

1. Most widely needed trace elements are Fe, Zn, and Mn. Iron (Fe) is present in ferredoxin and cytochrome and is an important cofactor. Iron also plays a regulatory role in some fermentation processes (e.g., iron deficiency is required for the excretion of riboflavin by *Ashbya gosypii* and iron concentration regulates penicillin production by *Penicillium chrysogenum*). Zinc (Zn) is a cofactor for some enzymes and also regulates some fermentations such as penicillin fermentation. Manganese (Mn) is also an enzyme cofactor and plays a role in the regulation of secondary metabolism and excretion of primary metabolites.

2. Trace elements needed under specific growth conditions are Cu, Co, Mo, Ca, Na, Cl, Ni, and Se. Copper (Cu) is present in certain respiratory-chain components and enzymes. Copper deficiency stimulates penicillin and citric acid production. Cobalt (Co) is present in corrinoid compounds such as vitamin B₁₂. Propionic bacteria and certain methanogens require cobalt. Molybdenum (Mo) is a cofactor of nitrate reductase and nitrogenase and is required for growth on NO₃ and N₂ as the sole source of nitrogen. Calcium (Ca) is a cofactor for amylases and some proteases and is also present in some bacterial spores and in the cell walls of some cells, such as plant cells.

Sodium (Na) is needed in trace amounts by some bacteria, especially by methanogens for ion balance. Sodium is important in the transport of charged species in eucaryotic cells. Chloride (Cl⁻) is needed by some halobacteria and marine microbes, which require Na⁺, too. Nickel (Ni) is required by some methanogens as a cofactor and Selenium (Se) is required in formate metabolism of some organisms.

3. Trace elements that are rarely required are B, Al, Si, Cr, V, Sn, Be, F, Ti, Ga, Ge, Br, Zr, W, Li, and I. These elements are required in concentrations of less than 10⁻⁶ M and are toxic at high concentrations, such as 10⁻⁴ M.

Some ions such as Mg²⁺, Fe³⁺, and PO₄³⁻ may precipitate in nutrient medium and become unavailable to the cells. *Chelating agents* are used to form soluble compounds with the precipitating ions. Chelating agents have certain groups termed *ligands* that bind to metal ions to form soluble complexes. Major ligands are carboxyl (—COOH), amine (—NH₂), and mercapto (—SH) groups. Citric acid, EDTA (ethylenediaminetetraacetic acid), polyphosphates, histidine, tyrosine, and cysteine are the most commonly used chelating agents. Na₂ EDTA is the most common chelating agent. EDTA may remove some metal ion components of the cell wall, such as Ca²⁺, Mg²⁺, and Zn²⁺ and may cause cell wall disintegration. Citric acid is metabolizable by some bacteria. Chelating agents are included in media in low concentrations (e.g., 1 mM).

Growth factors stimulate the growth and synthesis of some metabolites. Vitamins, hormones, and amino acids are major growth factors. Vitamins usually function as coenzymes. Some commonly required vitamins are thiamine (B₁), riboflavin (B₂), pyridoxine (B₆), biotin, cyanocobalamin (B₁₂), folic acid, lipoic acid, *p*-amino benzoic acid, and vitamin K. Vitamins are required at a concentration range of 10⁻⁶ M to 10⁻¹² M. Depending on the organism, some or all of the amino acids may need to be supplied externally in concentrations from 10⁻⁶ M to 10⁻¹³ M. Some fatty acids, such as oleic acid and sterols, are also needed in small quantities by some organisms. Higher forms of life, such as animal and plant cells, require hormones to regulate their metabolism. Insulin is a common hormone for animal cells, and auxin and cytokinins are plant-growth hormones.