

HISTORY OF CHROMIUM AND ITS RELATIONSHIP TO GLUCOSE METABOLISM

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INTRODUCTION

Studies by Schwartz and Mertz (1959) showed that trivalent chromium (Cr) was an essential component of a factor in brewers yeast (referred to as glucose tolerance factor) that corrected impaired glucose metabolism in rats fed a torula yeast-based diet. This discovery led to a number of studies in the 1960's evaluating Cr supplementation in humans with impaired glucose tolerance. Results obtained in these studies were variable but some individuals did show improvements in glucose metabolism following Cr supplementation. For example in one study 3 out of 6 adult-onset diabetics exhibited improved glucose tolerance following CrCl supplementation for 7-13 weeks (Glinsmann and Mertz, 1966).

Subsequent studies demonstrated that Cr functioned in insulin-sensitive tissues to potentiate the action of insulin. The mechanism by which Cr enhances insulin action is still unclear. In humans Cr is poorly absorbed (0.4 to 2.5%) and absorbed Cr is rapidly excreted in the urine (National Academies, 2001). Chromium in the blood is transported bound to the protein transferrin. There is believed to be little storage of Cr in the body. Based on research in humans, the Institute of Medicine established an adequate intake of Cr for humans (National Academies, 2001).

CHROMIUM IN ANIMAL NUTRITION

Chromium research in domestic animals was limited prior to the early 1990's because practical diets fed to domestic animals were generally assumed to provide adequate Cr to meet animal requirements. Steele et al. (1977) found that intravenous administration of a synthetic glucose tolerance factor, containing Cr, potentiated the hypoglycemic response following an insulin challenge in pigs. This study indicated that a Cr containing glucose tolerance factor was active in swine. The first animal production responses to Cr supplementation were reported in turkey poults. In a series of studies with turkey poults (Steele and Rosebrough, 1979, 1981; Rosebrough and Steele, 1981) supplementation of 20 mg Cr/kg (from CrCl) to a corn-soybean meal based diet increased body weight gain, liver glycogen, and hepatic lipogenesis from glucose. The first report in ruminants evaluating the effects of Cr on measures of insulin sensitivity was with growing lambs fed a high concentrate or high fiber diet (Samsell and Spears, 1989). Supplementing 10 mg Cr/kg diet (from CrCl) reduced fasting glucose concentrations in lambs fed a high concentrate diet and reduced serum free fatty acids after feeding in lambs fed a high fiber diet. Both of these responses are consistent with Cr affecting insulin sensitivity.

Chromium research with domestic animals accelerated in the 1990's. Research at the University of Guelph indicating that Cr supplementation could improve performance and reduce morbidity in stressed calves generated considerable interest in Cr in ruminant nutrition (Moonsie-Shageer and Mowat, 1993; Mowat et al., 1993). Chromium addition to swine diets was found to increase muscling and decrease fat thickness in grow-finish pigs (Page et al., 1993), and increase litter size in sows (Lindemann et al., 1995). Studies in calves (Bunting et al., 1994) and pigs (Amoikon et al., 1995) also demonstrated that Cr supplementation could increase glucose clearance rate following a glucose tolerance test. Research with broilers showed that Cr supplementation to practical diets often increased gain and improved carcass characteristics, especially under heat stress conditions (Lien et al., 1999; Sands and Smith, 1999).

Responses to supplemental Cr are greatest under conditions that decrease insulin sensitivity. Insulin resistance occurs in late gestation and continues during early lactation in both dairy and beef cows (Sano et al., 1993). Chromium supplementation (approximately 0.20 to 0.50 mg Cr/kg DM or 4 to 10 mg Cr/cow/day) of dairy cows during late gestation and early lactation has increased DM intake and milk production in a number of studies (McNamara and Valdez, 2005; Smith et al., 2005).

Hormones produced during stress (heat stress, weaning, shipping, etc) also decrease insulin sensitivity. Stress has also been shown to increase urinary losses of Cr in humans and rats (Spears and Trivedi, 2013). In dairy cows exposed to heat stress, Cr supplementation, at a level of 6 mg/cow/day, increased DM intake and milk production, and decreased serum cortisol concentrations (Soltan, 2009). Increased release of cortisol during stress is known to suppress a variety of immune responses, and Cr supplementation of stressed calves has increased immune responses in a number of studies (Spears and Trevedi, 2013). In a recent study stressed calves supplemented with 0, 0.10, 0.20, or 0.30 mg Cr/kg DM exhibited a linear improvement in gain and gain:feed during a 56-d receiving period (Bernhard et al., 2012). Morbidity during the receiving period was lower in calves supplemented with 0.30 mg Cr/kg compared with controls (7.5 vs. 25.9% of calves treated).

