Chapter 2

Balancing Vitamin A Supply for Cattle: A Review of the Current Knowledge

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Abstract

Among its many functions, vitamin A, also known as retinol, plays an essential role in growth, vision, immunity, cellular metabolism, bone development, and reproduction. Recent debate about retinol supplementation in commercial animal production is likely a result of its physiological importance, but also its high cost and susceptibility to oxidation. In cattle, inadequate vitamin A can reduce performance and increase susceptibility to diseases and reproductive problems. There is much to consider when determining an optimal vitamin A supply. Physiological condition, health, and nutritional status all affect retinol requirements in dairy and beef cattle. Estimated adequate vitamin A intake by scientific committees such as the National Research Council (NRC) or the National Academies of Sciences, Engineering, and Medicine (NASEM) consider the needs of healthy animals under optimal environmental conditions. In commercial production conditions, however, a higher vitamin supply is required for optimum weight gain, feed conversion, and health. Compounding balanced diets and achieving maximum performance in cattle requires an understanding of how vitamin A affects metabolism and health. This paper aims to review this complex subject, which has been rather neglected to date.

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Keywords: vitamin A, retinol, cattle, supplementation, requirement

Introduction

From a practical perspective, vitamin A is the most important vitamin (McDowell, 2000). Several forms of vitamin A exist, including retinol, the major circulating form; retinyl esters, the main form in which vitamin A is stored by cells; and the activated forms retinoic acid and retinaldehyde (Lespine et al., 1998). Since they are critical to the physiology of the retina, these oxidative states of retinol are all known as retinoids (Engelking, 2015). Retinol is essential for growth, vision, immunity, cellular metabolism, bone development, and reproduction (EFSA, 2013). Recently, retinol has attracted attention for its antioxidant capacities and its role in myogenesis, preadipocyte formation, and the reduction of milk protein allergens (Wang et al., 2018; Hufnagl et al., 2018; Harris et al., 2018; Yu et al., 2022). The main functions of vitamin A and manifestations of deficiency are presented in Table 1.

Table 1. Functions and manifestations of vitamin A deficiency

<table>
<thead>
<tr>
<th>Chemical form</th>
<th>Functions</th>
<th>Manifestations of deficiency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Retinol</td>
<td>Vision</td>
<td>Impaired immune function</td>
</tr>
<tr>
<td>Retinal</td>
<td>Cell growth and differentiation</td>
<td>Reproductive and fetal abnormalities</td>
</tr>
<tr>
<td>Retinoic acid</td>
<td>Immune modulation</td>
<td>Impaired bone development</td>
</tr>
<tr>
<td></td>
<td>Reproduction and fetal development</td>
<td>Growth retardation</td>
</tr>
<tr>
<td></td>
<td>Bone health</td>
<td>Bitot’s spots: Keratomalacia</td>
</tr>
<tr>
<td></td>
<td>Skin health</td>
<td>Dry eyes: Xerophthalmia</td>
</tr>
<tr>
<td></td>
<td>Gene expression</td>
<td>Night blindness: Nyctalopia</td>
</tr>
<tr>
<td></td>
<td>Antioxidant capacity</td>
<td>Skin problems: Hyperkeratosis or follicular hyperkeratosis</td>
</tr>
<tr>
<td></td>
<td>Anti-neoplastic properties</td>
<td>Anemia</td>
</tr>
</tbody>
</table>

Preformed types of vitamin A are only found in feed of an animal origin (Carazo et al., 2021). Some compounds in the class of polyisoprenoid plant pigments (carotenoids), may yield retinoids metabolically and, therefore, possess vitamin A activity (Combs and McClung, 2017). However, enzymatic processes can only convert a small percentage of carotenoids into retinoid precursors of retinol or retinoic acid in animals (Solomons, 1994). The extent to which they are utilized depends, among other factors, on the form of binding, animal species, diet composition and vitamin A supply status. Basal feedstuffs, such as cereal grains and roughages, commonly used in ruminant
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nutrition are deficient in vitamin A (Salinas-Chavira et al., 2014). It is therefore common practice to supplement herbivorous diets with sources of retinol (mostly in the form of retinyl acetate). The importance of providing an adequate amount of this vitamin, no matter how it is administered, has been well recognized (Lespine et al., 1998). Vitamin A requirements, however, depend on a wide range of environmental, genetic, and nutritional factors (Chen et al., 2015).

