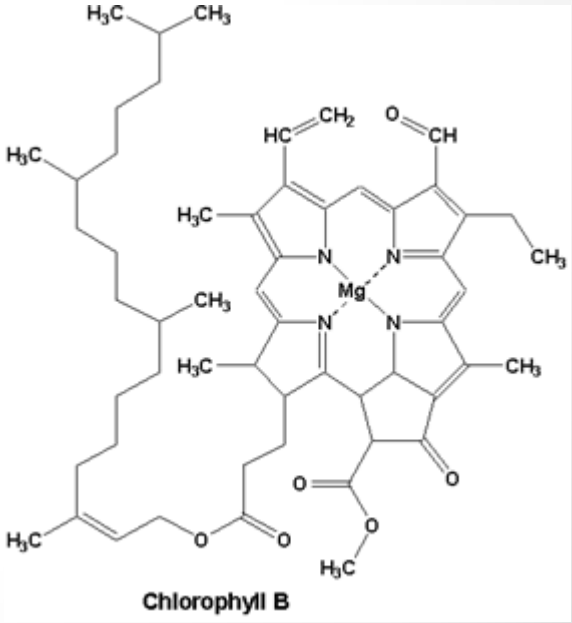
Kofaktory oxidoreduktas

- Fe-S klastry, příklady prostetických skupin bílkovin feredoxinového typu

Kofaktory oxidoreduktas

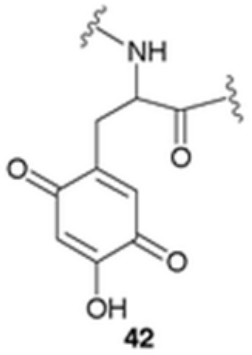
- Chlorofyly
  - Porfyrinová struktura, lipofilní substituent
  - Mg^{2+}
  - Fotosyntéza – transport e^-



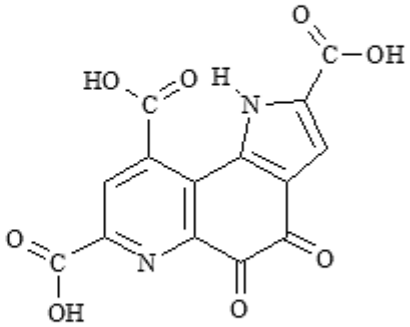


Kofaktory oxidoreduktas

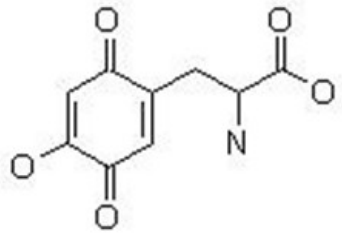
- Přeměněné AK
  - Prostetické skupiny
  - Bílkovinný původ



42



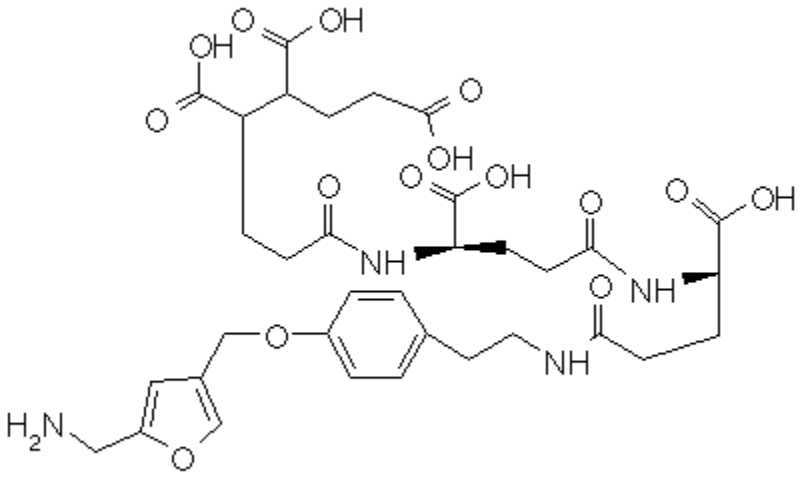
Pyrolochinolinochinon
PQQ



TOPAchinon
TrihydrOxyPhenylAlanin

Kofaktory oxidoreduktas

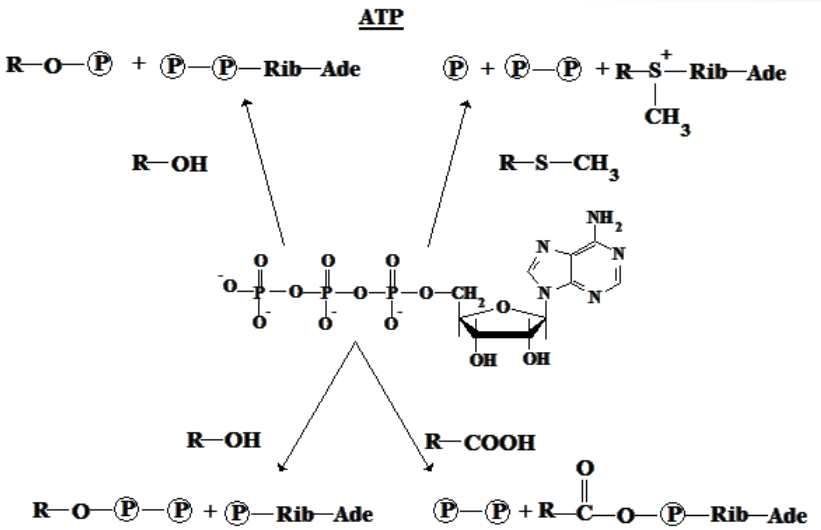
- Kofaktory metanogeneze

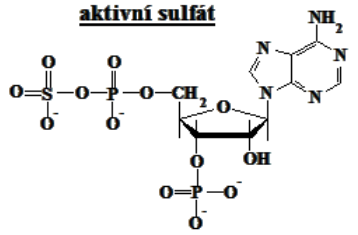


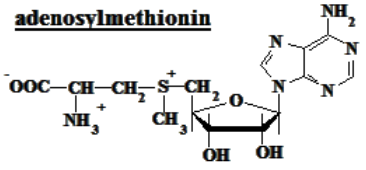
Metanofuran

Koenzymy transferas

- ATP
  - Přenos aktivních skupin
  - Aktivace metabolitů
- Reakce s R-OH
  - Voda – hydrolýza
  - sacharidy bílkoviny
    - kinasy
- Reakce s Met
  - Aktivní metyl
- Reakce s R-OH
  - Přenos PP, Rib-5P na P-Rib-PP
- Reakce s R-COOH
  - Aktivace acylů, aminoacylů
- Reakce se síranem
  - Aktivní kys. sírová



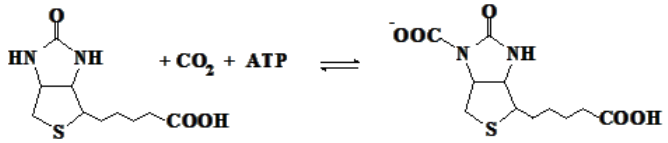




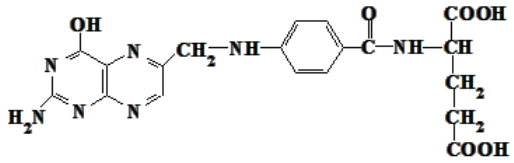
Koenzymy transferas

- Biotin
  - Vitamin B
  - Vázán na Lys enzymu
  - Aktivní karboxyl
- THF – tetrahydrofolát
  - Z folátu
  - Disociabilní
  - Aktivní 1C metabolity
  - Syntézy nukleotidů - bazí
- TPP – tiamindifosfát
  - Aktivní aldehydy (2C)
  - Prostetická skupina

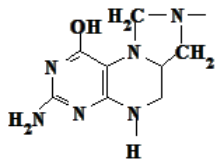
biotin



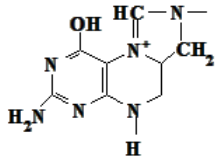
Kys. listová



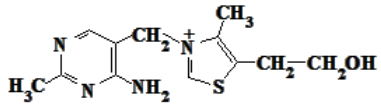
methylentetrahydrolistová k.

