PREFACE

Zinc is one of the most abundant transition metals in the human body, and it has various benefits as an essential trace element in the regulation of the living body. Nutritional deficiency of zinc is known to induce many chronic diseases such as immune system disorders, rheumatoid arthritis, diabetes, obesity, atherosclerosis, cancers, bone growth retardation, osteoporosis and others. This book introduces the recent topics concerning the characteristics, uses and benefits of zinc. This book will be helpful in research development and also in the understanding of the various physiological-pathophysiological roles of zinc.

Chapter 1 - A study of the effects of Inhibition Characteristic of Vegetable Extracts on the corrosion susceptibility of locally processed Al-base alloy in some media concentrations with varying volume of vegetable extracts (*Telferia occidentalis* and *Piper guinenses*) have been carried out. Virgin aluminum alloys containing 1.0% and 2.0% zinc were cast and machined to cylindrical coupons of initial surface area averaging 11.64cm^2. The pre-weighed samples were carefully immersed into 0.5 M and 1.0 M of the acid containing 50 cm^3 and 100 cm^3 of the extracts, respectively. The set-ups were allowed to stand for 28 days with a set withdrawn weekly for corrosion rate characterization. The trend of the results obtained were in tandem with that of passivating metals (or alloys) in simulated environments of initial steep rise in corrosion rate accompanied by a gradual decline as the exposure time increased. The vegetable extracts showed inhibition potentials with pronounced effects at higher extract concentrations. The best inhibiting property is found in Telferia occidentalis then, Piper guinenses.

Chapter 2 - A feasibility of ZnO-based materials was evaluated for a next-generation anode of Li-ion batteries. Composite thick-film electrodes of ZnO

and Si were prepared by a gas-deposition method using an Si powder and a radial-shaped ZnO powder synthesized by a precipitation method. We evaluated anode performance of the composite electrodes, comparing with electrochemical properties of a ZnO electrode without Si. After the 20th cycle, the ZnO electrode exhibited a stable cyclability and a moderate discharge capacity of 160–220 mA h g^{-1}. The ZnO/Si composite electrode exhibited a better cycle stability after the 20th cycle and relatively-large discharge capacities exceeding the theoretical capacity of graphite in practical use until the 370th cycle. In contrast, the composite electrode containing of crushed ZnO showed flatter surface morphology and lower electrode performance in comparison with that using the radial-shaped ZnO. These results revealed that microstructure of the radial-shaped ZnO is very favorable for improving efficiencies of electrode reactions due to its high surface area, and is effective in accommodating the strains induced by Li-insertion and Li-extraction in/from Si.

Chapter 3 - Zinc is a vital element in the nutrition of human beings, animals and plants. Although most experimental data have demonstrated the adverse effects of Zn deficiency on human and animal health, there is still evidence to support the hypothesis that Zn toxicity can also result in deleterious health effects. Conflicting views have been expressed regarding the role of Zn in carcinogenesis. Some studies emphasize the fact that Zn deficiency causes cancers, while others highlight that Zn is involved in tumour growth and development of neoplastic transformation. These conflicting observations suggest that the role of Zn in different organs may be different. Based on the results of a micro-beam synchrotron X-ray fluorescence technique (micro-SRIXE) applied to the quantitative analysis of Zn, we correlated Zn concentration levels with the clinical stage of prostate cancer at the time of operation (described by the Gleason grade system). Serial sections of prostate tissues were collected from patients undergoing radical prostatectomy. Our results seem to be valuable in light of determination of the potential changes in Zn concentration as a diagnostic marker and its etiologic involvement in the different stages of prostate diseases.

Chapter 4 - Atherosclerosis is a chronic inflammatory process, triggered by the presence of lipids in the vascular wall. The disease is associated with complex interactions among inflammatory cells, vascular elements, and lipoproteins, along with the expression of selected adhesion molecules and inflammatory cytokines. The strategy for protection against atherosclerosis has been a subject of intense research over the past decades. The important role zinc has been recognized in various biochemical and physiological functions

Early evidence indicates that zinc deficiency can cause growth retardation, delayed sex maturation, depressed immune response, and abnormal cognitive functions. Nutritional zinc deficiency is common in the developing countries. 30-40% of the elderly populations are estimated to have mild to modest zinc deficiency in the USA. Conditioned zinc deficiency is also present in many chronic diseases such as rheumatoid arthritis, diabetes, and cancers. The evidence from experimental, clinical, and epidemiological studies suggests that zinc has an atheroprotective function, potentially due to its anti-inflammatory and anti-oxidative stress effects, and other functions. However, the exact mechanism of zinc action in atherosclerosis is not fully understood. A large number of studies demonstrate that zinc deficiency increases the levels of inflammatory cytokines and oxidative stress, and induces apoptosis and endothelial cell dysfunction. Zinc supplementation reverses these adverse effects. Our recent *cell culture* studies have also demonstrated that zinc decreases the productions of oxidative stress and inflammatory cytokines, vascular cell adhesion molecule-1 (VCAM-1), as well as oxLDL-, and/or LPS-induced NF-κB activation in human monocyte-like and vascular endothelial cells. Our normal human subject study shows that zinc supplementation decreases the productions of oxidative stress biomarkers, TNF-α and IL-1β mRNAs, as well as TNF-α-induced NF-κB activation in isolated peripheral blood mononuclear cells (PMNC), compared to the placebo group. Normal elderly subjects show decreased levels of plasma and lymphocyte zinc, and increased generation of inflammatory cytokines and adhesion molecules in isolated PMNC cells, compared to normal young adult. Six months of zinc supplementation in normal elderly subjects increased plasma zinc and anti-oxidant capacity, and decreased plasma levels of C-reactive protein (CRP), IL-6, VCAM-1, MCP-1, and oxidative stress biomarkers, compared to the placebo-supplemented elderly subjects; this is consistent with the decreased incidence of infection. The data confirmed that zinc decreases the productions of inflammatory cytokines, oxidative stress, and atherosclerosis-associated biomarkers, suggesting that zinc may play a protective role in atherosclerosis through inhibition of inflammation and oxidative stress. In this chapter, we will discuss, in-depth, the molecular mechanisms of zinc action on the development and progression of atherosclerosis.