A comprehensive understanding of vitamin A metabolism in ruminants is essential for accurately assessing dietary requirements, identifying health risks associated with inadequate intake, and informing appropriate supplementation strategies. It is crucial to grasp the complex interplay between vitamin A metabolism, dietary intake, and supplementation for optimal health and wellbeing.

This review provides a thorough evaluation of the metabolism of vitamin A in cattle, including the effects of supplemental retinol on various aspects such as immune function, antioxidant capacity, reproduction, myogenesis, preadipocyte formation, the allergenic potency of milk proteins, and the considerations related to proper vitamin A supply in dairy and beef cattle.

**Metabolism of Vitamin A**

Ruminants, such as cattle, have a complex digestive system comprising of several stomach compartments, with the rumen being the largest. This compartment houses a diverse microbial ecosystem that plays a crucial role in feed digestion and fermentation (Castillo-Gonzalez et al., 2014). However, it is also a site of potential vitamin A loss or degradation, which can affect the overall metabolism of retinol in ruminants (Mitchell et al., 1967).

Vitamin A may be present in the paunch as both free forms and esterified forms. Retinyl esters can be cleaved by microorganisms, releasing free retinol (Rode et al., 1990), which can then be converted into other forms such as retinal and retinoic acid through a series of enzymatic reactions carried out by the microflora (Srinivasan and Buys, 2019). As a result, the rumen microbiome can play a critical role in determining the bioavailability and metabolism of vitamin A in cattle.

The metabolism of retinol in herbivores is a complex process that involves multiple organs and tissues, including the intestine and liver. In the small intestine, vitamin A esters are hydrolysed by pancreatic lipases, which release retinol into the intestinal lumen. Vitamin A as a fat-soluble vitamin is
predominantly absorbed in the proximal part of the small intestine (Goncalves et al., 2015). After absorption, retinol is re-synthesized into esters in the enterocytes and incorporated into chylomicrons. These chylomicrons are then transported through the lymphatic system and bloodstream to deliver vitamin A to the liver (O’Byrne and Blaner, 2013). Several factors affect the absorption of vitamin A in cattle, such as dietary fat content, intestinal health, and the presence of other micronutrients. Higher dietary fat content can enhance vitamin A absorption, while intestinal diseases can impede it in animals (Reboul, 2013; Amimo et al., 2022).

Once in the hepatic tissue, vitamin A is either stored or transported to other cells in the body. In the liver, vitamin A is esterified with long-chain fatty acids to form retinyl esters, which are stored in hepatic stellate cells (Grunet et al., 2013; Haaker et al., 2020). The liver can store large amounts of retinyl esters, which can be mobilized when needed. Retinol-binding protein (RBP) is the primary carrier protein for vitamin A in the circulation, and it binds to retinol to form a complex that is transported to other tissues (Berry and Noy, 2012). The cellular uptake of retinol is mediated by cells expressing the STRA6 membrane protein, which takes up the retinol-RBP complex (Kelly and von Lintig, 2015). Inside the cell, vitamin A is usually converted into its active form, retinoic acid, through two sequential oxidation reactions catalyzed by retinol dehydrogenases and retinal dehydrogenases (Bchini et al., 2013).

Retinaldehyde can be synthesized from dietary carotenoids, like β-carotene, which are absorbed through simple diffusion and cleaved by dioxygenases in the intestinal mucosal cells, as noted by Hynd (2019). The conversion of retinaldehyde to retinoic acid occurs through a two-step oxidation process, with retinaldehyde dehydrogenase catalyzing the addition of a carboxyl group to the aldehyde group in the first step, followed by aldehyde dehydrogenases converting it to retinoic acid (Belyaeva et al., 2019).

The conversion of carotenoids, such as β-carotene, to vitamin A in cattle is inconsistent probably due to the variable activity of the enzyme responsible for this conversion, β-carotene 15,15′-dioxygenase. While β-carotene has the potential to serve as a source of vitamin A in ruminants, its contribution is hindered by factors such as the highly variable content of β-carotene in feedstuffs, limited and unpredictable conversion rates, low stability, and various animal-related factors. Accurately estimating the amount of vitamin A obtained from β-carotene in cattle diets is therefore challenging. In their publication titled “Meeting the vitamin A requirement: the efficacy and importance of β-carotene in animal species,” Green and Fascetti (2016)
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thoroughly analyzed the effectiveness and significance of β-carotene in various animal species, and the reader is referred to this work for a comprehensive understanding of the topic.