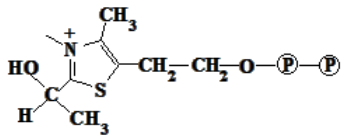


methenyltetrahydrolistová k.



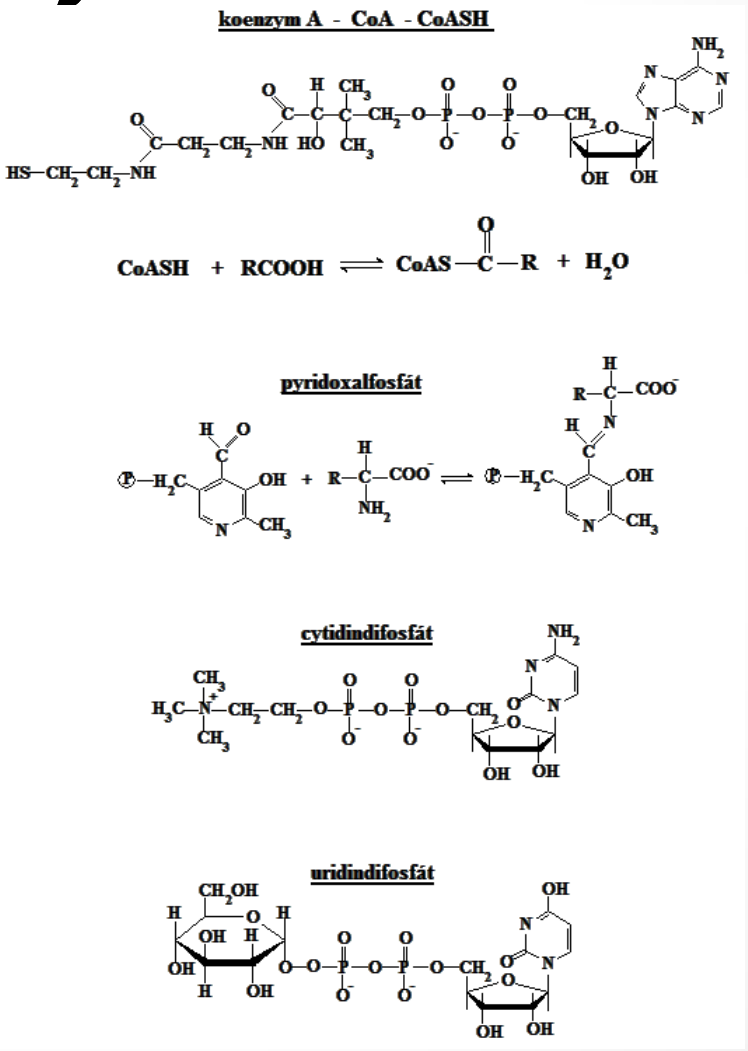
thiamin





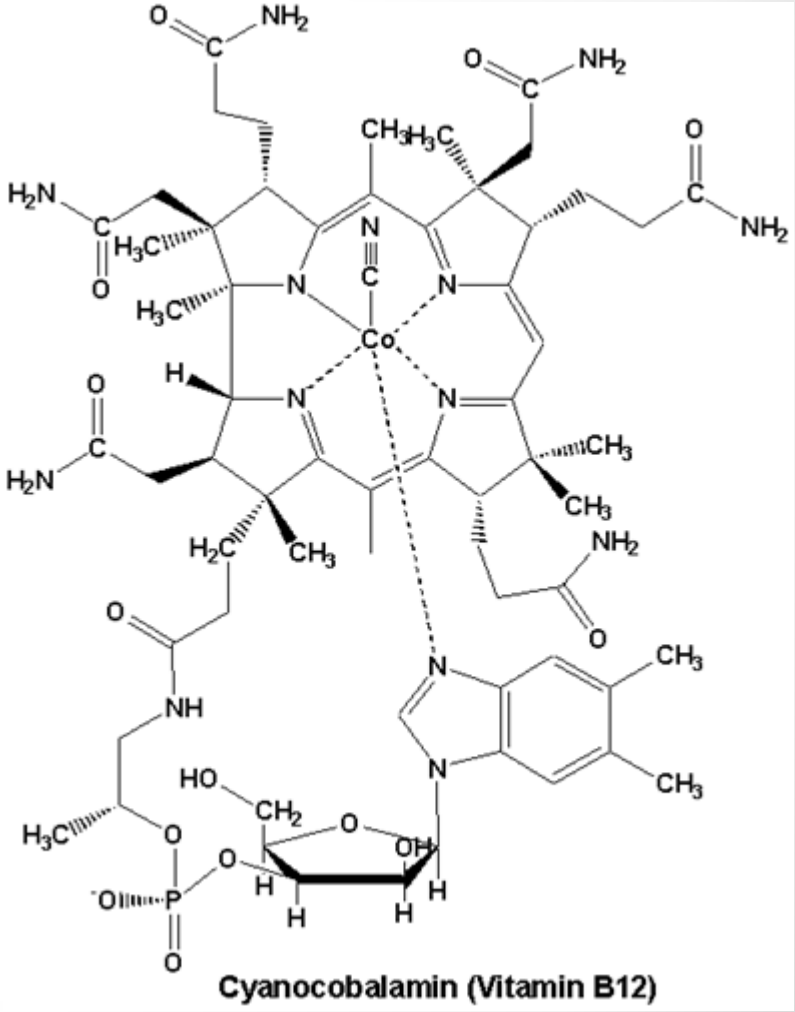
Koenzymy transferas

- Koenzym A
  - Z pantotenátu
  - Aktivní acyly
  - Spřaženo ATP = AMP + PP
- PALPO
  - Z pyridoxinu
  - Metabolismus aminů, AK
  - Tvorba Schiffovy báze
- CDP – netřeba vitamin
  - Aktivní báze PL
- UDP - dtto
  - Aktivní monosacharidy
  - UTP + Glc-1-P = UDP-Glc + PP



Koenzymy isomeras

- Vitamin B_{12}
  - Kobalamin
    - Korinoid + nukleotid
  - Ligandy
    - CN nejúčinnější
  - Transkarboxylace
  - Krvetvorba
    - Perniciosní anemie
  - Aplikace
    - Perorální nespolehlivá
    - Vnitřní faktor pro vstřebávání
  - Biotechnologická produkce
    - Výkaly přežvýkavců
    - Aktivovaný kal



