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The structural and functional effects of Hg(II) and Cd(II) on lipid model systems and human erythrocytes: A review

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ABSTRACT

The anthropogenic mobilization of mercury and cadmium into the biosphere has led to an increased and ineludible entry of these metals into biological systems. Here we discuss the impact of Hg(II) and Cd(II) on lipid model systems and human erythrocytes from a biophysical perspective. After a brief introduction to their implications on human health, studies that have investigated the effects of Hg(II) and Cd(II) on lipid model systems and human erythrocytes are discussed. In terms of lipids as toxicological target sites, predominantly variations in lipid head groups have been the source of investigation. However, as research in this field progresses, the effects of Hg(II) and Cd(II) on other structural features, such as acyl chain length and unsaturation, and other important lipid components and complex biomimetic lipid mixtures, will require further examinations.

This review provides an analysis of what has been learned collectively from the diverse methodologies and experimental conditions used thus far. Consequently, there is a need for more comprehensive and thorough investigations into the effects of Hg(II) and Cd(II) on lipid membranes under consistent experimental conditions such as pH, ionic strength, temperature, and choice of lipid model system.

Contents

Abbreviations: SM, sphingomyelin; PC, phosphatidylcholine; PE, phosphatidylethanolamine; (PS), phosphatidylserine; PG, phosphatidylglycerol; PA, phosphatidic acid; POPC, 1-palmitoyl-2-oleoyl-*sn*-phosphatidylcholine; POPE, 1-palmitoyl-2-oleoyl-*sn*-phosphatidylethanolamine; POPS, 1-palmitoyl-2-oleoyl-*sn*-phosphatidylserine; DMPC, dimyristoylphosphatidylcholine; DMPE, dimyristoylphosphatidylethanolamine; DMPS, dimyristoylphosphatidylserine; DMPA, dimyristoylphosphatidic acid; DMPG, dimyristoylphosphatidyl; DOPC, dioleoylphosphatidylcholine; DOPE, dioleoylphosphatidylethanolamine; DPPC, dipalmitoylphosphatidylcholine; DPPS, dipalmitoylphosphatidylserine; DPPA, dipalmitoylphosphatidic acid; DPPG, dipalmitoylphosphatidylglycerol; DPhyPC, diphytanoylphosphatidylcholine; BBPS, bovine brain phosphatidylserine; BSPS, bovine spinal chord phosphatidylserine; LUVs, large unilamellar vesicles; MLVs, multilamellar vesicles; DPH, 1,6-diphenyl-1,3,5-hexatriene; DCP, dicetylphosphate; SA, stearylamine; GP, generalized polarization; BLM, black lipid membrane; NMR, nuclear magnetic resonance; π–A, surface–pressure mean molecular area; GIXD, grazing incidence X-ray diffraction; XR, X-ray reflectivity.

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1. Introduction

Industrialization and anthropogenic activities since the 1800s have gradually increased the mobilization of heavy metals, such as mercury and cadmium, from the earth's crust into the biosphere (Pacyna, 1996). As a result of the rising levels of toxic metals in the environment, certain organisms are exposed to higher daily doses than ever before. The increased net influx of toxic metals into living systems could disrupt certain biological functions. Indeed, mercury and cadmium have been associated with an increased prevalence of cardiovascular disease (Peters et al., 2010; Virtanen et al., 2007) and kidney damage (Järup, 2003; World Health Organization, 1992). The predominant route of entry for mercury and cadmium into the body is via the digestive tract (Gailer, 2007). Cadmium is thought to pass through the intestinal membrane by the divalent metal transporter 1, especially during iron deficiency (Park et al., 2002). This protein has also been implicated in the transport of other metals across the apical membrane of enterocytes that line the small intestine (Park et al., 2002; Gunshin et al., 1997). Competition between various metals or metal ions determines the extent and types of metals transported across the small intestine. As a result, deficiencies in iron or zinc could facilitate the passage of toxic metals across the intestinal lining into the bloodstream. This is an important aspect, since any deficiency in essential elements like iron and zinc may increase the absorption of toxic metals into the bloodstream (Park et al., 2002; Gunshin et al., 1997).

