TABLE 9.3 **Common organic cofactors in metabolism.** (a) The name of the cofactor. (b) The vitamin from which the cofactor is derived. (c) The catalytic role of the cofactor in enzymatic catalysis. (d) The physiological roles of the cofactor, with emphasis on mammalian physiology. '*Antioxidation*' refers to reduction of chemical species during oxidative stress response. (e) Examples of enzymes that use the cofactor and correspond to the physiological role in (d). The biochemical pathway to which each enzyme belongs is shown in square parentheses. The enzymes are denoted by their common names. (f) Diseases associated with functional deficiency of the cofactor.

Abbreviations: α-KG – α-ketoglutarate; ACh – acetylcholine; ACoA – acetylcoenzyme A; AICAR – aminoimidazole carboxamide ribotide; Arg – arginine; BCKDC – branched-chain α-keto acid dehydrogenase complex; dTMP – deoxy-thymidine monophosphate; G6PD – glucose 6-phosphate; GAR – glycinamide ribotide; Glu – glutamate; His – histidine; HMG – hydroxy-methylglutaryl; Ile – isoleucine; Met – methionine; NO – nitric oxide; PC – phosphatidylcholine; Phe – phenylalanine; TAG – triacylglycerol; Thr – threonine; Trp – tryptophan; Tyr – tyrosine; Val – valine.

Name[a]	**Vitamin**[b]	**Catalytic Role**[c]	**Physiological Role**[d]	**Enzymes [Pathway]**[e]	**Deficiency-associated Disease or Condition**[f]
Thiamine diphosphate (ThDP, TPP, TDP)	B_1 (thiamine)	• Aldehyde transfer • Cleavage of bonds involving carbonyl-groups (decarboxylation, transketolation)	• Energy production • Carbohydrate breakdown	• Pyruvate dehydrogenase [pyruvate → ACoA] • α-Ketoglutarate dehydrogenase [Krebs cycle]	• Beriberi • Wernicke-Korsakoff syndrome • Demyelination of nerve cells
			• Fermentation	• Pyruvate decarboxylase [alcoholic fermentation]	
			• α-Keto acids and α-amino acids breakdown	• BCKDC [branched keto and amino acids breakdown]	
			• DNA/RNA synthesis	• Transketolase [pentose-phosphate cycle]	
			• Photosynthesis	• Transketolase [Calvin cycle]	
			• Cholinergic neurotransmission	• Pyruvate dehydrogenase [pyruvate → ACoA → acetylcholine]	

Name[a]	**Vitamin**[b]	**Catalytic Role**[c]	**Physiological Role**[d]	**Enzymes [Pathway]**[e]	**Deficiency-associated Disease or Condition**[f]
Flavin adenine dinucleotide (FAD)	B_2 (riboflavin)	• Redox	• Energy production • Carbohydrate breakdown	• Pyruvate dehydrogenase [pyruvate → ACoA] • Succinate dehydrogenase [Krebs cycle] • Mitochondrial glycerol 3-phosphate dehydrogenase [oxidative phosphorylation]	• Ariboflavinosis
			• Lipid metabolism	• Acyl-CoA dehydrogenase [fatty acid breakdown] • Cytochrome b5 reductase [fatty acid desaturation]	
			• α-Keto acids and α-amino acids breakdown	• BCKDC [branched α-keto and α-amino acids breakdown]	
			• Cellular signaling	• Nitric oxide synthase [Arg → NO]	
			• Antimicrobial activity	• NADPH oxidase [$O_2 \rightarrow H_2O_2$]	
			• Antioxidation	• Glutathione reductase [antioxidation]	
Flavin adenine mononucleotide (FMN)	B_2 (riboflavin)	• Redox	• Energy production	• NADH dehydrogenase [oxidative phosphorylation] • Pyridoxal 5′ phosphate synthase [PLP synthesis]	
			• Carbohydrate synthesis (glyoxylate cycle)	• 2-hydroxyacid oxidase	
			• Metabolism of dicarboxylic acids		
			• Synthesis of secondary metabolites		
			• Cellular signaling	• Nitric oxide synthase [Arg → NO]	