Vitaminy

- Vitaminy jako prekurzory kofaktorů
  - Většinou, některé nepotřebují
  - Některé jsou spíše metabolity (askorbát)
- Fyziologická role – zde druhořadé
- Výskyt – vlastnosti (polarita)
  - Rozpustné ve vodě – polární
  - Rozpustné v tucích – nepolární
  - Hledisko dietetické
- Následující přehled
  - Korelace struktur s kofaktory

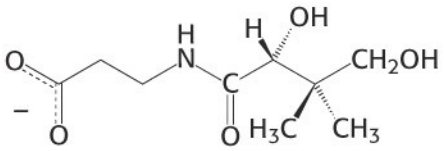
TABLE 8.9 Water-Soluble Vitamins

Vitamin	Coenzyme	Typical reaction type	Consequences of deficiency
Thiamine (B_1)	Thiamine pyrophosphate	Aldehyde transfer	Beriberi (weight loss, heart problems, neurological dysfunction)
Riboflavin (B_2)	Flavin adenine dinucleotide (FAD)	Oxidation–reduction	Cheliosis and angular stomatitus (lesions of the mouth), dermatitis
Pyridoxine (B_6)	Pyridoxal phosphate	Group transfer to or from amino acids	Depression, confusion, convulsions
Nicotinic acid (niacin)	Nicotinamide adenine dinucleotide (NAD^+)	Oxidation–reduction	Pellagra (dermatitis, depression, diarrhea)
Pantothenic acid	Coenzyme A	Acyl–group transfer	Hypertension
Biotin	Biotin–lysine complexes (biocytin)	ATP-dependent carboxylation and carboxyl-group transfer	Rash about the eyebrows, muscle pain, fatigue (rare)
Folic acid	Tetrahydrofolate	Transfer of one-carbon components; thymine synthesis	Anemia, neural-tube defects in development
B_{12}	5′-Deoxyadenosyl cobalamin	Transfer of methyl groups; intramolecular rearrangements	Anemia, pernicious anemia, methylmalonic acidosis
C (ascorbic acid)		Antioxidant	Scurvy (swollen and bleeding gums, subdermal hemorrhages)

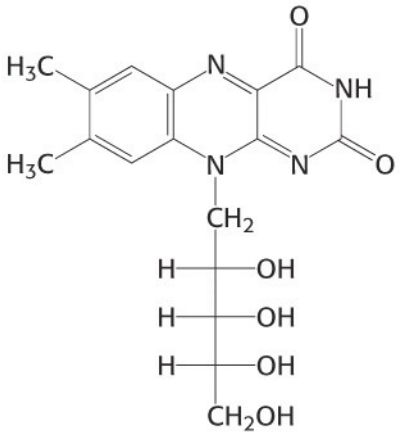
Přehozeny A a E!

TABLE 8.10 Fat-soluble vitamins

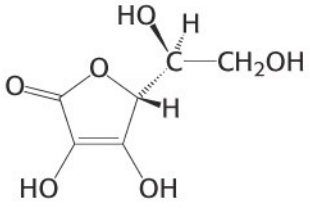
Vitamin	Function	Deficiency
A	Antioxidant	Inhibition of sperm production; lesions in muscles and nerves (rare)
D	Regulation of calcium and phosphate metabolism	Rickets (children): skeletal deformaties, impaired growth Osteomalacia (adults): soft, bending bones
E	Roles in vision, growth, reproduction	Night blindness, cornea damage, damage to respiratory and gastrointestinal tract
K	Blood coagulation	Subdermal hemorrhaging



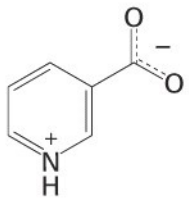
Vitamin B_5
(Pantothenate)



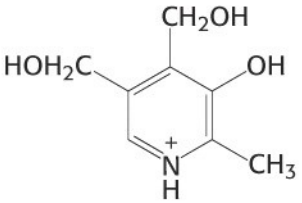
Vitamin B_2
(Riboflavin)



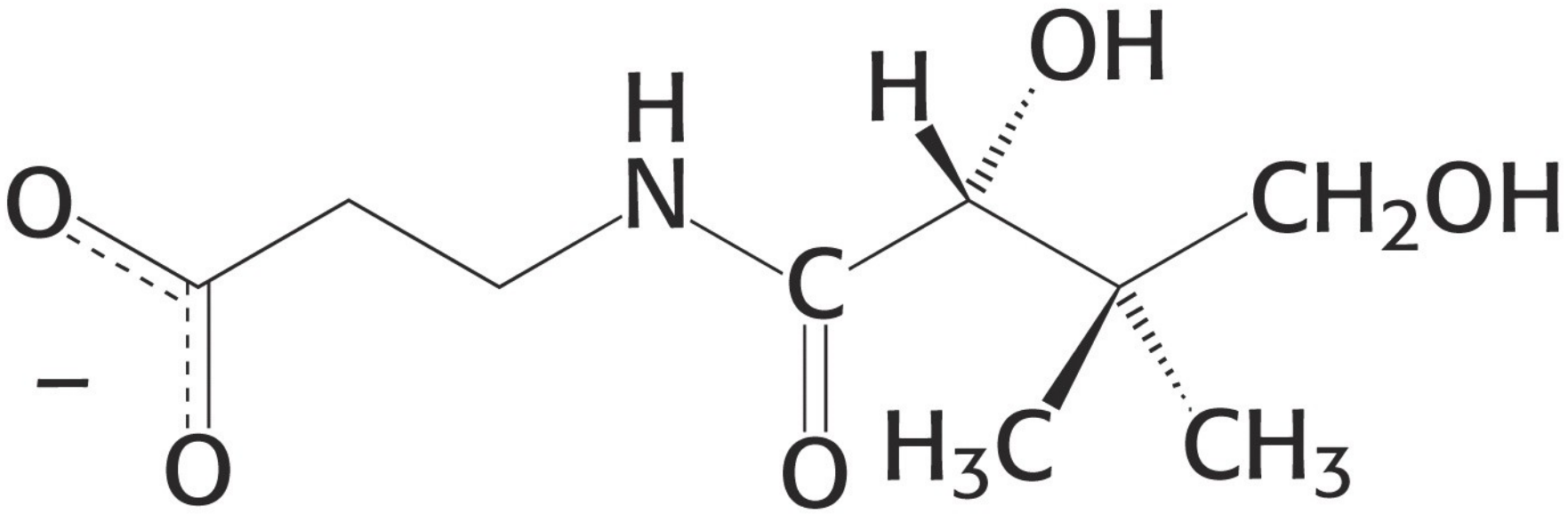
Vitamin C
(Ascorbic acid)