Chapter 5 - Zinc has recently emerged as an important trace element, capable of conferring cardioprotection and a variety of other benefits in the cardiovascular system and elsewhere. The events that occur subsequent to coronary artery occlusion are termed myocardial ischemia/reperfusion denoting that these are distinct phases of cellular injury with ATP depletion,

lactate accumulation and acidosis observed during ischemia and production of reactive oxygen species during reperfusion. Cell death during myocardial ischemia/reperfusion occurs by necrosis and apoptosis, both regulated by stress signals and results in "cardiac wasting." Although the mechanisms by which zinc accomplishes cardiac benefits remain largely unclear, proposals include both direct and indirect effects on an array of intracellular targets such as adenosine receptor, ErbB2, NADPH oxidase, PKC, Akt, GSK-3β and mPTP culminating in anti-apoptotic effects and improved functional recovery of contractile function. Interestingly, cardioprotection by zinc is manifested only in the presence of a lipophilic ionophore, such as pyrithione, in isolated neonatal and adult rat cardiac myocytes subjected to simulated ischemia /reperfusion, Langendorff isolated rat heart perfusion and ischemia/reperfusion injury in myocardial infarction. Thus, although great potential exists for zinc-based therapeutics, a number of questions remain. This review will discuss the available literature pertaining to zinc homeostasis in the myocardium and provide novel insights into the underlying molecular mechanisms towards better understanding of the therapeutic effect of zinc during ischemia /reperfusion. Attempts are made to identify the gaps in basic and translational science in the development of zinc ionophores as potential therapeutic compounds in the setting of myocardial ischemia reperfusion injury.

Chapter 6 - The trace element zinc is ubiquitous in the human body. It has catalytic, structural or regulatory functions in more than 300 enzymes. The importance of an adequate zinc intake is marked by its impact on biological functions such as DNA replication, RNA transcription, signal transduction and redox regulation. In particular, cells of the innate and adaptive immune system depend on zinc ions, e.g., for proliferation, differentiation, and the production of cytokines. Hence, a deficiency affects the susceptibility to infections and the development of inflammation and autoimmunity. Zinc deficiency is mainly caused by malnutrition, but can also occur as a result of genetic defects of zinc transport proteins (e.g., in *Acrodermatitis enteropathica*) or secondary to diseases such as type 2 diabetes or diarrhea. Although a variety of studies have been performed regarding the therapeutic usefulness of zinc supplementation the effects on several diseases remain unclear. Contradictory outcomes between different studies are caused by administration of diverse zinc salts and their varying bioavailability, the problematic determination of the patient's zinc status by plasma or serum zinc level, and differences in dosage and duration of the supplementation. For example, zinc is only effective in the treatment of the common cold if given within 24h of the onset of symptoms. Furthermore, zinc supplementation was shown to be beneficial for decreasing

the frequency of diarrhea and pneumonia, diseases which contribute significantly to the high infant mortality in developing countries. On the other hand, zinc excess may result in increased susceptibility to infections by inhibiting leukocyte function. This review gives an overview on populations at risk of zinc deficiency, available supplements, and the impact of zinc administration on immune cells and several diseases.

Chapter 7 - Zinc is known as an essential nutritional factor in the growth of the human and animals. Bone growth retardation is a common finding in various conditions associated with dietary zinc deficiency. Bone zinc content has been shown to decrease in aging, skeletal unloading and postmenopausal conditions, suggesting its role in bone disorder. Zinc has been demonstrated to have a stimulatory effect on osteoblastic bone formation and mineralization; the metal directly activates aminoacyl-tRNA synthetase, a rate-limiting enzyme at translational process of protein synthesis, in the cells, and it stimulates cellular protein synthesis. Zinc has been shown to stimulate gene expression of the transcription factors runt-related transcription factor 2 (Runx 2) that is related to differentiation into osteoblastic cells. Moreover, zinc has been shown to inhibit osteoclastic bone resorption due to inhibiting osteoclast-like cell formation from bone marrow cells and stimulating apoptotic cell death of mature osteoclasts. Zinc has a suppressive effect on the receptor activator of nuclear factor (NF)-κB ligand (RANKL)-induced osteoclasto-genesis. Zinc transporter has been shown to express in osteoblastic cells and osteoclastic cells. Zinc protein is invloved in transcription. The intake of dietary zinc causes an increase in bone mass. β-Alanyl-L-histidinato zinc (AHZ) is a zinc compound, in which zinc is chelated to β-alanyl-L-histidine. The stimulatory effect of AHZ on bone formation is more intensive than that of zinc sulfate. Zinc acexamate has also been shown to have a potent-anabolic effect on bone. The oral administration of AHZ or zinc acexamate has the restorative effect on bone loss under various pathophysiological conditions including aging, skeletal unloading, aluminium bone toxicity, calcium- and vitamin D-deficiency, adjuvant arthritis, estrogen deficiency, diabetes, and fracture healing. Zinc compounds may be designed as new supplymentation factor in the prevention and therapy of osteoporosis.