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The Role of Lead and Molybdenum and Their Effects on Oxidative Stress in Ruminant Animals: Subject Review

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Abstract. *Ruminant animals have significantly improved global food security, particularly in rural and semi-arid lands, where milk, meat, and wool are food producers, among other items. Their production and health may be altered by several environmental conditions. There is also critical exposure to heavy metals and trace elements. Oxidative stress is an important biological process that links environmental pollution to reduced physiological actions. The imbalance between reactive complimentary radicals and antioxidants causes cellular damage to essential tissues lowering growth and condition, affecting immune functions, and reducing ruminant reproductive efficiency. Lead increases reactive oxygen species production while reducing antioxidant enzymes superoxide dismutase and catalyze effectiveness, increasing the formation of several oxidative stress markers, including malondialdehyde. Molybdenum, however, is a trace element that helps activate several important enzymes in this study, including sulfur and purine metabolism aggravation. With a protective potential, it can have a dual role in oxidative stress: a beneficial for ruminant animals when applied the recommended doses and degradation: it can help and compromise other minerals while provided unreasonably. It analysis recent original research on the performance of ruminants based on current high-level research evidence concerning lead and molybdenum. Further, I will explain a physiological concept, groundbreaking research, and expert views to offer an explanation of how these two elements work and influence their oxidative balance in ruminants.*

Keywords: Ruminants, Oxidative stress, Heavy metals, Lead (Pb), Molybdenum (Mo).

INTRODUCTION

Ruminous animals, including cattle, sheep, and goats, make a vital contribution to ensuring food security and agricultural sustainability, particularly in areas that are engaged in pastoralism or semi-intensive production of livestock. Apart from their important economic significance, these animals are characterized by the ability to transform low-quality fibers of plant origin into highly valuable products, such as milk and meat [1]. However, the biological and productive parameters of ruminants directly depend on their health, which can be compromised by multiple environmental factors, most prominently the exposure to heavy and trace metals, responsible for the direct impact on metabolic, Moreover, although in ruminants lead, in high loads, also affects the neurological, hepatic, and renal functions, a high level of the metal in the feeder water or LED has been linked to the decreased reproductive performance and elevated oxidative stress levels. On the other hand, molybdenum Mo is another trace metal used in different medical procedures due to the critical role that it plays as it involves the formation of various enzymes and their activation. The pharmacologic action is, however, two-way: first, its deficiency is associated with metabolic imbalance and the resulting low level of detoxification and, on the other hand, the high level of the component, especially in interaction with copper and sulfur, affects metabolism level resulting in metabolic disorders related to the osmotic and ionic balance disruption [2], [3], [4]. The condition leads to generalized oxidative damage, including lipid peroxidation, protein oxidation, DNA damage, compromising fertility, growth, and disease susceptibility in ruminants. In this context, [5] lead Pb appears to be one of the most toxic heavy metals. The metal has no essential pharmacological functions and multiple adverse effects on many critical systems, including the immune ones. According to the literature, lead enhances the production of ROS and inhibits the activity of anti-oxidant enzymes, promoting an elevated level of malondialdehyde MDA, a molecule typical for cellular membrane lipids damage [6], [7], [8] ,[9].

Lead exposed ruminants suffer neurological, hepatic and renal damage and exposure to high level of lead in feed and water has also been associated with reproductive disorders and oxidative stress [10], [11], [12]. On the other hand, molybdenum (Mo) is a trace element which is required for the generation and the activation of many enzymes including xanthine oxidase, sulfite oxidase and aldehyde oxidase. By contrast, molybdenum Mo is a trace element critical for the formation and activation of several enzymes, such as xanthine oxidase, sulfite oxidase, and aldehyde oxidase. However, its pharmacological role is two-faced because, on the one retreat, the lack of Mo causes metabolic disturbance and the bumming of detoxification capability, and, on the other, its excess, specifically in conjunction with Cu and S disturbs metabolism resulting in metabolic disorders affecting osmotic or ionic equilibrium [13], [14], [15]. There is inconsistent evidence regarding the effects of molybdenum on the anti-oxidant system, suggesting that it may enhance levels of oxidative stress if administered in excessive doses or outside optimal mineral ratios [16], [17]. However, due to the interactions between various minerals within the animal, the evaluation of the independent impact of each looks insufficient, and one shall take into opposites the influence of one type of mineral on the absorption or biological activity of others. For example, some authors have claimed that molybdenum might have a protective effect against lead toxic exposure, due to the formation of non-absorbable compounds in the gastrointestinal tract, while others have stressed that molybdenum over-dosage leads to an anti-oxidal action by disturbing copper balance and oxidal stress [18], [19], [20].