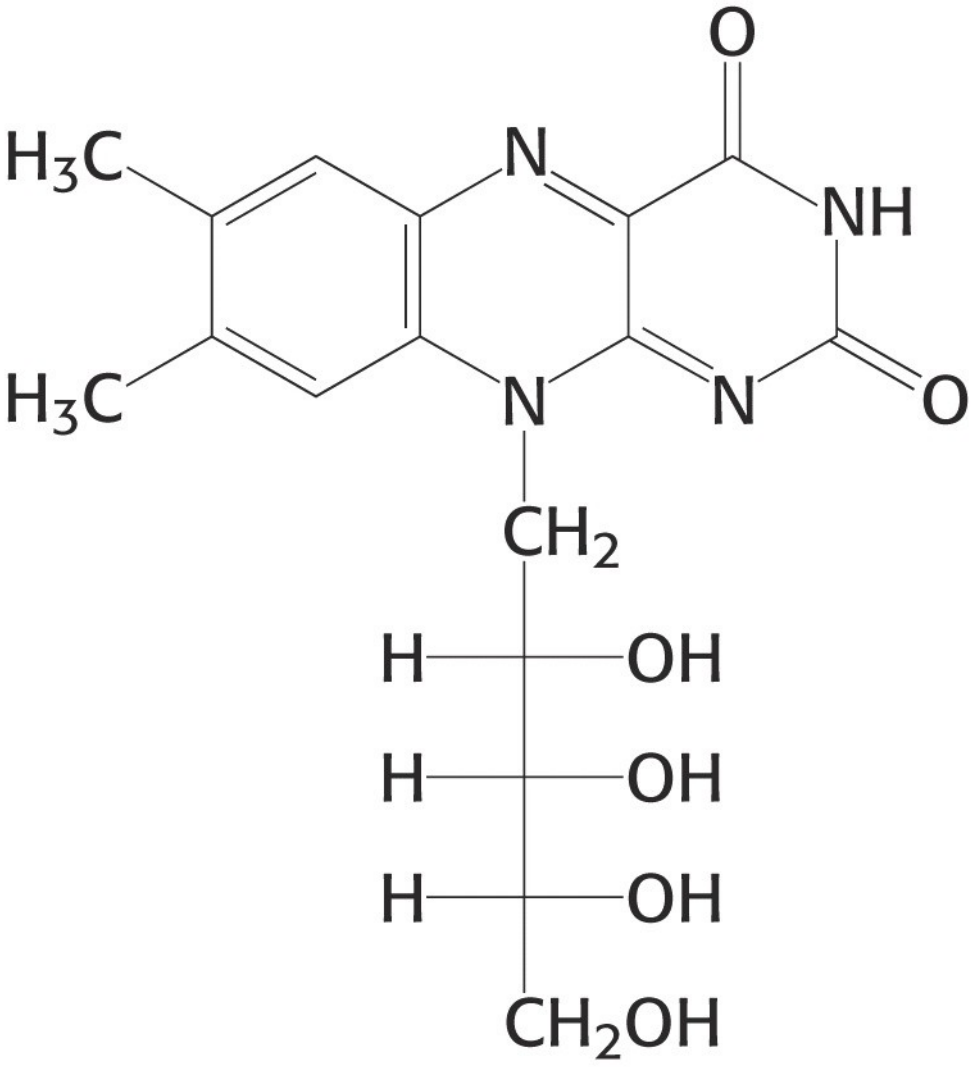
Vitamin B_3
(Niacin)



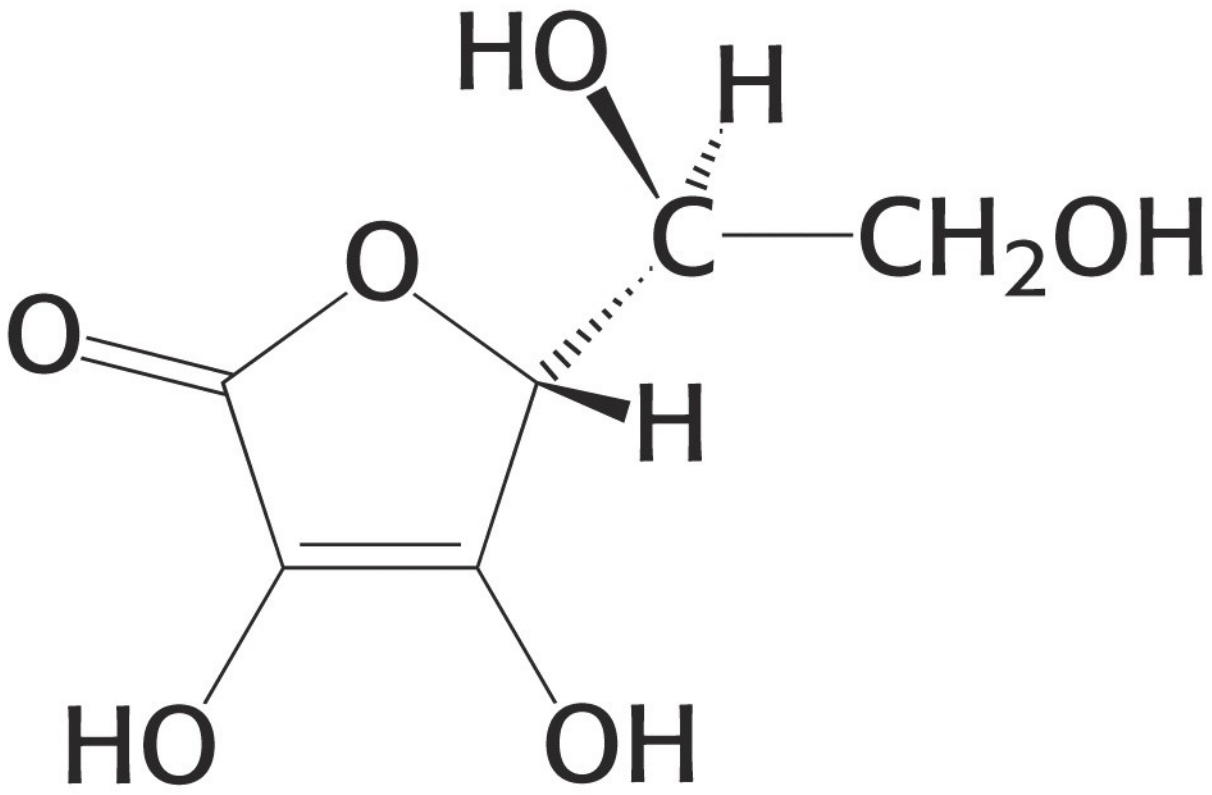
Vitamin B_6
(Pyridoxine)