In the animal cells, retinoic acid binds to nuclear receptors, including retinoic acid receptors and retinoid X receptors, to regulate gene expression (Huang et al., 2014). The specific functions of vitamin A in cattle depend on the tissue and cell type, but it is essential for vision, immune function, and reproduction.

Vitamin A plays a crucial role in vision, particularly in the process of dark adaptation, which is the ability of the eye to adjust to low levels of light. The visual pigment in the retina, known as rhodopsin, is composed of a protein called opsin and a molecule called 11-cis-retinal, which is derived from vitamin A (Palczewski, 2014). In bright light, rhodopsin is bleached, and 11-cis-retinal is converted into all-trans-retinal, leading to a decrease in visual sensitivity (Chen et al., 2009). However, in low light, enzymes convert all-trans-retinal back into 11-cis-retinal, which can then recombine with opsin to form rhodopsin, restoring visual sensitivity (Kono et al., 2008). Therefore, a deficiency of vitamin A can lead to impaired dark adaptation, night blindness, and even complete blindness (Debelo et al., 2017). Additionally, vitamin A is also involved in maintaining the health of other parts of the eye, such as the cornea and conjunctiva.

Promoting cellular differentiation is one of the most essential functions of vitamin A in growth. Retinol is necessary for the proper differentiation of cells into specialized tissues and organs during embryonic development and throughout the growing period (Barber et al., 2014). Epithelial tissues, which are found in vital areas such as the skin, respiratory system, urinary tract, and digestive tract, depend on vitamin A for their growth and maintenance (Timoneda et al., 2018).

Apart from its role in cellular differentiation, vitamin A also plays a significant role in the growth and development of bones. Retinol deficiency in cattle can impair bone growth and increase the risk of bone malformations (Hayes et al., 1968). Vitamin A’s role in promoting the production and activation of osteoblasts, which are responsible for building new bone tissue, can be attributed, at least in part, to its effect on bone health (Henning et al., 2015). Additionally, retinol is involved in regulating bone resorption, which is the natural process of breaking down old bone tissue and replacing it with new bone tissue (Yee et al., 2021).

Given its essential role in a variety of physiological functions, vitamin A is a fundamental micronutrient, and its insufficiency can result in adverse
health outcomes, underscoring the importance of ensuring adequate intake. In
the following sections of this scientific review paper, we will provide a
comprehensive analysis of the impact of vitamin A supplementation on several
physiological functions, such as immune function, antioxidant capacity,
reproductive performance, myogenesis and preadipocyte formation, and effect
on allergenic potency of milk proteins.

**Effect on Immune Function and Antioxidant Capacity**

In 1928, Green and Mellanby discovered the role of vitamin A in immune
modulation, naming it the “anti-infective vitamin.” The results of subsequent
animal studies revealed that vitamin A supplementation improved resistance
to gram-negative and gram-positive bacteria, and prevented parasitic
infections (Chew, 1987).

The impact of hypovitaminosis A on respiratory infections in young
animals is well known. To address this issue, a recent study by McGill et al.
(2019) focused on bovine respiratory syncytial virus (BRSV), a pathogen that
causes lower respiratory tract disease. The researchers developed a
nanovaccine containing BRSV proteins encapsulated in polyanhydride
nanoparticles. However, when tested on calves with vitamin A deficiency, the
vaccine was ineffective, and the most animals did not receive protection from
BRSV challenge (Table 2). Moreover, the study found that acute BRSV
infection had an adverse effect on both serum and hepatic retinol levels (Figure
1). These findings highlight the critical role of vitamin A in regulating
respiratory mucosal immunity in animals.