Once in the bloodstream, Hg(II) and Cd(II) can interact with various blood and cellular components (Fig. 1) such as human serum albumin (HSA) (Li et al., 2007), erythrocyte membrane proteins, glutathione, and intracellular proteins and metabolites (Trisak et al., 1990; Lou et al., 1991). Since it is well established that both Hg(II) and Cd(II) have a strong affinity for sulfhydryl groups (Hughes, 1957; Rabenstein et al., 1983; Rabenstein, 1989; Gwoździński, 1995; Bridges and Zalups, 2005), an appreciable amount of work has been directed directed toward better understanding the binding of Hg(II) and Cd(II) to endogenous proteins and metabolites. Comparatively less information, however, is available on how these toxic metals may adversely impact the cellular membrane.

Several studies show that environmental pollutants, such as cadmium and mercury, are nephrotoxic (Järup, 2003; Järup et al., 1998; Madden and Fowler, 2000; Zalups, 2000; Satarug et al., 2010) and cause adverse health effects in humans (Järup, 2003; Satarug et al., 2010; Tchounwou et al., 2003). For the general population, Hg (II) and Hg^0 exposure is primarily by dental amalgam fillings that contain mercury (World Health Organization, 1991; Barregard et al., 1995; Sallsten et al., 1996; Clarkson and Magos, 2006), but may also involve the utilization of skin-lightening cosmetic creams (McRill et al., 2000; Sin and Tsang, 2003; Chan, 2011). Dermal absorption of Hg(II) may occur across the epidermis (Chan, 2011; Park and Zheng, 2012) via the sebaceous gland, sweat glands, and hair follicles (Fig. 2). The organ which typically contains the highest concentration of Hg(II) is the kidney from absorption through the gastrointestinal tract (Park and Zheng, 2012). In addition, the oxidation of Hg^{2+} to Hg^0 by the enzyme catalase, a common mammalian intracellular protein, is also carried out by some bacteria found in the oral cavity and the gastrointestinal tract (Barkay et al., 2003). The resistance of bacteria to toxic metals has been reviewed (Summers, 2002), and non-occupational exposure to Hg(II) is most commonly via 'silver' dental amalgams, which can contain up to 50% of mercury. Exposure of bacteria to toxic metals

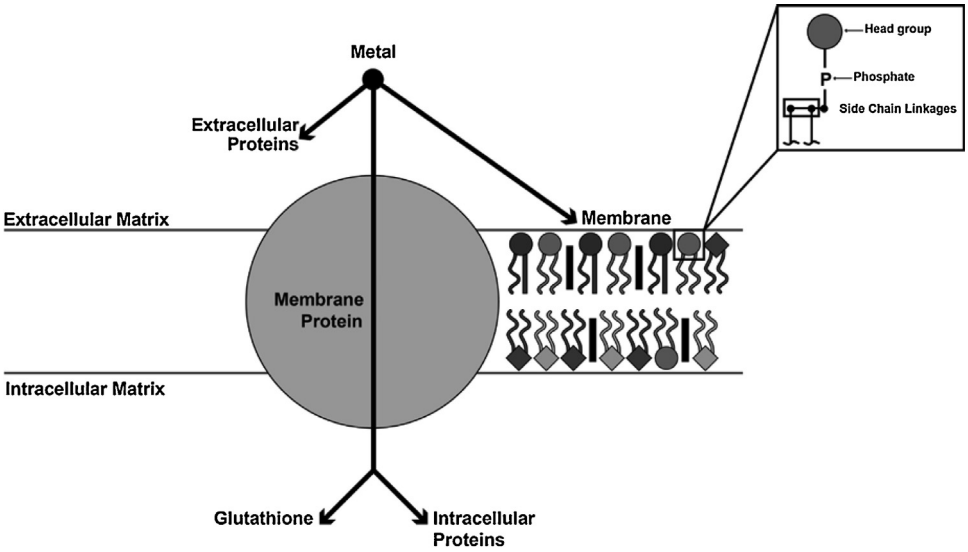

Fig. 1. Potential macromolecular targets of toxic metals in mammalian organisms.