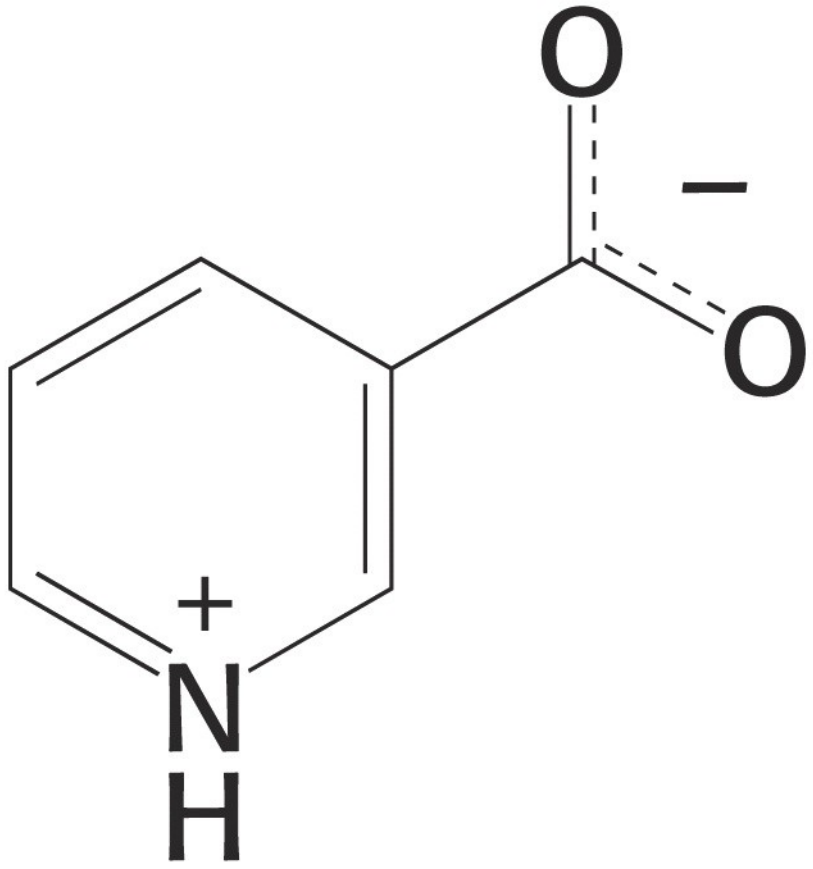
Vitamin B_5 (Pantothenate)



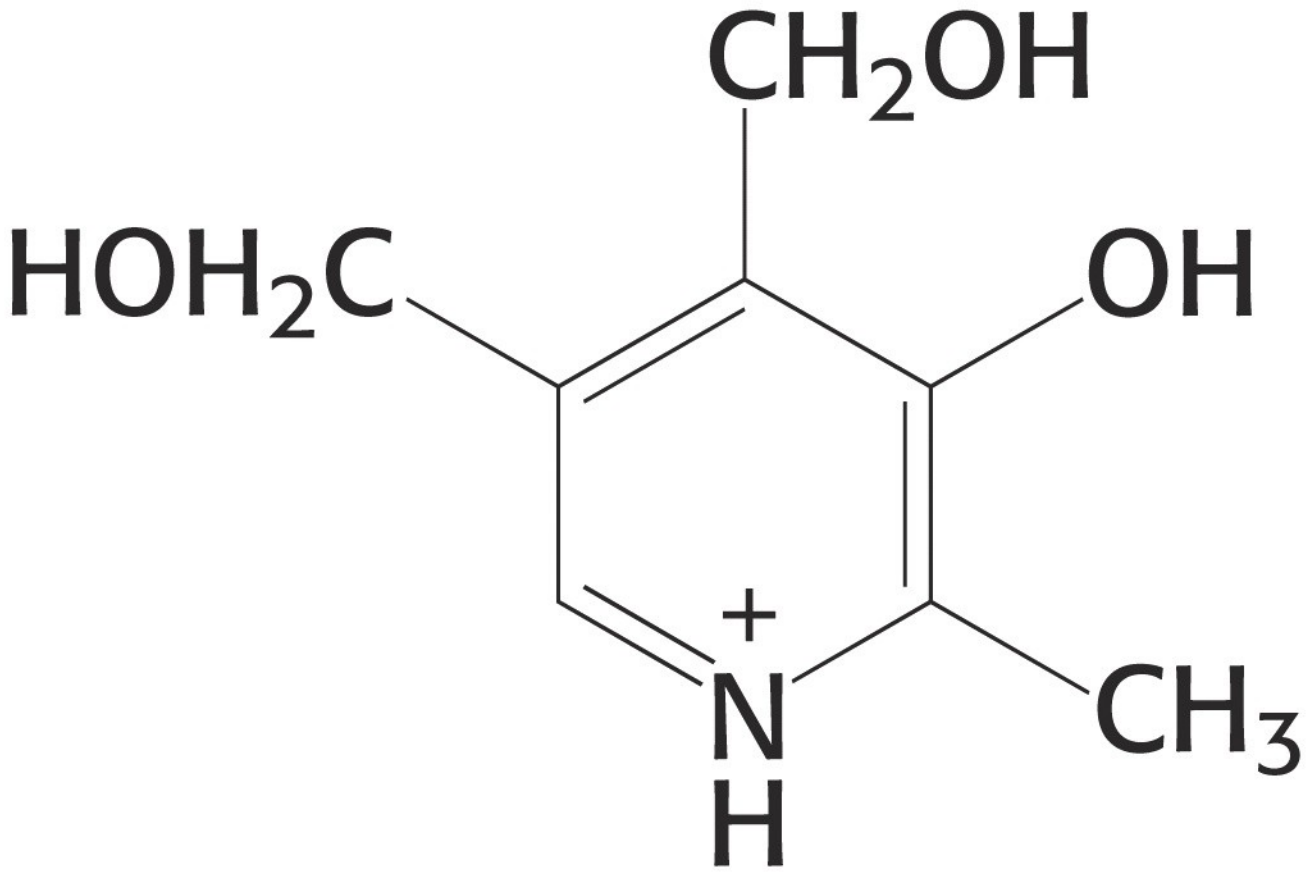
Vitamin B_2
(Riboflavin)



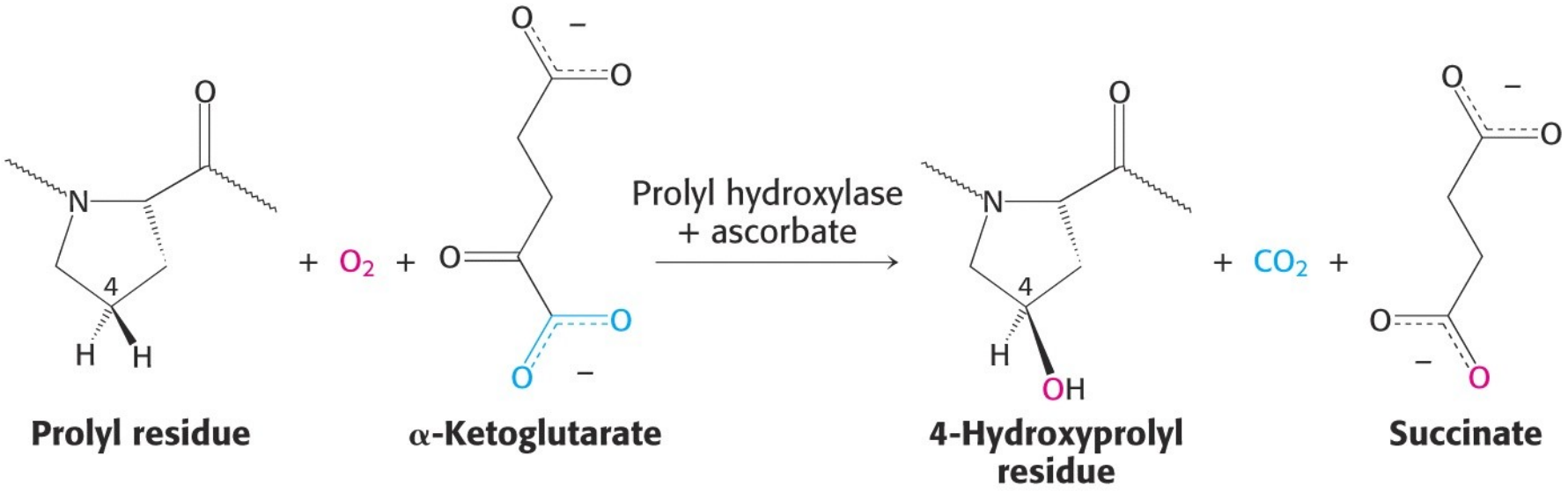
Vitamin C
(Ascorbic acid)

