**Could Your Trace Mineral Program Be Doing More Harm Than Good?**

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## Introduction

Although trace minerals are one of the smallest components of the diet, they are also one of the most important. Copper, zinc, and manganese are vital to animal health and well-being due to their involvement in immunity, fertility, metabolism, and production. Trace mineral supplementation started with oxide forms in the 1930s and moved to the more available sulfate forms in the 1950s when World War II technology advances allowed for more efficient sulfate production. To further improve bioavailability and effectiveness, organic trace minerals were introduced in the 1970s. While many organic trace minerals delivered improved results, their high cost meant producers only replaced a small fraction of the animal's total trace mineral requirement. Hydroxy trace minerals (IntelliBond®) were developed in the 1990s as a more cost-effective improved trace mineral source. The differences in trace mineral sources and their effectiveness mainly lie in the type of chemical bond that binds the metal to its ligand (Figure 1). Sulfate trace minerals contain a metal ion bound to a sulfate ion via an ionic bond. This ionic bond breaks apart easily in an aqueous environment, releasing a free metal ion at liberty to interact with other nutrients or microbes in the rumen. Organic and IntelliBond trace minerals contain stronger covalent bonds that protect the metal from being released too early in the feed or digestive tract, giving them an advantage in diet stability, palatability, digestibility, and bioavailability over sulfate trace minerals.