**Table 2. Virus recovered from nasal swabs in BRSV challenged calves**

(McGill et al., 2019)

<table>
<thead>
<tr>
<th>Days p.i.</th>
<th>VAS Unvac</th>
<th>VAS BRSV NP</th>
<th>VAD Unvac</th>
<th>VAD BRSV NP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 0</td>
<td>0/6</td>
<td>0/13</td>
<td>0/6</td>
<td>0/12</td>
</tr>
<tr>
<td>Day 2</td>
<td>2/6</td>
<td>1/13</td>
<td>3/6</td>
<td>4/12</td>
</tr>
<tr>
<td>Day 4</td>
<td>6/6</td>
<td>5/13</td>
<td>6/6</td>
<td>10/12</td>
</tr>
</tbody>
</table>

*VAS=vitamin A sufficient; VAD=vitamin A deficient; Unvac=unvaccinated; BRSV
NP=nanovaccine containing BRSV. Nasal swab samples were collected on days 0, 2, 4 and 7
after BRSV challenge. Virus isolation was performed on bovine turbinate cells to determine virus
shedding. Results are presented as a ratio of BRSV positive samples/total samples.
Figure 1. Liver retinol level in BRSV challenged calves (McGill et al., 2019). Liver retinol was measured at necropsy, on day 7 after BRSV infection. $^{a,b}P < 0.001$ by student’s t-test.

A controlled gene expression appears to enhance both antibody-mediated and cell-mediated immune responses when retinol is provided in an optimal quantity (Oliveira et al., 2018). Jin et al. (2014) found that by supplementing dairy cows with vitamin A at twice the amount recommended by the NASEM (2001), immunoglobulins A, M and G, interleukin-1, glutathione peroxidase, superoxide dismutase and catalase activities were significantly increased along with total antioxidant capacity and the ability to inhibit hydroxyl radicals. In the group supplemented with increased amounts of vitamin A, the authors also observed a significant reduction in the somatic cell count in milk, and a significant reduction in soluble CD8, malonaldehyde and reactive oxygen species.

The prevalence of immune dysregulation is clearly associated with oxidative stress. The immune system uses reactive oxygen species to function, and thus requires adequate levels of antioxidant defences sequentially to prevent the harmful effects of excess free radical production (Victor et al., 2004). It has been shown that fat-soluble vitamins E and A boost immune responses in individuals exposed to specific environmental sources of free radicals (Hajian, 2015). The findings of Jin et al. (2014) suggest that greater vitamin A supplementation (220 IU vs 110 IU/kg BW) in dairy cow diets may improve both antioxidant and immune function. The authors also indicated that adequate vitamin A intake requirement estimates of NASEM (2001) may be insufficient to maintain immunity and antioxidant capacity in dairy cattle.
A study by Ma et al. (2005) found that supplementing beef cattle with 3300 or 4400 IU of vitamin A per kg of DM increased glutathione peroxidase and superoxide dismutase activities in serum significantly more than 1100 IU or 2200 IU of vitamin A per kg of DM. A further increase in vitamin A supplementation levels to 4400 and 5500 IU/kg DM significantly reduced malondialdehyde levels in blood serum. As a result, the authors recommended supplementing beef cattle with 3300 IU vitamin A/kg DM intake. The optimal level of antioxidative protection would, however, require an intake of 5500 IU of vitamin A/kg DM.

As Semba (1999) points out, using supplemental vitamin A should reduce infectious disease morbidity and mortality by enhancing immunity. Among dairy cattle, mastitis is the most common and costly disease in this regard (Halasa et al., 2007). It is often associated with intramammary bacterial infections (Lundberg, 2015). A notable protective role of dietary vitamin A supplementation against mastitis has been demonstrated in ruminant studies (Chew et al., 1982; Chew et al., 1984; Johnson and Chew, 1984; Chew and Johnson, 1985; Van Merris et al., 2004).

By 1982, Chew et al. had already shown that blood plasma levels of vitamin A and β-carotene had a highly significant correlation with California Mastitis Test scores. In the study, dairy cows with low plasma vitamin A and β-carotene levels scored higher than those with higher levels.

Unlike the previously described studies, Oldham et al. (1991) reported no effect of vitamin A on udder health. However, dairy cows supplemented with higher levels of vitamin A (170,000 IU/day) produced significantly more fat-corrected milk than animals receiving only 50,000 IU of vitamin A per day, or 50,000 IU of vitamin A+300 mg β-carotene per day.

More recent studies show that retinoic acid is important for modulating the immune response during acute mastitis, indicating that the metabolism of vitamin A changes profoundly during the course of this disease (Van Merris et al., 2004).