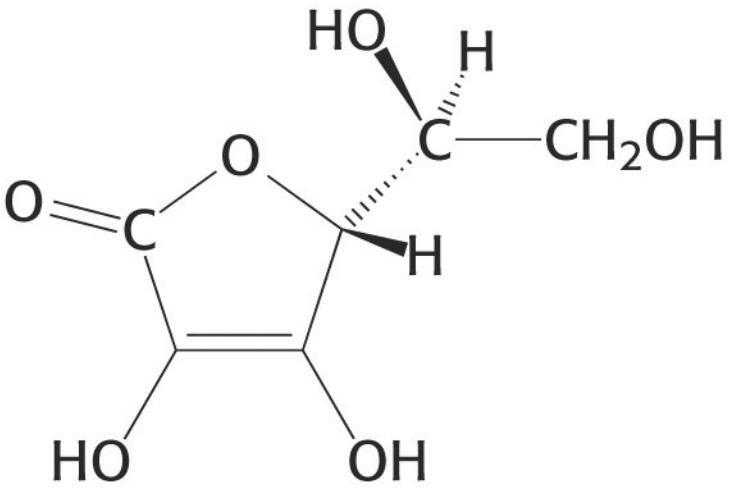


Vitamin B_3 (Niacin)

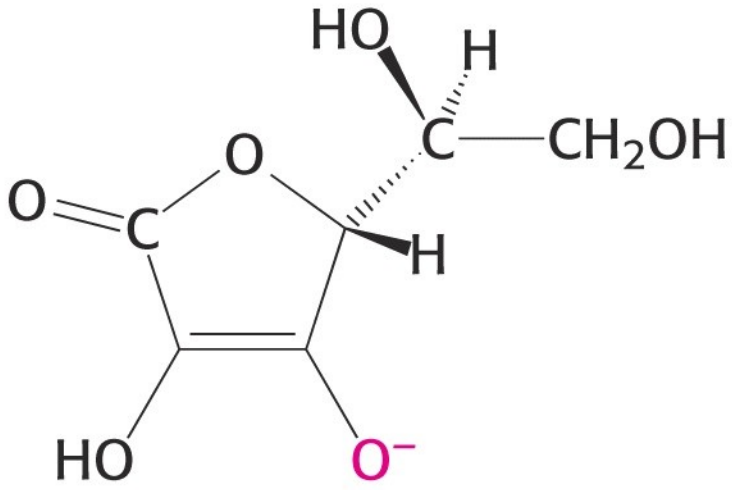


Vitamin B_6 (Pyridoxine)

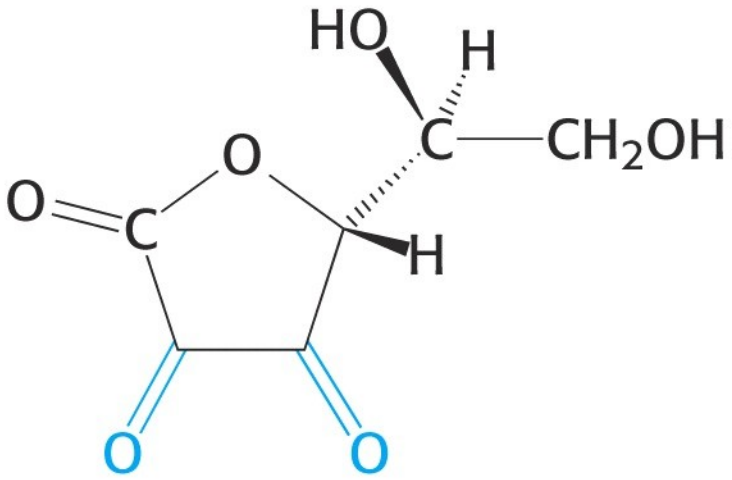

Prolyl hydroxylase
+ ascorbate
+ O2 +
+ CO2 +
Prolyl residue
α-Ketoglutarate
4-Hydroxyprolyl residue
Succinate