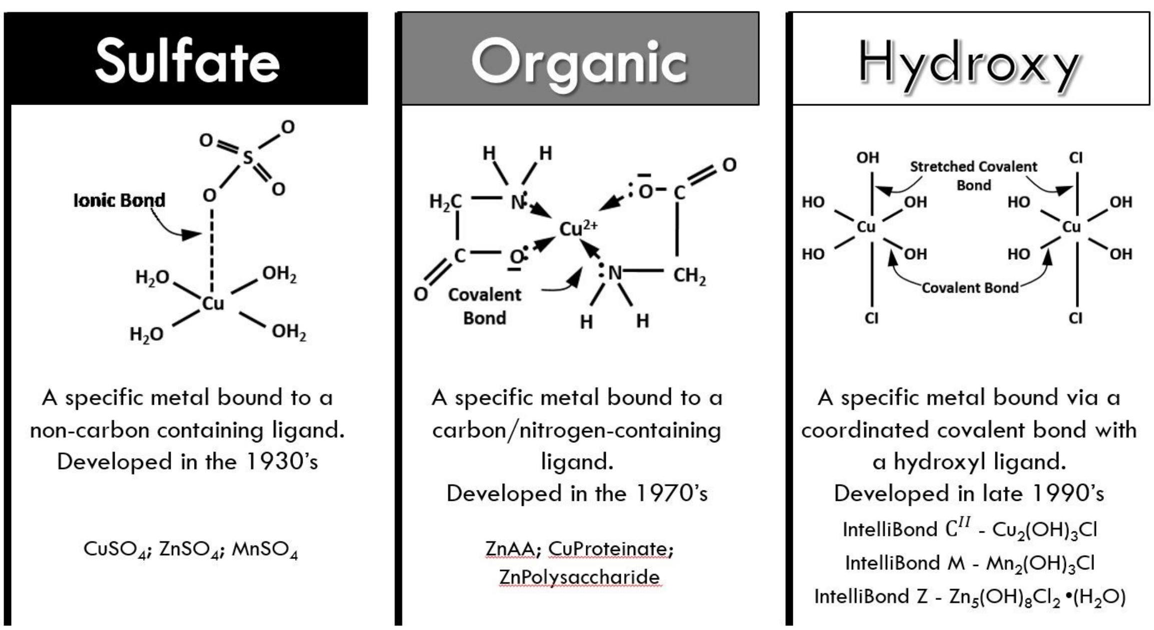


Figure 1. Chemical characteristics of different trace mineral sources

## Feed Stability

Some nutrients and additives included in a complete ration may be susceptible to oxidative free metals released by sulfate trace minerals. Vitamins are sensitive to their environment because they are comprised of unsaturated carbon atoms and double bonds vulnerable to oxidation. Coelho (2002) reported on a variety of ruminant premix processing protocols and found that vitamin stability is often compromised when trace minerals were included in the premix. Furthermore, when sulfate or free metals were included in the premix, stability of vitamins A, E, and K were decreased to a greater extent compared to chelated (organic) or oxide trace minerals, indicating that trace mineral source impacted vitamin availability. Research with IntelliBond copper has shown 10-70% more vitamin E retention in complete poultry diets containing 200 ppm copper versus copper sulfate after 10-40 days of storage (Lu et al., 2010; Figure 2), which later corresponded to higher liver and plasma vitamin E levels when these diets were fed to chicks. Lipids are another class of compounds susceptible to oxidation. Miles et al. (1998) found that replacing poultry diets containing 300 ppm copper sulfate with 300 ppm IntelliBond copper resulted in 17-35% less primary lipid oxidation and 7-45% less secondary lipid oxidation. Enzymes added to the diet are also susceptible to degradation by free metals. Phytase fed to improve phosphorus availability in poultry diets showed 16% greater retention in feed when formulated with IntelliBond copper compared to copper sulfate, indicating a prevention of phytase degradation during feed storage (Liu et al., 2005). Using a less reactive trace mineral source appears to protect vitamins, lipids, and enzymes in feed, ensuring the nutrients formulated retain their optimum quantity and quality.

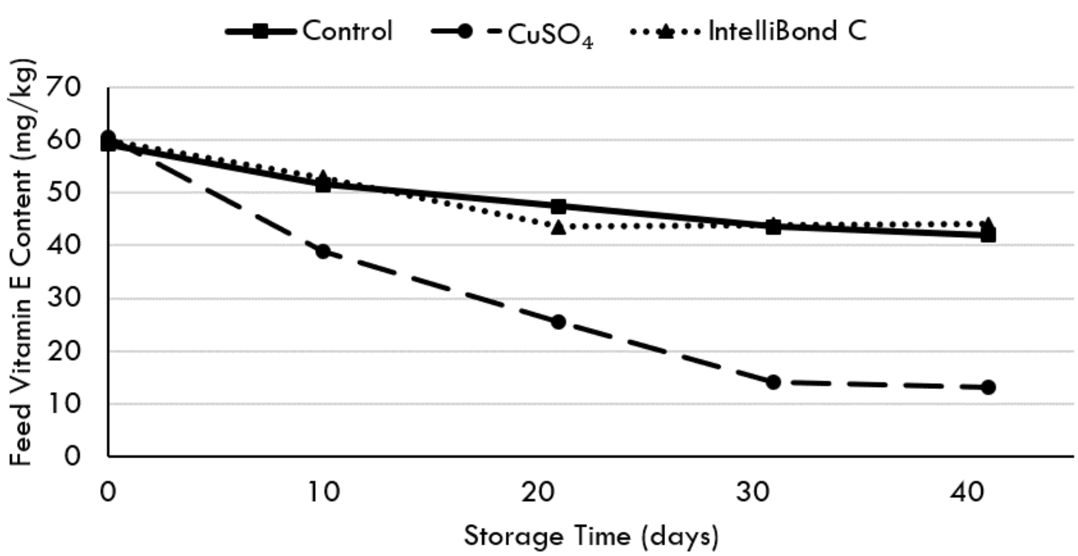


Figure 2. Lu et al., 2010. Feed vitamin E content over time in a poultry diet containing no added copper (Control) or 200 ppm copper from either copper sulfate ($CuSO_4$) or IntelliBond C

## Palatability

Studies across a variety of species have shown that, when given the choice, animals prefer to consume IntelliBond rather than sulfate sources of trace minerals. The reason behind increased palatability may be related to the high reactivity of sulfate trace minerals due to their weak ionic bond and release of free metal stimulating an averse metallic taste. In both broilers and layers, as copper sulfate is added to a diet, intake gradually decreases. However, when the copper sulfate is replaced with IntelliBond copper, intake is maintained (Miles et al., 1998; Kim et al., 2016). Similarly, when pigs are presented a choice between feeds formulated with either copper sulfate or IntelliBond copper, a greater proportion of IntelliBond-formulated feed is consumed (Coble et al., 2014). Ruminant studies have also shown an increase in preference of IntelliBond copper, zinc, and manganese over both sulfate and organic sources in a creep-fed pre-weaning supplement, a weaned calf supplement, and a cooked molasses block (Wiebusch et al., 2015; Caramalac et al., 2017; Ranches et al., 2018; Figure 3). To further investigate, Caramalac et al. (2017) conducted four separate trials looking at how each individual metal source (Cu, Zn, or Mn) affected preference. When given the opportunity to select between sulfate, organic, and IntelliBond sources, calves consumed more supplement containing IntelliBond versus organic or sulfate sources of copper (Trial 1), zinc (Trial 2), or manganese (Trial 3). In the fourth trial, all three elements were combined within a single supplement, and the calves had an overwhelming preference for IntelliBond mineral over organic or sulfate sources (82.9, 10.4, and 6.7% of total supplemental intake, respectively). It is remarkable these effects are consistently seen across livestock species, and this partiality may be explained by an evolved aversion to metallic-tasting compounds in their free ionic state.