Retinoids, as noted by Semba (1999), influence the immune system in a variety of ways, including humoral immune responses such as the expression of mucin and keratin, cytokines, and adhesion molecules such as ICAM-1. Furthermore, retinoids impact cellular immune responses such as hematopoiesis, neutrophil development, differentiation, and function, natural killer cells, monocytes/macrophages, Langerhans cells, T and B lymphocytes, immune responses resembling T helpers type 1 and 2, immunoglobulin production, and apoptosis.
In a recent study by Agustinho et al. (2021), lactating cows supplemented with vitamin A prepartum had a lower milk somatic cell count than those without vitamin A (Figure 2). The authors attributed this observation to a balanced immune response resulting from retinol supplementation. Consequently, improving both immune and antioxidant functions in ruminants through vitamin A supplementation can be considered essential to health, growth, milk quality and udder antioxidant activity (Jin et al., 2014).

**Figure 2.** Somatic cell count for multiparous Holstein dairy cows (n = 80, total) that were fed diets with or without vitamin A (110 IU/kg body weight or none) during prepartum period (from day -35 to the day of calving; adapted from Agustinho et al., 2021). All cows received a common lactation ration postpartum. *Dietary vitamin A interaction (P = 0.04).

**Effect on Reproductive Function**

Vitamin A plays a crucial role in maintaining the structure and function of the reproductive tract in both males and females. In males, it is required for the normal development and maturation of spermatozoa, and its deficiency can lead to reduced sperm count and motility (Hogarth and Griswold, 2010). In females, vitamin A is involved in the regulation of follicular development, ovulation, and the maintenance of pregnancy (Clagett-Dame and Knutson, 2011). Its deficiency can cause irregular estrous cycles, embryonic death, and fetal abnormalities (McDowell, 2000). To stimulate the production of
testosterone in males, Leydig cells need to differentiate, a process that can be facilitated by retinol. Similarly, retinol also helps to promote the differentiation of theca cells in females, which are responsible for estrogen production (Yang et al., 2018). Therefore, it is important to ensure adequate vitamin A intake in the diet of cattle to maintain optimal reproductive health and productivity.

The study conducted by Shaw et al. (1995) demonstrated that administering vitamin A (retinol palmitate) in beef cows during superovulation had a positive impact on embryo quality. The results showed that the cows treated with vitamin A had a significantly higher \( (P < 0.05) \) mean number of high-quality and total transferable embryos than the control group that received corn oil alone. Moreover, the mean number of blastocysts was also greater in the cows treated with vitamin A, suggesting an improvement in embryo development. Notably, the administration of vitamin A did not affect ovulation rate or the total number of embryos recovered, indicating that its positive impact was solely on embryo quality. These findings are significant because they suggest that vitamin A supplementation during superovulation in cattle may lead to improved embryo quality, which could ultimately result in higher conception rates and increased productivity. Overall, the study highlights the importance of vitamin A in reproductive performance and the potential benefits of supplementing vitamin A in cattle breeding programs.

It is well established that heat stress during the summer months affects milk yields and fertility in dairy cows (Al-Katanani et al., 1999). It has been observed that when bovine oocytes are exposed to high temperatures, vitamin A has a safeguarding effect (Lawrence et al., 2004).

In their study, Lawrence et al. (2004) investigated the potential protective effects of retinol on bovine oocytes subjected to elevated temperature stress during \textit{in vitro} development. The study found that oocyte development was significantly compromised at 41.0°C, resulting in reduced blastocyst development and fewer total nuclei in derived blastocysts. However, when retinol was administered to the maturation medium, it prevented heat-induced reductions in oocyte development to the blastocyst stage \( (P < 0.05) \). These results suggest that retinol may have a protective effect on oocytes exposed to heat stress, potentially improving their development and viability. The results of this study are noteworthy in the context of reproductive management in cattle, as heat stress can be a common and challenging issue in many production systems.

\textit{In vitro}, retinol was also found to be beneficial for challenged oocytes, as shown by Livingston et al. (2002). The researchers explored the effects of
adding retinol to media containing developing bovine embryos in both low and atmospheric oxygen atmospheres. In the first experiment, bovine oocytes were matured with varying concentrations of retinol, fertilized, and cultured in a modified synthetic oviductal fluid under low oxygen conditions. The results showed that retinol treatment tended to increase blastocyst formation compared to controls. When blastocyst development rates fell below 20% in the control groups, retinol treatment improved embryonic development significantly ($P < 0.02$). In the second and third experiments, the addition of 5 micromolar retinol to the embryo culture medium did not improve cleavage or blastocyst rates under low oxygen conditions, but significantly increased ($P < 0.001$) blastocyst development under atmospheric conditions. These findings suggest that retinol supplementation to the maturation medium can improve embryonic development of bovine oocytes. This positive effect of retinol on stressed oocytes is unclear but Lawrence et al. (2004) questioned whether it might result from its role in the cell’s antioxidative system.