According to the above, the objectives of this review are to summarize the last scientific findings on the effects of both lead and molybdenum on oxidative stress in ruminants. The objective of this paper is to review the existing information, to put forward pathophysiological mediation, to review interventions provided and the treatments given, and to discuss the possibility of preventive or therapeutic approaches through balanced mineral nutrition.

A. Oxidative stress in ruminants

Oxidant stress is one of the serious physiological factors affecting the well-being and performance in ruminants. P The urgency of this problem has been aggravated in recent years, also because of vast metalloid contamination of the environment and more intensive loads of immunological and nutritional stress in ruminants. Oxidative stress, resulting from an imbalance that is caused when the amount of free radicals produced in a body exceeds that which the body's defense systems (the antioxidants) can neutralize., overproduction of reactive oxygen species (ROS) is termed oxidative stress. That being said, in the normal functioning of the body free radicals have important roles that extend to the protection against several pathogenic microorganisms and other biological processes.. However, over the critical levels of accumulation in the body, when the body can no longer regulate the accumulation and distribution processes, free radicals cause molecular and cellular damage by interacting with lipids, DNA, and proteins, which leads to the occurrence of destructive changes in living tissues [2], [21], [8]. It is noteworthy to re-emphasize that radicals are endogenously generated by the body due to metabolic processes,that takes place in the mitochondria essentially during cellular respiration. The most toxic reactive oxygen species (ROS) are considered to be the superoxide radical O_2^-, hydrogen peroxide H_2O_2 and hydroxyl radical OH•. Under adverse environmental conditions, such as chronic lead exposure or a lack of minerals in a valid ration, “wicked” forms of metabolic products, including ROS, synthesized and oxidative stress are enhanced and develop. Numerous studies have shown that oxidative stress in ruminants weaken reproduction, reduce immune status, decrease milk and meat production, and heighten the susceptibility to inflammatory processes, including mastitis and the development of food infections [22], [5], [23] ,[24].

Twoof these, seleniumand zinc, are important to the health of animals. Such components are implicated into hormonal and enzymic regulations as well as in the defence reaction of the antioxidant-protection of the body of an animal in adaptation to the normal work of the systems of metabolism, immune regulation. At the same time, dose effect of the SU can be also positive (synergy) in case that their action is additive or synergetic, andnegative (antagonism) as a result of antagonistic reaction of SU [23] ,[24]. Integrative system ofantioxidants and antioxidant enzymes prevents the complex formation of free radicals in the body. The most appropriate ones are have some effect over the superoxide dicmutation, that is the Superoxide dismutase, the catalyst that converts hydrogen peroxide to water and oxygen, the Catalase and the Gultathione peroxidase that making use of the reduced form of the glutathione makes the reduction of peroxides. These enzymes function as a fundamental defense against oxidative stress in animal cells. Their behaviour is very sensitive to these mineral 14 balances, especially the inclusion of trace elements (selenium, zinc and copper).This can lead to non-specific pathologies [25] ,[17]. Heavy metals like lead have been reported in literature to inhibit the activity of these enzymes, leading to an increase in oxidative stress [18] ,[6]. To assess how much oxidative stress occurs in ruminant health, a battery of biomarkers in blood and tissues is utilised. The most important of these is probably malondialdehyde (MDA), a product of the lipid oxidation and marker of cell membrane damage. The content of reduced glutathione (GSH) is often used as a marker of cellular resistance to oxidant challenge, because diminution of GSH level is a sign of exhausted endogenous antioxidant defense system. The activity of the three key enzymes (SOD, CAT, and GPx) are analyzed as a direct indication of the efficiency of the antioxidant system and the TAC of the total antioxidant capacity are also a comprehensive and comprehensive evaluation of the overall balance between oxidation and biological defense in the body [18] ,[6] [16].