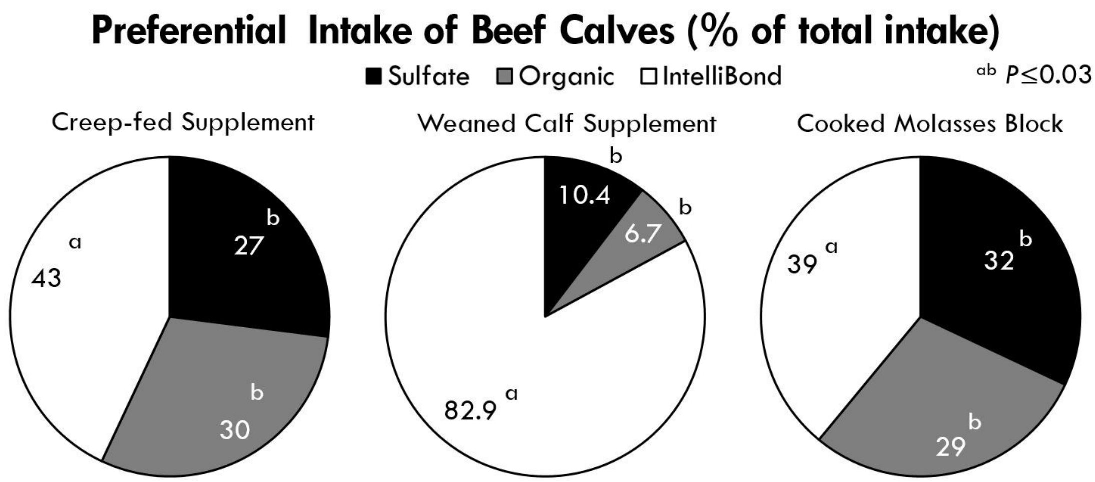


Figure 3. Preferential intake of beef calves as a percentage of total intake when fed a creep-feed mineral (left; Wiebusch et al., 2015), meal supplement (center; Caramalac et al., 2017), or a cooked molasses block (right, Ranches et al., 2018) formulated with minerals from sulfate, organic, or IntelliBond sources of Zn, Cu, and Mn

## Bioavailability

One of the goals of trace mineral supplementation is to ensure minerals are available to the animal during different situations that might affect trace mineral bioavailability. Dietary antagonists such as fiber, molybdenum, sulfur, iron, and imbalances in zinc and copper have the potential to affect absorption of different metals (Spears, 2003). Most antagonistic reactions occur in the rumen. If free metals are released in this environment, there is the potential to bind to antagonists, rendering them too tightly bound and causing them to pass through the lower GI tract and past absorption sites in the small intestine. Thus, the reactivity of trace minerals in the rumen is a large determining factor in the potential to bind with antagonists. When dosed in the rumen, sulfate sources of copper, zinc, and manganese were shown to be significantly more soluble than IntelliBond trace minerals (Caldera et al., 2019; Figure 4). Because copper, zinc, and manganese sulfate are bonded to their ligand via ionic bonds, solubility in the rumen is analogous to dissociation, meaning soluble sulfate trace mineral sources release free ionic metals and animals are more prone to antagonist-induced deficiencies. Furthermore, Caldera et al. (2019) investigated the binding strength of these minerals in digesta 12 hours post-bolus using dialysis against chelating agents. The chelating agent released more metal from rumen digesta of IntelliBond- versus sulfate-dosed animals, indicating the marked increase in rumen soluble mineral from sulfates resulted in the metal becoming too tightly bound to antagonistic complexes. IntelliBond begins to solubilize in acidic conditions (Spears et al., 2004) such as the abomasum and gradually throughout the intestinal tract. These data indicate IntelliBond sources avoid antagonistic interactions early in the digestive tract (i.e., the rumen), ensuring trace minerals reach their site of absorption in an available form with as little interference as possible.

