

**TABLE 2.8 Cellular and physiological roles of key cationic metals in living organisms** (<sup>[512,513]</sup> **and references therein**). Examples of proteins (in italics), processes, or structural motifs associated with some of the roles are in parentheses. Abbreviations: CCO – cytochrome c oxidase; CP450 – cytochrome P450; GS – glutamine synthetase; GT – glycosyltransferase; ND – NADH dehydrogenase; PC – plastocyanin; PEPCK – phosphoenolpyruvate carboxykinase; PK – pyruvate kinase; SD – succinate dehydrogenase; SOD – superoxide dismutase.

<b>Metal</b>	<b>Cellular and Physiological Roles</b>	<b>Nutritional Deficiency</b>
Fe <sup>2+/3+</sup> (iron)	<ul style="list-style-type: none"> <li>• Enzymatic catalysis (electron transport, substrate or cofactor binding and stabilization)</li> <li>• Energy metabolism (<i>ND</i>, <i>SD</i>) and production (electron transport chain)</li> <li>• DNA synthesis (<i>ribonucleotide reductase</i>)</li> <li>• Photosynthesis (electron transport chain)</li> <li>• Oxygen transport (<i>hemoglobin</i>, <i>myoglobin</i>)</li> <li>• Nitrogen fixation</li> <li>• Anti-oxidation (<i>catalase</i>, <i>peroxidases</i>)</li> <li>• Detoxification of drugs and toxins (<i>CP450</i>)</li> <li>• Brain development in infants</li> <li>• Nitrogen fixation by certain bacteria (<i>nitrogenase</i>)</li> </ul>	Anemia
Cu <sup>+2+</sup> (copper)	<ul style="list-style-type: none"> <li>• Enzymatic catalysis (electron transport, substrate or cofactor binding and stabilization)</li> <li>• Energy production (<i>CCO</i> in electron transport chain)</li> <li>• Synthesis of connective tissue proteins, red blood cells, melanin, certain hormones and neurotransmitters</li> <li>• Iron metabolism (<i>ceruloplasmin</i>)</li> <li>• Bone mineralization</li> <li>• Anti-oxidation (<i>SOD</i>)</li> <li>• Oxygen transport in invertebrates (<i>hemocyanin</i>)</li> <li>• Photosynthesis in plants (<i>PC</i> in electron transport chain)</li> </ul>	Hematological and neurological disorders (very rare)

Metal	Cellular and Physiological Roles	Nutritional Deficiency
Mg <sup>2+</sup> (magnesium)	<ul style="list-style-type: none"> <li>• Enzymatic catalysis (substrate or cofactor binding, stabilization and activation)</li> <li>• DNA replication, repair, and stabilization</li> <li>• Energy production and biosynthesis</li> <li>• Nerve and muscle function</li> <li>• Formation of bones and teeth</li> <li>• Photosynthesis in plants (<i>chlorophyll</i>)</li> </ul>	Neuromuscular, cardiovascular and metabolic dysfunction (rare)
Zn <sup>2+</sup> (zinc)	<ul style="list-style-type: none"> <li>• Enzymatic catalysis (substrate or cofactor binding, stabilization and activation in over 300 enzymes <sup>[514]</sup>)</li> <li>• DNA replication and transcription (zinc fingers in <i>DNA/RNA polymerases</i> and <i>transcription factors</i>)</li> <li>• Stabilization of cell membranes</li> <li>• Development of skeletal and reproductive systems</li> <li>• Wound healing (<i>matrix enzymes and proteins</i>)</li> <li>• Immune response</li> <li>• Brain function and learning</li> <li>• Blood pH buffering and CO<sub>2</sub> transport (<i>carbonic anhydrase</i>)</li> <li>• Cellular signaling and neurotransmission</li> <li>• Programmed cell death</li> </ul>	Multiple, from hair loss, impotence and diarrhea to impaired growth and development, and susceptibility to infections
Ca <sup>2+</sup> (calcium)	<ul style="list-style-type: none"> <li>• Enzymatic catalysis (substrate or cofactor activation)</li> <li>• Cellular signaling (e.g., <i>calmodulin</i>)</li> <li>• Muscle contraction</li> <li>• Neurotransmission</li> <li>• Blood clotting (<i>coagulation factors</i>)</li> <li>• Structural element in bones and teeth</li> </ul>	<ul style="list-style-type: none"> <li>• Rickets</li> <li>• Clotting problems</li> <li>• Osteoporosis</li> </ul>
Mn <sup>2+</sup> (manganese)	<ul style="list-style-type: none"> <li>• Enzymatic catalysis (substrate or cofactor binding and stabilization)</li> <li>• Energy production and biosynthesis (<i>PK, PEPCK, GS</i>)</li> <li>• Nitrogen metabolism (<i>arginase</i> in urea cycle)</li> <li>• Anti-oxidation (<i>SOD</i>)</li> <li>• Wound healing (<i>prolidase</i> in collagen formation)</li> <li>• Bone development (<i>GT</i> in proteoglycan synthesis)</li> <li>• Photosynthesis in plants (water splitting center)</li> </ul>	<ul style="list-style-type: none"> <li>• Bone demineralization</li> <li>• Impaired growth</li> </ul>
Co <sup>2+</sup> (cobalt)	<ul style="list-style-type: none"> <li>• Enzymatic catalysis (substrate or cofactor binding and stabilization)</li> <li>• Vitamin B<sub>12</sub>-dependent processes, e.g., DNA synthesis and amino acid metabolism</li> </ul>	—

Metal	Cellular and Physiological Roles	Nutritional Deficiency
$\text{Mo}^{3+/4+/6+}$ (molybdenum)	<ul style="list-style-type: none"> <li>• Enzymatic catalysis (electron transport, substrate binding, stabilization and activation)</li> <li>• Purine nucleotides breakdown (<i>xanthine oxidase</i>)</li> <li>• Amino acid metabolism (<i>sulfite oxidase</i>)</li> <li>• Metabolism and clearance of drugs and toxins (<i>aldehyde oxidase</i>)</li> <li>• Nitrogen fixation by certain bacteria (<i>nitrogenase</i>)</li> </ul>	—
$\text{Cr}^{3+}$ (chromium)	<ul style="list-style-type: none"> <li>• Glucose transport into cells (by potentiation of insulin action)</li> </ul>	<ul style="list-style-type: none"> <li>• Impaired glucose tolerance</li> <li>• Increased insulin requirement</li> <li>• Diabetes</li> </ul>