Finally, Michal et al. (1994) examined the effect of vitamin A and β-carotene supplementation on the reproductive performance of Holstein cows during the periparturient period. The results showed that cows supplemented with β-carotene had higher concentrations of plasma β-carotene and retinol than unsupplemented cows. β-Carotene and vitamin A supplementation also increased plasma retinol levels and reduced the incidence of retained placenta and metritis ($P < 0.1$), two common reproductive disorders in cows. These findings suggest that dietary supplementation with β-carotene and vitamin A can positively impact the reproductive health of cows during the periparturient period.

Therefore, in dairy cows, it can be concluded that vitamin A promotes the reproductive process and can reduce fertility problems.

**Effect on Myogenesis and Preadipocyte Formation**

Vitamin A plays a crucial role in animal growth and development. It appears that retinoic acid signaling has a major impact on myogenic differentiation in mammals (Zhu et al., 2009; Ryan et al., 2012). Wang et al. (2018) reported that vitamin A administration improved cattle growth by increasing PAX7 positive satellite cells and the expression of myogenic marker genes including PAX7, MYF5, MYOD and MYOG. As a result of retinyl palmitate treatment during an early stage, muscle fiber sizes were larger in vitamin A-treated cattle.
at harvest (Figure 3). The authors suggested that vitamin A levels in beef cattle need to be carefully managed in order to achieve optimal growth performance.

![Figure 3](image-url)  
*Figure 3. Average latissimus dorsi muscle fiber diameter at harvest (adapted from Wang et al., 2018). Angus steer calves were administered with 0 (control) or 150,000 IU vitamin A (retinyl palmitate) per calf at birth and 1 month of age. The resulting steers were harvested at 14 months of age. *$P < 0.05$; Mean, $n = 9$.

Beef palatability is greatly influenced by intramuscular fat content, or marbling (Moore et al. 2012). The study by Yu et al. (2022) showed that vitamin A/retinoic acid promoted vascular endothelial growth factor A and increased intramuscular adipose progenitors, resulting in the development of adipocytes within muscle tissue. The authors concluded that beef marbling can be promoted by vitamin A when administered at neonatal stage, without effects on overall fat content. Similarly, Harris et al. (2018) found that administering vitamin A at birth resulted in higher weaning weights in beef cattle due to improved muscle growth and enhanced marbling fat production (Table 3). As a result, vitamin A administration during early development could offer beef cattle producers a practical way to enhance marbling and improve beef production efficiency.
### Table 3. Impacts of neonatal vitamin A administration on cattle growth performance* (adapted from Harris et al., 2018)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>0 IU (n=9)</th>
<th>150,000 IU (n=7)</th>
<th>300,000 IU (n=9)</th>
<th>SE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth to weaning</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Birth weight, kg</td>
<td>35.1</td>
<td>35.6</td>
<td>35.6</td>
<td>0.58</td>
</tr>
<tr>
<td>Average daily gain, kg/d</td>
<td>0.88b</td>
<td>0.98b</td>
<td>1.00a</td>
<td>0.02</td>
</tr>
<tr>
<td>Backgrounding</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weaning weight at d 210, kg</td>
<td>219.2</td>
<td>248.7</td>
<td>246.0</td>
<td>5.98</td>
</tr>
<tr>
<td>Gain:Feed ration, kg</td>
<td>0.149</td>
<td>0.153</td>
<td>0.156</td>
<td>0.031</td>
</tr>
<tr>
<td>Finishing</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weight at 308 d, kg</td>
<td>312.1b</td>
<td>333.0ab</td>
<td>339.7a</td>
<td>8.65</td>
</tr>
<tr>
<td>Feed:Gain ration, kg</td>
<td>4.35</td>
<td>4.76</td>
<td>4.79</td>
<td>0.13</td>
</tr>
</tbody>
</table>

*Angus steer calves (n = 30) were randomly allocated to three treatment groups at birth, receiving 0, 150,000, or 300,000 IU of vitamin A at both birth and one month of age. a,b Mean values within a row with no common superscript differ significantly (*P* < 0.05).