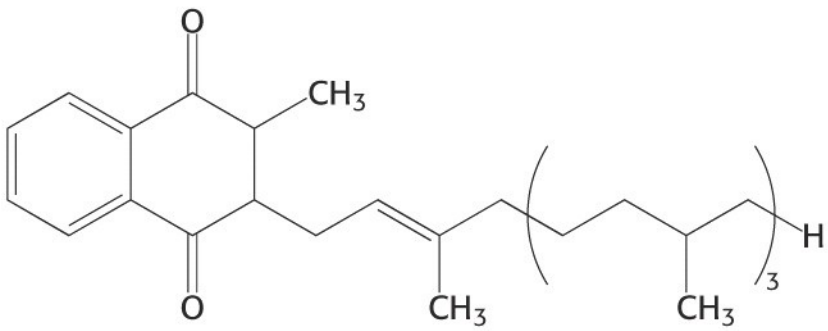
Ascorbic acid



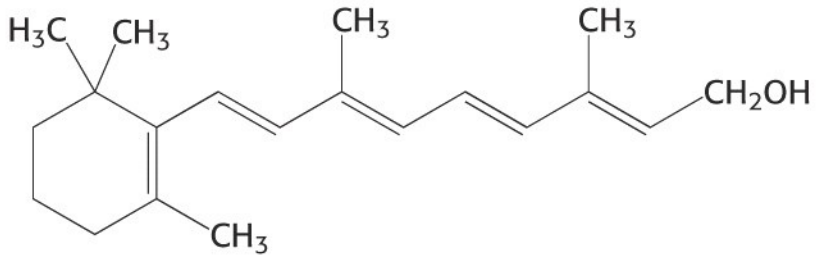
Ascorbate



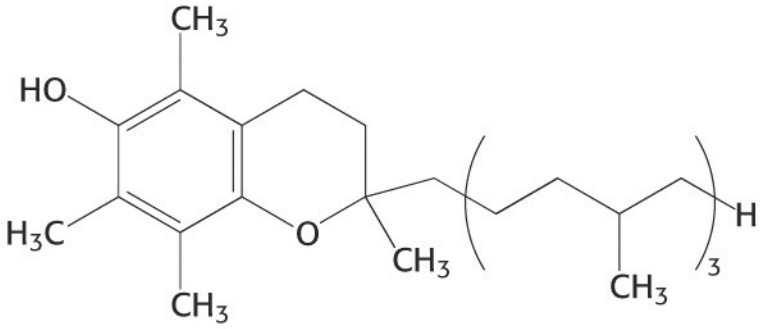
Dehydroascorbic acid



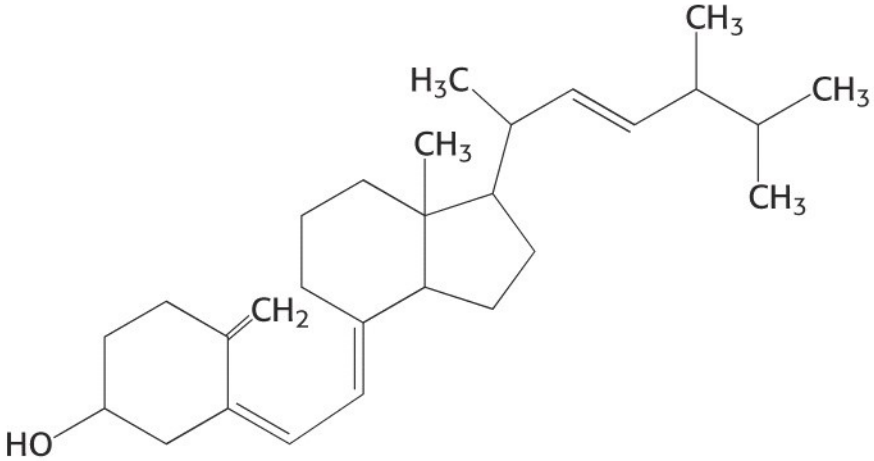
Vitamin K_1



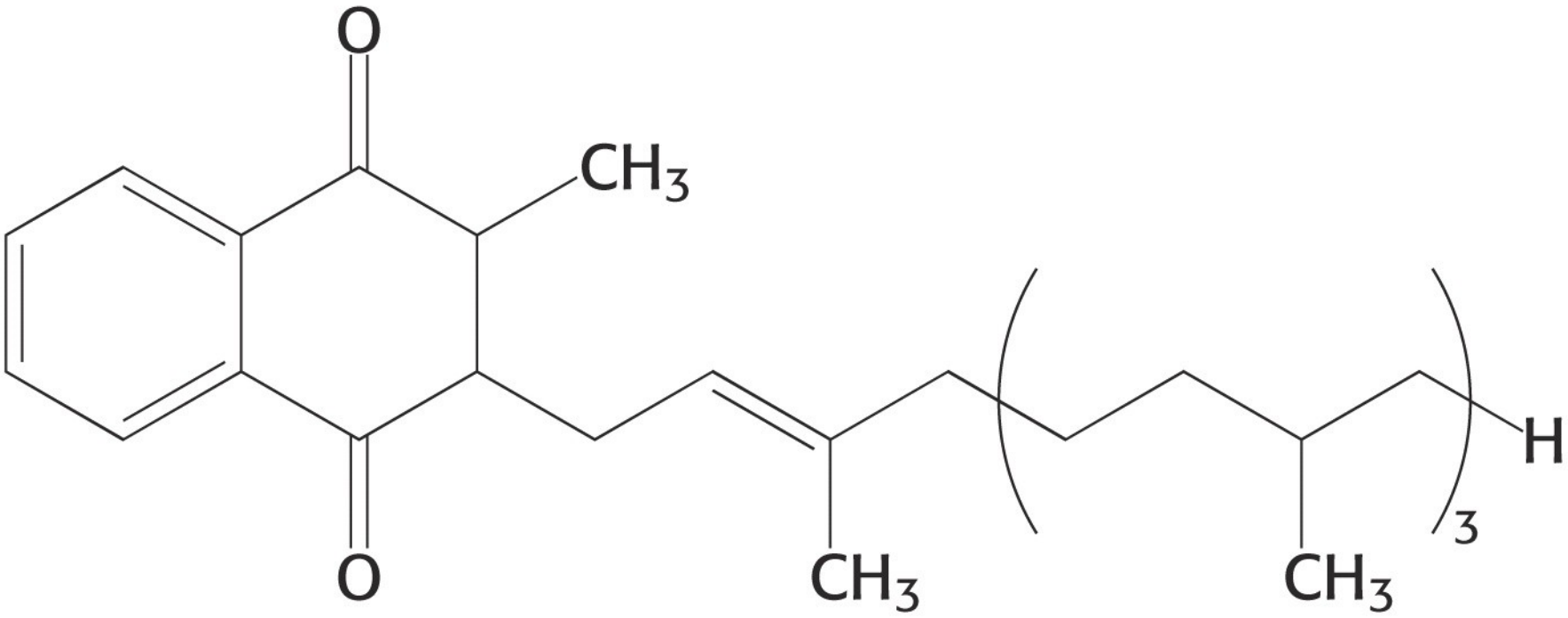
Vitamin A (Retinol)



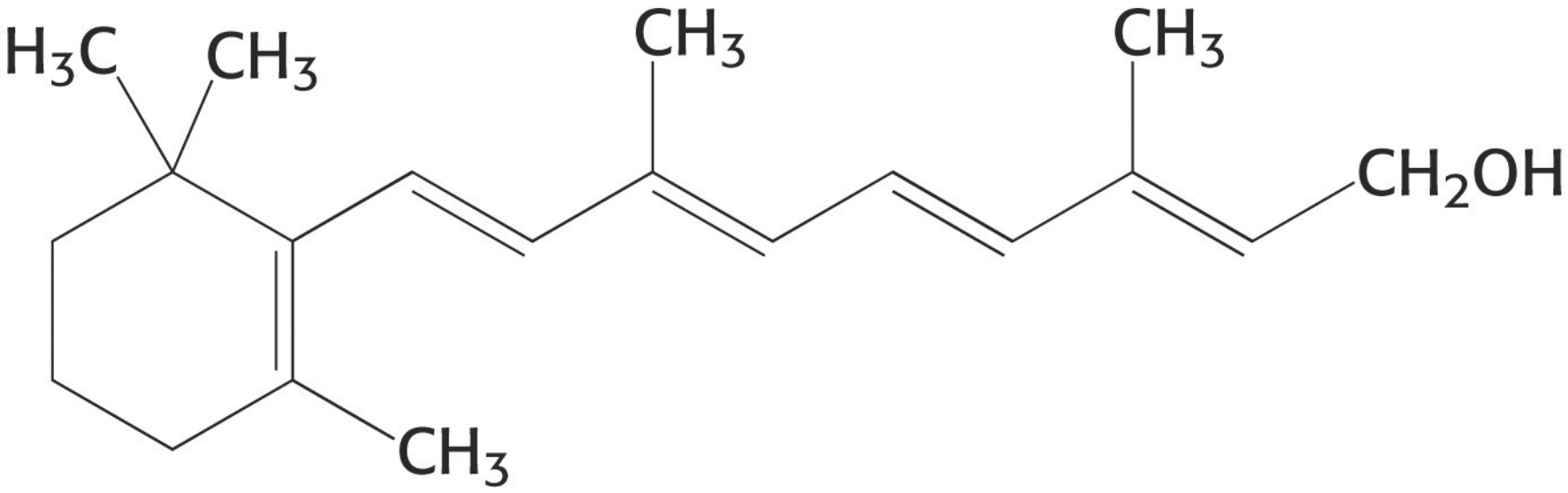
Vitamin E (α-Tocopherol)



