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CHAPTER 1

Role of Metals and Metalloids in Redox Biology[1]

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1.1 INTRODUCTION

Oxidation-reduction (redox) reactions play a critical role in biological systems [1]. These involve the basic functions of life ranging from respiration to metabolism. Alterations in these redox reactions may lead to changes in physiological processes and promote progression of various diseases that can even prove fatal to the body [2]. An imbalance in homeostasis of reactive oxygen species (ROS) is the main cause of several diseases [3,4]. Basically there are two types of ROS: (a) primary ROS, generated via metabolic process or after oxygen activation by physical irradiation, and (b) secondary ROS, generated by primary ROS via interacting with enzyme/metal-catalyzed reaction [5]. Cellular antioxidant defense systems damage signaling pathways and biomolecules when overwhelmed with high levels of free radical production. Imbalance between free radicals and antioxidants in the human body is termed as oxidative stress, which takes place as a result of increased ROS production and decreased elimination [6]. Oxidative stress is frequently implicated in a number of biochemical physiological and pathological reactions and pathways [6]. Pathological processes such as cardiovascular dysfunction, diabetes, atherosclerosis, inflammation, and apoptosis occur during oxidative stress [6].

In human physiology, metals and metalloids play pivotal roles as active molecules that participate in several physiological processes including enzyme–substrate reaction, metal transporter system, and redox signaling pathway. Most of the metals are required by the human body at optimum levels since high concentration of metals is toxic for the body [7]. Heavy metals such as lead and mercury have been proven to be fatal to human health when ingested through food. These heavy metals can access the human body through numerous routes including skin, respiration, and contaminated water or food. Some of these metals react with other constituents of the body such as oxygen and chloride. The reaction of these metals inside the body eventually produces ROS that causes oxidative stress which ultimately leads to impaired kidney function, neurological diseases, endocrine diseases, and different types of cancers [8].

High concentration of iron in the body gives rise to free radicals that overpower the cellular antioxidant defense mechanisms, degrade biomolecules, and dysregulate cell signaling pathways [9]. Copper has the potential to induce oxidative stress either by catalyzing ROS formation through a Fenton-like reaction or by significantly decreasing the glutathione levels [10]. Chromium is considered as an occupational carcinogen that not only targets the lungs but also leads to adverse health conditions including gastrointestinal symptoms, hypotension, hepatic and renal failures, and sometimes stomach tumors [11]. The trivalent forms of the metalloid arsenic (As^{3+}) are the most toxic and react with the thiol groups of proteins leading to neurological disorders [12]. Hallmarks of chronic exposure to arsenic include skin lesions, peripheral neuropathy, and anemia. Zinc deficiency is associated with poor diet and related to increased oxidative damage that results in increased lipid, protein, and DNA oxidation [13]. Cadmium enters the human body through the lungs and skin, and accumulates in the intestine and kidneys [14]. Cadmium-induced testicular damage and necrosis have been well documented. Lead damages cellular components via increased oxidative stress through direct ROS generation and *via* depletion of the cellular antioxidant pool [10]. Roles of some important metals and metalloids in redox biology and their implications in physiology and pathological states will be discussed in this chapter.

1.2 IRON

Iron is one of the most essential trace elements of the earth which exhibits biological activities from bacteria to mammals. It has a wide range of oxidation states, i.e., –2 to +6, but biologically active oxidation states are +2 and +3. Fe^{+2} is soluble in mostly all biological fluids. Iron acts as the major metal component in many proteins (hemoglobin) and enzymes, and also plays important