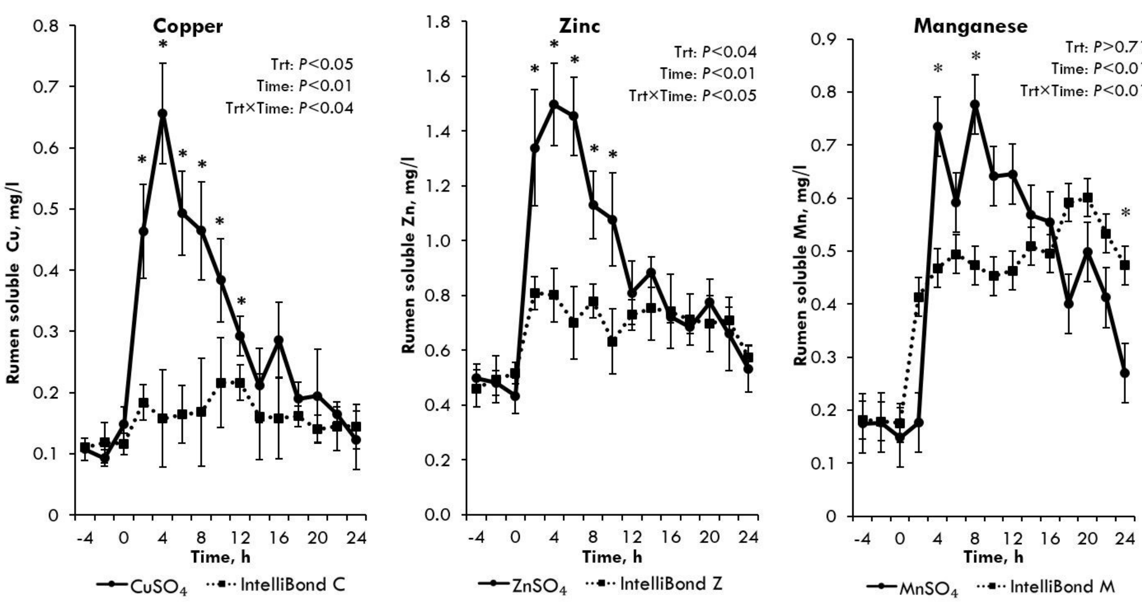


Figure 4. Caldera et al., 2019. Influence of trace mineral source on rumen soluble copper (left), zinc (center), and manganese (right) concentrations

Bioavailability is expressed relative to a standard source, and there are two main approaches: 1) feed mineral at dietary concentrations much higher than the animal's requirement and measure accumulation in tissues, or 2) feed mineral at dietary concentrations below the animal's requirement and measure a specific function. The latter is more practical because it measures the bioavailability of the mineral in a situation when mineral is limiting. However, it is difficult to formulate diets deficient in certain trace minerals using practical feedstuffs (Spears and Hansen, 2008). Therefore, the addition of dietary antagonists are often used to test the ability of mineral sources to overcome the antagonistic challenge. When sulfur and molybdenum (Cu antagonists) were fed to copper-depleted steers, the bioavailability of IntelliBond copper was 1.96x and 1.12x compared to copper sulfate based on liver copper concentrations (Spears et al., 2004; VanValin et al., 2019; Figure 5). Additionally, when steers were depleted and then fed 25 ppm zinc from either zinc sulfate or IntelliBond zinc, the bioavailability of IntelliBond zinc was 2.04x compared to zinc sulfate based on retained zinc as measured via total fecal and urine collection (Shaeffer et al., 2017; Figure 5).