It is recognised from experimental evidence that ruminant's oxidative stress is influenced not only by endogenous factors, but also on low concentrations of metals in environment and of food that both have the oxidant toxicity potential (lead) and act as protective enzyme factor (molybdenum and selenium). This confirms the necessity of the control of OS by animal health programs, particularly under the conditions of a high occurrence of metal pollution, which directly affects the security and quality of ruminants' products [6] ,[16], [15].

B. Lead (pb) and its effect on oxidative stress in ruminants

Lead (Pb) is a highly toxic and common heavy metal distributed in the environment. It plays no beneficial biological function in the body of ab acter male; but it is somehow involved in toxic effects at multiple levels. Various researches have reported that ruminants are sensitive to bioaccumulation of lead through consumption of contaminated feed, water, and exposure to dust followed by industrial activity and traffic along highways [7] [15]. Polluted soil with industrial waste and pesticides is the leading culprit of lead mediated pollution in the animal food chain. Lead gets deposited on plants and is eaten by ruminants, and accumulative effects are seen in their vital organs [26] [17]. At a cellular level, lead is an oxidant indirectly. It does not form free radicals directly, but by interfering with antioxidant enzymes, by disturbing essential metal ions such as zinc and selenium, by damaging sprecific enzymes, such as SOD, CAT and GPx, its structure and function are affected. In addition, lead can bind to the sulfhydryl (-SH) group of proteins and inhibit the activity of sulfhydryl-SH-dependent enzymes, interfere with DNA repair to induce negative genetic effects [27] ,[18], [8].

Biochemically, the exposure to lead resulted in a marked elevation in MDA levels, an index of oxidative damage to membrane lipids, along with diminished level of GSH, a principal non-enzymatic antioxidant for maintaining cellular homeostasis. In the same way, a drastic reduction in the level of antioxidant enzyme activities of SOD, CAT, and GPx activities in blood, liver and muscle tissues of lead exposed animals showed a weakened defensive mechanism against the oxidative stress [6] ,[25], [28].

Applied studies carried out on ruminants employing Awassi ewes showed that oral intake of water containing more than recommended dose of lead caused severe hematological changes such as decrease in haemoglobin concentration and elevation in damage markers of liver (ALT, AST) as well as increase in serum and liver MDA and depletion of GSH [18]. Furthermore, in dairy cows, chronic exposure to low levels of lead causes accumulation of lead in adipose and liver tissues, decrease in milk production, decline in cell immunity, and increase in the level of oxidative stress, and so on [29] ,[16], [11].

These results suggest that Pb is not only a hazard substance but is correlated with the disturbance of an equilibrium of the minerals and enzymes in the body of the animal, which is a long-term risk that can affect its general condition and productivity for ruminants. This deserves the monitoring of the environmental, water and feed sources of contamination as well as periodic biomarkers of oxidative stress.

C. Molybdenum and its effect on oxidative stress in ruminants

Molybdenum (Mo) is a trace element necessary for animals in very low amounts, as a cofactor in the regulation of several biological pathways (mainly redox pathways). This metal is a necessary cofactor of the oxidoreductase enzymes, which are involved in many important processes such as purine metabolism, detoxification of sulfite and conversion of toxic aldehydes to less toxic products [13] ,[15]. According to the function of these enzymes, it is expected therefore, an indirect role of molybdenum in the maintenance the oxidative balance of the cell since causes the formation of intermediatemolecules, such as hydrogen peroxide (H2O2), which must be rapidly detoxified by antioxidant enzymes such as catalase and glutathione peroxidase [25] ,[17].

Absence of molybdenum or molybdenum availability at suboptimal levels would suppress the action of these enzymes and the buildup of toxic compounds with an indirect increase in oxidative stress. However, high flaxseed reduces the bioavailability of copper in gastrointestinal tract of the animal due to the presence of high amounts of molybdenum, in situations where the plants require the micro-mineral in different proportions, as for high levels of sulfur in the environment, for example, when the activity of copper-dependent enzyme superoxide dismutase become depleted, as a result of a severe depletion of the oxidative defense system [14] ,[15]. This imbalance had been reported to be accompanied by increased oxidation markers like malondialdehyde (MDA) and a decrease in reduced glutathione (GSH) levels which weaken the animal‟s capacity to withstand environmental stress [18].