Name[a]	**Vitamin**[b]	**Catalytic Role**[c]	**Physiological Role**[d]	**Enzymes [Pathway]**[e]	**Deficiency-associated Disease or Condition**[f]
Nicotinamide adenine dinucleotide (NAD^+)	B_3 (niacin)	• Redox	• Energy production • Carbohydrate breakdown	• Cytosolic glyceraldehyde 3-phosphate dehydrogenase [glycolysis] • Pyruvate dehydrogenase [pyruvate → ACoA] • Isocitrate, α-KG and malate dehydrogenases [Krebs cycle] • NADH dehydrogenase [oxidative phosphorylation]	• Pellagra • G6PD deficiency (NADPH)
			• Glucose synthesis	• Cytosolic glyceraldehyde 3-phosphate dehydrogenase [gluconeogenesis]	
			• Fermentation	• Lactate dehydrogenase • Alcohol dehydrogenase	
			• Lipid metabolism	• Cytosolic glyceraldehyde 3-phosphate dehydrogenase [TAG and phospholipid synthesis] • β-Hydroxyacyl-CoA dehydrogenase [fatty acid breakdown] • β-HB dehydrogenase [ketone bodies metabolism]	
			• α-Keto acids and α-amino acids breakdown	• Glutamate dehydrogenase • BCKDC [branched α-keto acids and α-amino acids breakdown]	

Name[a]	Vitamin[b]	Catalytic Role[c]	Physiological Role[d]	Enzymes [Pathway][e]	Deficiency-associated Disease or Condition[f]
Nicotinamide adenine dinucleotide phosphate ($NADP^+$)	B_3 (niacin)	• Redox	• Energy production	• Isocitrate dehydrogenase [Krebs cycle]	• Pellagra • G6PD deficiency (NADPH)
			• Carbohydrate metabolism	• G6PD and 6-phosphogluconate dehydrogenase [pentose-phosphate pathway]	
			• Amino acid breakdown and synthesis	• Glutamate dehydrogenase • Glutamate-5-semialdehyde dehydrogenase • Pyrolline-5-carboxylate reductase • Dihydrofolate reductase (indirect)	
			• Lipid biosynthesis	• Fatty acid synthase and malic enzyme [fatty acid synthesis] • Fatty acyl-CoA desaturase [fatty acid desaturation] • HMG-CoA reductase [cholesterol synthesis] • Squalene synthase [cholesterol synthesis] • Squalene mono-oxygenase [cholesterol synthesis] • 5-Hydroxyeicosanoid dehydrogenase [eicosanoid synthesis]	
			• Nucleotide biosynthesis	• G6PD and 6-phosphogluconate dehydrogenase [pentose-phosphate pathway] • Dihydrofolate reductase (indirect)	
			• Signaling	• Nitric oxide synthase	
			• Antioxidation	• Glutathione reductase	
			• Detoxification of drugs and toxins	• P-450 oxidase	
			• Anti-pathogenic	• NADPH oxidase	

Name[a]	Vitamin[b]	Catalytic Role[c]	Physiological Role[d]	Enzymes [Pathway][e]	Deficiency-associated Disease or Condition[f]
Coenzyme A (CoA)	B_5 (pantothenate)	• Acyl group transfer	• Energy production • Carbohydrate breakdown	• Pyruvate dehydrogenase [pyruvate → ACoA] • α-Keto glutarate dehydrogenase [Krebs cycle]	• Paresthesia (uncommon)
			• Lipid metabolism	• Fatty-acyl-CoA synthase [fatty acid synthesis] • Carnitine acyltransferase II [fatty acid breakdown] • Thiolase [fatty acid breakdown, ketone bodies metabolism, cholesterol synthesis] • HMG-CoA reductase [cholesterol synthesis]	
			• α-Keto acids and α-amino acids breakdown	• BCKDC [branched α-keto acids and α-amino acids breakdown] • α-Amino-β-ketobutyrate lyase [Thr breakdown]	
			• Neurotransmitter synthesis	• Choline acetyltransferase [acetylcholine synthesis]	
Pyridoxal phosphate (PLP)	B_6 (pyridoxine)	• $-NH_2$ group transfer • Racemization • Decarboxylation • β/γ-Elimination	• Amino acid metabolism	• Amino transferases [amino acid breakdown] • Aromatic L-amino acid decarboxylase • Serine dehydratase	• Diverse conditions
			• Glycogen breakdown	• Glycogen phosphorylase	
			• Synthesis of bioactive compounds	• Aromatic amino acid decarboxylase [synthesis of catecholamines and serotonin] • Glutamate decarboxylase [GABA synthesis] • Aminolevulinic acid synthase [porphyrins synthesis]	
Biotin	B_7 (H)	• $-CO_2$ group transfer (carboxylations, decarboxylations)	• Glucose synthesis	• Pyruvate carboxylase and Propionyl-CoA carboxylase [gluconeogenesis]	• Neurological and growth disorders (infants)
			• Lipid metabolism	• ACoA carboxylase [fatty acid synthesis]	
			• Amino acid breakdown	• Propionyl-CoA carboxylase [Met/Val/Ile breakdown] • β-Methylcrotonyl CoA carboxylase [Leu breakdown]	