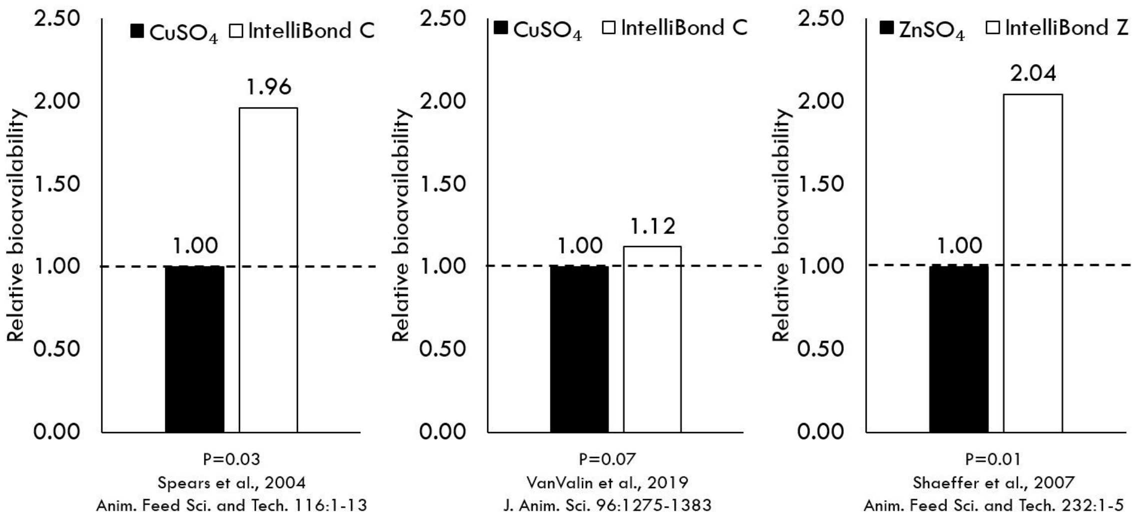


Figure 5. Bioavailability of IntelliBond C during a Mo and S antagonist challenge (left and center; Spears et al., 2004; VanValin et al., 2019) or IntelliBond Z following a Zn depletion period (right; Shaeffer et al., 2017) expressed relative to respective sulfate sources

## Digestibility

It is well understood that microbial activity in the rumen is essential to promote optimized neutral detergent fiber digestibility (NDFd), which is fundamental to the production of volatile fatty acids as an important energy source for the ruminant. Metals such as copper, silver, and zinc have known antimicrobial properties that are utilized as antimicrobial agents and antibiotic alternatives in other industries (Lemire et al., 2013). Therefore, reactive trace mineral sources are counterproductive because, once broken down in the rumen, the metal ion (zinc or copper) originally linked within the sulfate ligand now possesses these antimicrobial properties. Consequently, these free metal ions can potentially harm the beneficial fibrolytic bacteria. Research investigating how trace minerals may affect microbial function dates back to the 1950s. Several in vitro studies have indicated even very low amounts of added copper are highly toxic to cellulolytic bacteria (Sala, 1957; Hubbert et al., 1958; Martinez and Church, 1970; Ward and Spears, 1993). There is a recognized rumen microorganism requirement for zinc (Durand and Kawashima, 1980); however, the rumen microbe requirement for zinc appears to be quite low. Two separate studies conducted using washed suspensions of rumen microorganisms (therefore eliminating any soluble zinc from the basal diet) found either no change or an increase in cellulose digestion with low levels of added zinc (Hubbert et al., 1958; Martinez and Church, 1970). However, the rumen zinc requirement is likely quite small and readily met by zinc within the basal diet, as dry matter digestibility was similar in lambs and calves fed a zinc-deficient diet compared to those supplemented with adequate amounts of zinc (Miller et al., 1966; Somers and Underwood, 1969). Additionally, both washed rumen microbe studies found that continuing to add increasing levels of zinc inhibited cellulose digestion in these suspensions. A more recent in vitro study observed reduced cellulose digestion and cellulolytic bacteria concentration after 24 hours of incubation with 50 µg/mL zinc (Eryavug and Dehority, 2009). Therefore, the zinc requirements of rumen microorganisms appear to be very low relative to zinc requirements of the animal.

To further evaluate the impact of trace mineral source on a more practical level, researchers from multiple universities have looked at how level or source of trace mineral impact digestibility in vivo. Lambs supplemented 100 ppm copper for 30 days had 7.7 points lower dry matter digestibility compared to those receiving 5 ppm copper (Goodrich and Tillman, 1966). Additionally, digestible dry matter intake tended to decrease with increasing ruminal doses of zinc in heifers (Arelovich et al., 2000). In terms of source, supplementing a covalently bonded trace mineral source can prevent the negative digestibility effects of reactive trace minerals by minimizing the amount of free ionic metal in the rumen. In lambs supplemented with organic trace minerals, increased NDFd and ADF digestibility have been observed (Garg et al., 2008; Hassan et al., 2011). In a wide range of studies comparing how sulfate trace minerals affect NDFd relative to IntelliBond trace minerals, research has found an improvement in NDFd ranging from 1.1 to 4.6 points with IntelliBond trace minerals relative to sulfate sources (Figure 6). As Oba and Allen (1999) suggest, a one-point change in NDFd can translate to a 0.17 kg increase in dry matter intake and a 0.25 kg increase in 4% fat-corrected milk. These studies were conducted under practical trace mineral feeding levels (5-25 ppm Cu [average 12 ppm Cu], 30-120 ppm Zn [average 56 ppm Zn], and 15-60 ppm Mn [average 36 ppm Mn]) indicating that a component as seemingly insignificant as trace mineral source can have a profound impact on digestibility and energy status in today's high producing ruminants.