Supplementation of ruminant rations with molybdenum has been found to enhance the efficiency of the body antioxidant system in applied studies. In a study on sheep, [31] found that the timed intro3 duction of molybdenum supplements caused a decrease of MDA levels and an increment of CAT and GPx activities, along with recovery of MIR signals. By contrast, in a dairy calves model of high dietary Mo intake, a high level of molybdenum inhibited Cu absorption and Cu-dependent enzymes (those SOD and GPx) activity, and increased oxidative stress markers, and is generally associated with suppression of the animal's physiological performance [18] ,[8].

However it must be kept in mind that molybdenum is a very limited homeostatic element: the range of safe intake for this element is low (recommended molybdenum concentration in ruminant diets is from 0.1 to 5 mg per kg of dry matter). Beyond this level it can result in secondary metal toxicity, reduced reproductive efficiency, weight loss, or even altered liver function [13] ,[15]. Therefore controlling its dietary levels is essential for a healthy oxidative system.

Molybdenum, it would seem, is an essential element that can also harm you (but don't blame the element, it is simply a tool). When it exists at ideal levels (usage), it will help improve the resistance of animals to oxidative stress and thereby improve production performance. But if it gets out of balance, or if it has a negative interaction with other substances, including iron and copper, it can itself become an engine of damage. Thus, supplementation of molybdenum and monitoring its biochemical status are necessary for the maintenance of ruminal health, particularly in regions with an uneven distribution of mineral content in the soil and water.

D. Lead and molybdenum interaction in ruminants

One of the most serious problems of biosynthesis is interaction of mineral elements in ruminant diet. The lead and molybdenum interaction is an obvious example of damage by this type. Although the two elements have different properties, i.e., Pb is classified as a biologically non-essential toxic element in animals and molybdenum is an essential trace element confirmed several studies that they associate with a complicated way of complex absorption mechanisms, toxicities and oxidative impacts in animal's body [18] ,[14], [15].

Medical studies have demonstrated that molybdenum can inhibit lead absorption and its toxic cost to the body. One of the major reasons for this effect is the formation of insoluble complexes of molybdenum, sulfur and lead within the gastro-intestinal tract, which in turn decrease the absorption of lead into the circulation and hence the accumulation into tissues [27] ,[8]. Molybdenum may also have a role in increasing activity of some detoxification enzyme, which consequently resulted in increased lead removal from animals [15].

But it's not always positive. Molybdenum may interfere with the absorption of copper, part of the antioxidant enzyme, superoxide dismutase (SOD), in the body at excessive levels according to some studies. This depletion may render the animal more vulnerable to injury caused by oxidative stress, particularly that induced by lead as an environmental toxicant [13] ,[25]. The effect of molybdenum on the toxicity of lead, therefore, appears to be related to dosage and the mineral status of the diet in general. In sheep, nutritional supplements of molybdenum compounds [15]. lowered lead deposits in liver and kidney, also have been demonstrated to adjust antioxidant parameter including GSH and CAT.

A possible example is a field experiment in Awassi ewes, where molybdenum administered in controlled dose for 30 days successfully suppressed the toxic effects of chronic lead exposure levels in drinking water, where the MDA concentrations decreased (as opposed to an increased activities of antioxidant enzymes) in comparison to the control group [18].The effect of molybdenum and environmental contamination on lead toxicosis in young calves was also investigated, in an earlier report from the same group2. Molybdenum decreased lead uptake up to 28% and liver and blood parameters were ameliorated as compared with the untreated animals. It was documented that effectiveness of the latter effect was also associated with the diet's copper and selenium balance [29] ,[17] , [30].

From the results of the present investigation, one could argue that molybdenum has a realistic potential to counteract some of the deleterious effects of lead toxicity in ruminants. This effect is, however, not universal, and diet formulation, dose, duration, feed constitution, as well as the relative balance of other minerals, such as copper, exert an influence. As a result, the systematic monitoring of molybdenum concentrations in feed and water, particularly in environments with known elevated lead contamination, is imperative in order to prevent negative influences through overuse of this element.