Name[a]	Vitamin[b]	Catalytic Role[c]	Physiological Role[d]	Enzymes [Pathway][e]	Deficiency-associated Disease or Condition[f]
Tetrahydrofolate (THF, FH_4)	B_9 (folic acid)	• Single-carbon groups transfer	• Nucleotide synthesis	• Thymidylate synthase [dTMP biosynthesis] • GAR formyltransferase [purine biosynthesis] • AICAR formyltransferase [purine biosynthesis]	• Megaloblastic anemia • Birth defects (pregnant women) • Elevated homocysteine (risk factor for cardiovascular diseases)
			• Amino acid metabolism • Keeping low homocysteine levels	• Methionine synthase [homocysteine → methionine] • Serine hydroxymethyl transferase [glycine → serine] • Glu formiminotransferase [His → Glu]	
			• Signaling	• Nitric oxide synthase	
Cobalamin	B_{12}	• Molecular rearrangements (radical catalysis) • $-CH_3$ group transfer • Dehalogenation	• Glucose synthesis	• Methylmalonyl-CoA mutase [fatty acids → succinyl-CoA → glucose]	• Megaloblastic anemia (*via* THF deficiency) • Methylmalonic-related pathologies (acidemia, myelin destabilization) • Elevated homocysteine (risk factor for cardiovascular diseases)
			• DNA synthesis	• Ribonucleotide reductase [DNA synthesis]	
			• Amino acid metabolism • Keeping low homocysteine levels	• Methionine synthase [homocysteine → methionine] • Methylmalonyl-CoA mutase [Met/Val/Ile breakdown]	
			• Lipid metabolism	• Methylmalonyl-CoA mutase [fatty acids → succinyl-CoA] • Glycerol dehydratase [glycerolipid metabolism]	
			• Folic acid regeneration	• Methionine synthase [methyl-THF → THF]	
Ascorbic acid	C	• Hydroxylation • Redox	• Collagen synthesis • Antioxdiation	• Prolyl/Lysyl hydroxylase [collagen synthesis] • ε-*N*-trimethyl-L-lysine hydroxylase [carnitine synthesis] • Dopamine β-hydroxylase [norepinephrine synthesis]	• Scurvy
Tetrahydrobiopterin (TH_4)		• $-OH$ group transfer • Redox	• Amino acids metabolism	• Phe/Tyr/Trp hydroxylases	• Alzheimer's disease • Parkinson's disease • Depression
			• Neuronal signaling	• Phe/Tyr/Trp hydroxylases [catecholamine and serotonin synthesis] • Nitric oxide synthase [NO synthesis]	

Name[a]	**Vitamin**[b]	**Catalytic Role**[c]	**Physiological Role**[d]	**Enzymes [Pathway]**[e]	**Deficiency-associated Disease or Condition**[f]
Coenzyme Q (CoQ, ubiquinone)		• Redox	• Energy production	• Electron transport chain, mitochondrial glycerol 3-phosphate dehydrogenase [oxidative phosphorylation]	
			• Antioxidation (non-enzymatic)		
Lipoic acid		• Redox • Acyl group transfer	• Energy production • Carbohydrate breakdown	• Pyruvate dehydrogenase [pyruvate → ACoA] • α-Ketoglutarate dehydrogenase [Krebs cycle] • Transketolase [pentose-phosphate cycle]	
			• α-Keto acids and α-amino acids breakdown	• BCKDC [branched keto and amino acids breakdown]	
			• Antioxidation		
Menaquinone	K_2	• γ-Carboxylation of glutamate residues	• Blood clotting	• γ-Glutamylcarboxylase [Glu carboxylation]	• Hemorrhagic syndrome
			• Antioxidation		
			• Bone formation		
S-Adenosyl-methionine (SAM, AdoMet)		• $-CH_3$ group transfer • Aminopropyl group transfer • Radical catalysis	• DNA/RNA methylation	• DNA/RNA methyltransferases	
			• Lipid synthesis	• PEMT [PC synthesis]	
			• Amino acid metabolism	• Methylases [homocysteine synthesis] • Methionine adenosyltransferse [methionine breakdown]	
			• Neurotransmission	• PNMT [epinephrine synthesis]	
			• Polyamines synthesis	• AdoMet decarboxylase (spermidine synthesis)	