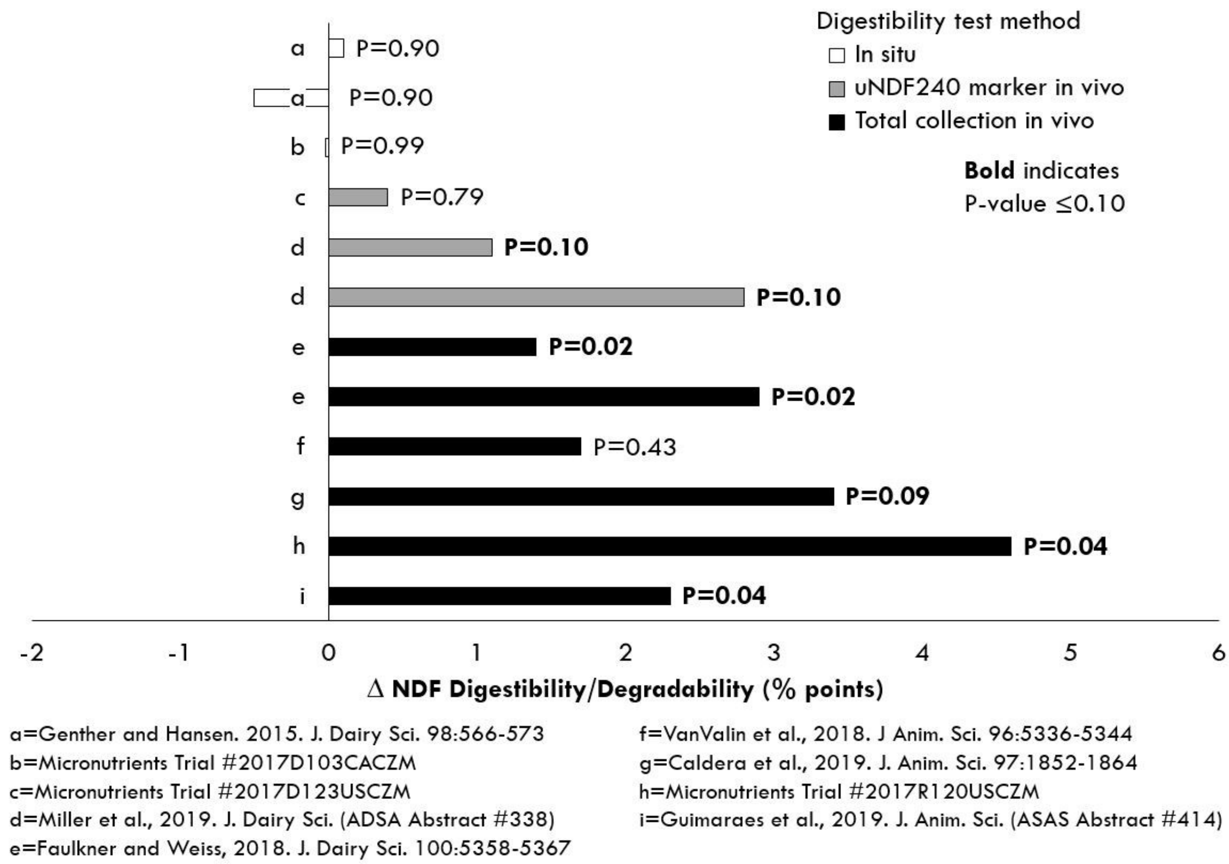


Figure 6. Change in neutral detergent fiber (NDF) digestibility relative to sulfate sources of trace minerals in various studies.

## Summary

The primary goals of trace mineral supplementation are to meet the nutritional demands of today's high producing animals and to provide a bioavailable mineral source that does its job without negatively interacting with other components of the diet. Providing a high-quality improved trace mineral source as a replacement for sulfate trace minerals ensures proper trace mineral nutrition without the negative side-interactions sulfate minerals may have on diet stability, palatability, bioavailability, and digestibility that may do more harm than good.

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