APPROVALS OF CHROMIUM IN ANIMAL DIETS

Until recently, Cr was not considered as a substance generally recognized as safe for addition to animal diets in the United States. Therefore, U.S. Food and Drug Administration (FDA) permission or approval is required for any Cr source to be supplemented to animal diets. Two Cr sources are permitted for supplementation to swine diets at a concentration up to 0.20 mg/kg diet (Lindemann, 2007). In 1996 FDA stated that it would not object to Cr picolinate being supplemented to swine diets. The FDA indicated in 2000 that it would not object to Cr propionate being supplemented to swine diets. Permission from the FDA to use these two Cr sources was based on changes in glucose metabolism and related safety data.

The FDA issued a regulatory discretion letter in 2009 which permitted the use of Cr propionate in cattle diets. Chromium propionate is the only Cr source currently permitted for supplementation to cattle diets in the US, and can be added at levels up to 0.50 mg Cr/kg DM. Permission to use Cr propionate in cattle diets was largely based on utility and human food safety studies. The utility study was a dose-titration study examining glucose and insulin metabolism in growing heifers supplemented with 0, 3, 6, or 9 mg supplemental Cr per animal daily (Spears et al., 2012). These daily doses of supplemental Cr corresponded to 0 (control diet analyzed 0.20 mg Cr/kg DM), 0.47, 0.94, and 1.42 mg supplemental Cr/kg DM. All levels of supplemental Cr reduced insulin release and insulin:glucose ratios following intravenous glucose infusion. The lower release of insulin and decreased insulin:glucose ratio in Cr-supplemented heifers clearly indicated that their tissues were more sensitive to insulin. Furthermore, insulin concentrations and insulin:glucose ratios did not differ among heifers supplemented with 0.47, 0.94, and 1.42 mg Cr/kg DM.

The human food safety study involved demonstrating that Cr propionate supplementation would not increase Cr concentrations in meat and milk to levels that might cause a human health concern. Supplementation with Cr propionate for 120 days at 4 times (2 mg Cr/kg) the permitted level did not increase Cr concentrations in milk, muscle, or fat, the major animal products consumed by humans (Lloyd et al., 2010). Chromium supplementation did result in small increases in liver and kidney concentrations. Based on the maximum intake of liver and kidney that would be consumed by humans, it was determined that Cr propionate supplementation even at 4 times the permitted level would have minimal effect on Cr intake by humans.

Recently (June, 2016) Cr propionate was approved by U.S. FDA for supplementation to broiler diets at a level not to exceed 0.20 mg Cr/kg diet. This action was in response to a food additive petition submitted by Kemin Industries, Inc. The food additive petition included a utility study showing increased insulin sensitivity in broilers supplemented with Cr propionate (Brooks et al., 2016), animal and human food safety studies, environmental assessment, identity of chemical structure, stability of Cr propionate, manufacturing chemistry, and a mixing and homogeneity study, among other required regulatory components. Chromium is the first new trace mineral approved for use in U.S. broiler diets since selenium in 1974.

CHROMIUM IN ANIMAL FEEDSTUFFS

Little is known regarding Cr concentrations naturally present in practical feedstuffs, and even less is known regarding bioavailability of Cr from common feedstuffs. Chromium analysis of feedstuffs and total diets is challenging due to the low levels of Cr normally present and problems with Cr contamination of samples during collection, processing, and laboratory preparation of samples for analysis (NRC, 2005). Soil contamination of samples during harvesting will increase Cr concentrations in feedstuffs. Chromium derived from metal during harvesting and processing of feedstuffs is likely a major source of Cr contamination.

Li et al. (2005) reported Cr concentrations in homegrown and imported feeds from 54 dairy farms in Wisconsin. Mean Cr concentrations in homegrown feedstuffs ranged from 0.33 mg/kg DM for corn grain to 0.91 mg/kg DM for alfalfa haylage. Of the imported feed ingredients mineral supplements contained by far the highest concentrations of Cr (69 mg Cr/kg). Chromium would be expected to occur as a contaminant in most mineral ingredients. Average Cr concentrations in unground wheat samples from different areas in Australia ranged from 0.013 to 0.041 mg/kg (Jones and Buckley, 1977). They also reported Cr concentrations in oats and barley of 0.020 and 0.024, respectively.

We recently analyzed a number of feedstuffs obtained from different areas of the US for Cr. Samples of corn, soybeans, wheat, and oats analyzed whole averaged 0.026, 0.063, 0.041, 0.025 mg Cr/kg DM, respectively. Grinding whole samples of corn, soybeans, and wheat in a Wiley mill using a stainless steel screen more than doubled analyzed Cr concentrations. Samples of processed corn also analyzed considerably higher than whole corn samples. Corn silage samples averaged 0.22 mg Cr/kg DM and samples of alfalfa hay and haylage averaged 0.52 mg Cr/kg DM. Of the major feed ingredients that we have analyzed only beet pulp and corn steep liquid analyzed over 1.0 mg Cr/kg DM. These results indicate that Cr concentrations naturally occurring in most feedstuffs are low, and that much of the Cr in feedstuffs is due to contamination.

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