2.16: The Natural Catalysts

Table 2.1 lists metalloenzymes that catalyze hydrolytic and related reactions. According to the above guidelines the hydrolysis of peptide bonds is catalyzed by enzymes called peptidases that belong to the class of hydrolases (according to the official enzyme classification). Two peptidases (carboxypeptidase and thermolysin) are known in great detail, because their structures have been elucidated by high-resolution x-ray crystallography. They share many features; e.g., their metal ions coordinate to the same kind of protein residues. A discussion of the possible mechanism of carboxypeptidase A will be given in Section V.A. Metallopeptidases are zinc enzymes: generally they are single polypeptide chains with molecular weights in the range 30 to 40 kDa. Metallohydrolases of carboxylic and phosphoric esters are also often zinc enzymes. Alkaline phosphatase will be described in Section V.B as a representative of this class. Magnesium is sometimes involved in hydrolytic reactions. This is common when phosphate groups are involved, probably because the affinity of Mg^{2+} for phosphate groups is high.[1] However, hydrolytic reactions can be performed by other systems (not treated here) like urease, which contains nickel(II),[2] or acid phosphatase, which contains two iron ions,[3] or aconitase, which contains an Fe_4S_4 cluster.[4]

Table 2.1 - Representative metalloenzymes catalyzing hydrolytic and related reactions

Enzyme	Metal(s)	Function
Carboxypeptidase	Zn^{2+}	Hydrolysis of C-terminal peptide residues
Leucine aminopeptidases	Zn^{2+}	Hydrolysis of leucine N-terminal peptide residues
Dipeptidase	Zn^{2+}	Hydrolysis of dipeptides
Neutral protease	Zn^{2+}, Ca^{2+}	Hydrolysis of peptides
Collagenase	Zn^{2+}	Hydrolysis of collagen
Phospholipase C	Zn^{2+}	Hydrolysis of phospholipids
β-Lactamase II	Zn^{2+}	Hydrolysis of β-lactam ring
Thermolysin	Zn^{2+}, Ca^{2+}	Hydrolysis of peptides
Alkaline phosphatase	Zn^{2+}, Mg^{2+}	Hydrolysis of phosphate esters
Carbonic anhydrase	Zn^{2+}	Hydration of CO_2
α-Amylase	Ca^{2+}, Zn^{2+}	Hydrolysis of glucosides
Phospholipase A_2	Ca^{2+}	Hydrolysis of phospholipids
Inorganic pyrophosphatase	Mg^{2+}	Hydrolysis of pyrophosphate
ATPase	Mg^{2+}	Hydrolysis of ATP
Na^+ - K^+ - ATPase	Na^+, K^+	Hydrolysis of ATP with transport of cations
Mg^{2+} - Ca^{2+} - ATPase	Mg^{2+}, Ca^{2+}	Hydrolysis of ATP with transport of cations
Phosphatases	Mg^{2+}, Zn^{2+}	Hydrolysis of phosphate esters
Creatine kinase	M^{2+}	Phosphorylation of creatine
Pyruvate kinase	M^+, M^{2+}	Dephosphorylation of phosphoenolpyruvate
Phosphoglucomutase	Mg^{2+}	Phosphate transfer converting glucose-I-phosphate to glucose-6-phosphate
DNA polymerase	Mg^{2+} (Mn^{2+})	Polymerization of DNA with formation of phosphate esters
Alcohol dehydrogenase	Zn^{2+}	Hydride transfer from alcohols to NAD^+

Examples of enzymes catalyzing nucleophilic addition of OH^- (other than hydrolysis) and H^- are carbonic anhydrase and alcohol dehydrogenase. Both are zinc enzymes. In the official biochemical classification of enzymes, carbonic anhydrase belongs to the class of lyases. Lyases are enzymes that cleave C-C, C-O, C-N, or other bonds by elimination, leaving double bonds, or conversely add groups to double bonds. Carbonic anhydrase has a molecular weight around 30 kDa, and is among the most-studied metalloenzymes. It catalyzes the deceivingly simple CO_2 hydration reaction. The subtleties of its biological function, unraveled by a combination of techniques, make it an ideal example for bioinorganic chemistry. Section IV is fully dedicated to this enzyme. Alcohol dehydrogenase is a 90-kDa enzyme that catalyzes the reversible transfer of a hydride ion from alcohols to NAD^+. Although it is a redox enzyme (in fact, classified as an oxidoreductase) and not a hydrolytic one, it will illustrate a different use that Nature makes of zinc to catalyze nucleophilic attack at carbon (Section V.C). Finally, the enzymatic transfer of organic radicals by enzymes involving coenzyme B_{12} will be briefly considered.