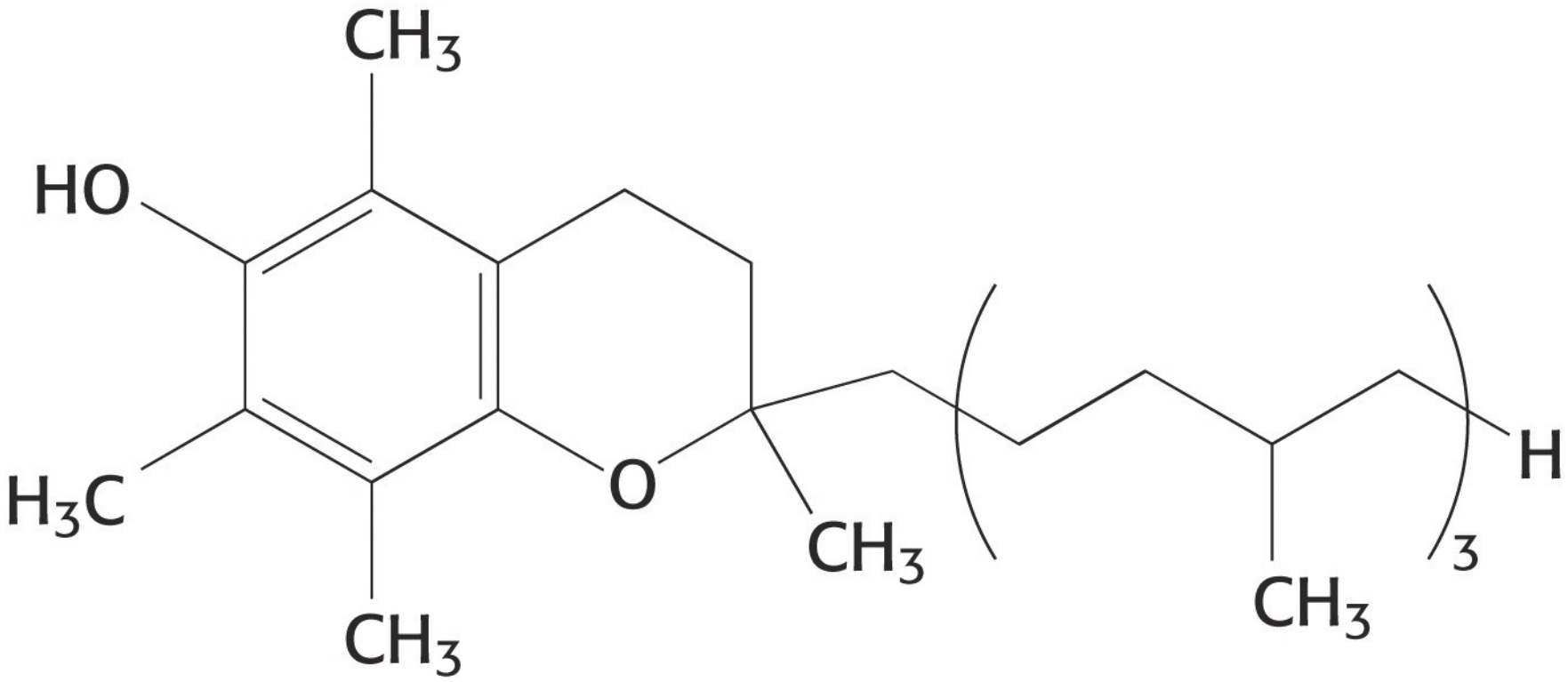
Vitamin D_2 (Calciferol)



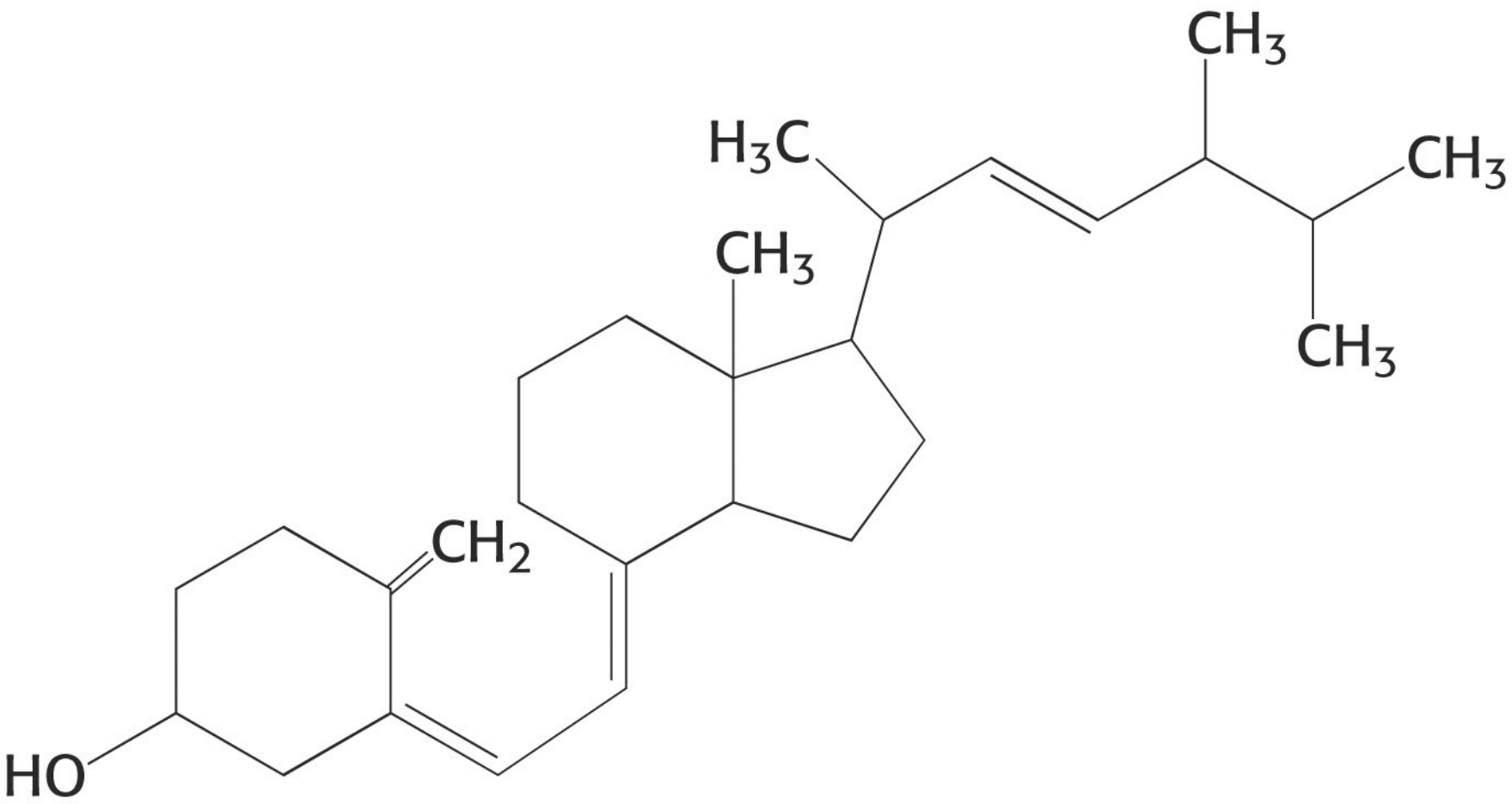
Vitamin K_1



Vitamin A (Retinol)



Vitamin E (α-Tocopherol)



Vitamin D_2 (Calciferol)