E. Recent studies on the effect of lead and molybdenum on oxidative stress in ruminants

Heavy metals and trace elements in the environment: The past, the present and the future Controversy between heavy metals as essential or toxic elements in ruminant livestock Recent years have seen a marked increase in interest in studying the effects of heavy metals and trace elements on ruminant biology, reflected by the grow-ing number of sources of environmental pollution due to industrial and agricultural activity. [31] Many studies have been devoted to the oxidation effect of either lead or molybdenum alone or their interaction, in order to explain the consequences on the physiological processes and the health status of animal.

[32] also described oxidative stress as a main factor in explaining suppressed immunity and high rates of infection in cattle (particularly in metal polluted areas), while [21] earlier suggested that OS is central for explaining reduced immunity and increased incidences of infection in ruminants. This tendency was supported by Celi (2011) who reported that excessive heavy metals accumulation (mainly lead) results in the reduction of antioxidant enzymes and the rise of the concentration of malondialdehyde (MDA) in blood and also tissues. In the present recent work we will refer to, in a previous work (publishe.2024), [33] explored the combined effect of lead on tissue of dairy cow. This study found that there were significant differences in concentrations of MDA, SOD and GSH between experimental cows and control cows with regard to lead exposure through fodders and drink waters. The authors also observed a suppression of milk yield and a poor hepatic and hematological profile, thus indicating the overall severity of lead-induced oxidative stress.

The study by [15] demonstrated that the balance of this element in diet is directly associated to integrity of enzymatic activity related to an oxidative activity. It was revealed that molybdenum deficiency is the basis for endotoxin accumulation, while its excessive content is responsible for the disruption of copper absorption and damage to the oxidative system. Another practical research of [31] on heat-stressed ewes in examination that molybdenum supplementation at low levels enhanced the antioxidant status of animals, which influenced the antioxidant capacity and resulted in enhanced GPx and CAT activities and reduced MDA. An enhanced immune response and ability to balance blood electrolyte was also detected.

Similarly, [34] studied an interaction of heavy metals, and showed that molybdenum may serve as a protective factor against lead-induced toxicity via lowering lead concentration in liver and kidneys and ameliorating oxidative stress biomarkers. These results were confirmed by investigations on pigs and cattle, increasing their biological relevance to different species. Recent research demonstrated that hormonal treatments significantly increased the reproductive and haematological characteristics of Awassi ewes, suggesting hormonal management can improve the productivity of livestock[35],[36]. (Alwan, Majid, & Ismail, 2018a; 2018b). Supplementation of selenium or zinc fortified yeast improved antioxidant status and decreased the liver and kidney usage indexes in the local Iraqi goats [37], [38], [39].

Conversely a comparison study by [18] raised concerns about overuse of molybdenum. High doses were shown by the researchers to cause acute mineral imbalances, with reduced copper and selenium absorption and thus an impairment of the antioxidant system and chronic toxicity symptoms. In conclusion, the findings from these studies support that an appropriate balance between lead and molybdenum and management of the copper and selenium ratios in the diet are the basis for the support of ruminant health and tolerance to oxidative stress. These should be considered for inclusion in surveillance programs in production regions with known environmental contamination or on farms depending on dubious feed sources.

CONCLUSION

The present study findings suggested the importance of interactions between mineral elements, especially lead and molybdenum and oxidative damage in ruminants and that such study would be relevant for ruminants to maintain their health and enhance production of ruminants due to increase environmental contamination by metallic pollutants. The lead was found to afford a marked cellular damage by increasing the oxidative stress markers such as MDA and reduced the essential antioxidants like glutathione and protective enzymes. Mo, on the other hand, showed two-way function; helpful when nutritionally balanced, toxic when present more in concentration as well as behavior of other elements. Therefore, the study suggests that periodical feed and water surveillance, feeding of mineral balanced diet, periodic determination of anti-oxidative stress borne biomarkers and cautious molybdenum supplementation can be useful in reducing lead toxicity. It further suggests that local applied studies be stimulated to determine the physiological points of interaction of these elements in the economic environmental conditions of ruminants in the specific region. These results support and validate the effectiveness of environmental preventive measures, nutritional management, and biological monitoring against the deleterious effects of oxidative stress induced by lead and molybdenum in developing sustainable and efficient animal production strategies.

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