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Review

Bioavailability as an issue in risk assessment and management of food cadmium: A review

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ABSTRACT

The bioavailability of cadmium (Cd) from food is an important determinant of the potential risk of this toxic element. This review summarizes the effects of marginal deficiencies of the essential nutrients zinc (Zn), iron (Fe), and calcium (Ca) on the enhancement of absorption and organ accumulation and retention of dietary Cd in laboratory animals. These marginal deficiencies enhanced Cd absorption as much as ten-fold from diets containing low Cd concentrations similar to that consumed by some human populations, indicating that people who are nutritionally marginal with respect to Zn, Fe, and Ca are at higher risk of Cd disease than those who are nutritionally adequate. Results from these studies also suggest that the bioavailability of Cd is different for different food sources. This has implications for the design of food safety rules for Cd in that if the dietary source plays such a significant role in the risk of Cd, then different foods would require different Cd limits. Lastly, the importance of food-level exposures of Cd and other potentially toxic elements in the study of risk assessment are emphasized. Most foods contain low concentrations of Cd that are poorly absorbed, and it is neither relevant nor practical to use toxic doses of Cd in experimental diets to study food Cd risks. A more comprehensive understanding of the biochemistry involved in the bioavailability of Cd from foods would help resolve food safety questions and provide the support for a badly needed advance in international policies regarding Cd in crops and foods.

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Contents

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1. Introduction

In the context of this paper, bioavailability is defined as the degree to which a nutrient, toxin, or other substances become available for body use or deposition after exposure. When exposure to the substance is oral, bioavailability generally includes absorption, body utilization, and/or deposition. Cadmium (Cd) is generally considered a toxic element where food is the major source of acquisition. Up to a point, intestinal absorption of Cd is proportional to the concentration in the diet, and in the past, the amount of the element in food has been regarded as the overriding risk factor that determines the body burden of Cd. However, other factors influence the rate of intestinal absorption and organ retention of Cd.

Perhaps the most important factor in this regard is the interaction between Cd and other mineral nutrients that are antagonistic to Cd absorption. The rate of Cd absorption from various food sources is reduced if the nutritional status of zinc (Zn), iron (Fe) or calcium (Ca) of the individual is high (Evans et al., 1970; Kello and Kostial, 1977; Koo et al., 1978; Fox et al., 1979; Jacobs et al., 1983; Fox, 1983; Fox, 1988; Ferguson et al., 1990; Brzóska and Moniuszko-Jakoniuk, 1998). However, if the general nutritional status of these minerals in the consumer is low, then Cd absorption will be enhanced. Flanagan et al. (1978) were among the first to show that Fe deficiency caused an increase in Cd absorption in both mice and humans. More recent work has shown that marginal dietary deficiencies of Fe, Zn, and Ca also have a strong effect on the bioavailability of Cd from food (Reeves and Chaney, 2001; Reeves and Chaney, 2002; Reeves and Chaney, 2004; Reeves et al., 2005). The following is a review of this work and a discussion of how these findings might influence risk assessment and management of food cadmium.

2. Research outcomes

A recent series of experiments evaluated the effects of marginal dietary intakes of Zn, Fe, and/or Ca and their interactions on Cd absorption and its accumulation and retention in various organs (Reeves and Chaney, 2001; Reeves and Chaney, 2002; Reeves and Chaney, 2004; Reeves et al., 2005). The term "marginal" was defined as that concentration of dietary Zn, Fe, or Ca that is less than the requirement for the rat as defined by the U.S. National Research Council (NRC) (1995), but not low enough to initiate frank signs of deficiencies such as reduced weight gain. The general study design was to use food-based diets made with sunflower kernel (SFK) or rice containing concentrations of Cd that are found naturally — 0.25–0.45 mg Cd/kg. In addition, the diets contained adequate Zn, Fe, and/or Ca as defined by the National Research Council, or marginal concentrations amounting to approximately 70, 30, and 50% of the respective adequate concentrations. The SFK (0.6–0.8 mg Cd/kg) were roasted, ground, and incorporated into the diet at 20%. Rice was cooked with Cd in the water, dried (0.6 mg Cd/kg), and incorporated into the diet at 40%. Please note that these foods were formulated into the diets to account for their inherent nutrient content. Rats were fed their respective diets for five weeks and then given a 1.0 g-meal labeled with ^{109}Cd. The amount of label retained in the body was monitored by whole-body-counting for up to 16 days. Absorption was calculated according to the procedure outlined by Reeves and Chaney (2001, 2002).

Cd absorption in animals fed either SFK or rice was not affected by marginal dietary Zn unless both Fe and Ca were also marginal. Marginal Fe, on the other hand, enhanced Cd absorption by 50 to 60% in diets with either food component. Marginal dietary Ca had a similar effect. In rats fed the 40% rice diets, marginal intakes of Fe and Ca combined caused a 6-fold increase in Cd absorption over that in animals consuming adequate intakes of these minerals. In addition, rats fed the rice-based diet with marginal Fe and Ca absorbed significantly more Cd than rats fed the SFK-based diet with a marginal supply of these minerals (Fig. 1).

In these and subsequent studies, it was found that marginal Zn, Fe, and/or Ca status seemed to correlate with a slower transit time of Cd through the gut of rats. The fecal excretion of a dose of ^{109}Cd incorporated into the food was delayed in those marginally deficient in Fe and Ca, when compared to rats with adequate mineral status (Reeves and Chaney, 2001; Reeves and Chaney, 2002). In rats receiving adequate Fe and Ca, up to 90% of the unabsorbed ^{109}Cd was excreted in the feces over the first 4 days after dosing. However, during the same period, only about 60% was excreted in rats fed the marginal diet (data not shown). When Zn was marginal as well, the delay in Cd excretion was even more pronounced. Importantly, these diets contained Cd concentrations that occur in natural foods (0.25–0.45 mg/kg), not toxicological concentrations as used in most studies of this nature.

To determine whether marginal mineral status affected gut retention of dietary Cd, studies were performed to monitor the changes in Cd concentrations of the gut enterocytes over time. Rats were fed the 40% rice diet as described above, except that only groups adequate or marginal in all three minerals; Zn, Fe,

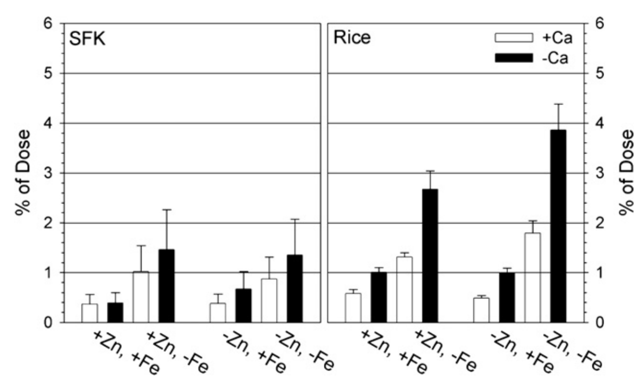

Fig. 1 – Whole body retention of ^{109}Cd is affected by mineral nutrient status of rats. Female rats were fed diets containing either 20% ground sunflower kernels or 40% cooked dried rice, each containing 0.25 mg Cd/kg. Each diet also contained marginal or adequate amounts of Zn, Fe, or Ca. After 5 weeks, each rat was given 1.0 g of diet labeled with ^{109}Cd. After 16 days, the amount of label remaining in the body was monitored and expressed as a percentage of the initial dose. Values are means ± SEM for eight replicates. Graph reconstructed from data in Reeves and Chaney (2001, 2002).