### Effect on Allergenic Potency of Milk Proteins

Cow’s milk is one of the most common causes of food allergies in children and can also develop in adults. It is usually caused by bovine β-lactoglobulin (Selo et al., 1999; Hochwallner et al. 2014). This protein has the ability to bind a variety of hydrophobic molecules, for example retinoic acid (Konuma et al., 2007). In a recent study conducted by Hufnagl et al. (2018), retinoic acid was shown to inhibit the immunogenicity of β-lactoglobulin by binding to, and masking, its main cell epitope. According to the authors, feeding vitamin A to cows can enhance the loading of β-lactoglobulin with retinoic acid, thereby reducing the development of allergies to this component of cow’s milk. Further research is warranted to assess whether such a strategy would be effective and feasible.

### Guidance for Proper Vitamin A Supplementation

There are insufficient data to establish definitive vitamin A requirements for cattle, therefore “Adequate Intake” levels have been set by the NASEM (2000, 2001) and NASEM (2016, 2021). In ruminant nutrition, vitamin A supplementation must be considered for the prevention of deficiency symptoms, and to support optimum health, reproduction and performance. As Weiss stated (2017), the absence of a deficiency does not imply an adequate
dietary vitamin A level. Typically, healthy immune function requires higher vitamin A levels than those related to performance or reproduction (Weiss, 1998). Considering the benefits, the severe degradation of vitamin A in the rumen, and very high tolerability (up to 1.3 million IU vitamin A/d), feeding twice the adequate vitamin A intake requirement estimates of NASEM (2001) is justifiable (Jin et al., 2014).

According to the new NASEM (2021) recommendations, dry cows, growing heifers and lactating animals giving less than 35 kg of milk per day do not need more vitamin A than the value estimated by the NASEM (2001). The adequate retinol intake for animals producing more than 35 kg milk per day is now calculated as follows: 110 × BW + 1000 × (milk - 35). Thus, to replace the retinol secreted in milk by high performing dairy cows, an additional 1000 IU of vitamin A must be supplemented for each kilogram of milk. Despite this adjustment, nutritionists usually only consider the NASEM estimates for vitamins to be the minimum levels required to prevent clinical deficiencies (McDowell, 2018). According to McDowell (2006), however, the optimum vitamin supplementation level is the quantity that achieves the best growth rate, feed utilization, and health (including immune competency), while also providing adequate body reserves.

Finally, antioxidant capacity must be considered. To produce one liter of milk, 540 liters of blood are perfused into the udder (Potapow, 2010). Consequently, the higher the milk yield, the more oxidative stress occurs in the mammary glands (Bae et al., 2017). It therefore seems logical to give high-performing dairy cows more fat-soluble antioxidant vitamins such as retinol and α-tocopherol due to the increased redox imbalance. Vitamin A supplementation of 1000 IU per additional liter of milk (animals with >35 L/head/d) is unlikely to compensate for the increased oxidative stress in high-performing dairy cows. Similarly, modern beef cattle breeds, which are genetically enhanced to produce fast growth and meat deposition, exhibit increased metabolic turnover and oxidative stress. Retinol supplementation above the levels defined as adequate by NASEM (2016; 2021) (Tables 4 and 5) is required by high-performing animals under stress to maximize antioxidant and immune function (Ma et al., 2005; Jin et al., 2014). Furthermore, supplemental retinyl acetate may sustain significant losses during storage and processing, which cannot be accounted for in scientific vitamin norms (Hirai et al., 2023).

To close this gap and finally establish vitamin A requirements for cattle, high-quality dose-response trials are needed. These are costly and require a
significant number of animals, making studies of large ruminants difficult. It is nevertheless imperative in the years to come that considerable effort is made to understand retinol requirements in dairy and fattening cattle at all stages of production.

Table 4. Estimated adequate vitamin A intake in dairy cattle, NASEM (2001) and NASEM (2021)

<table>
<thead>
<tr>
<th>Committee</th>
<th>Adequate intake of vitamin A, IU/kg BW</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Growing heifers</td>
</tr>
<tr>
<td>NASEM 2001</td>
<td>110</td>
</tr>
<tr>
<td>NASEM (2021)</td>
<td>110</td>
</tr>
</tbody>
</table>

Table 5. Estimated adequate vitamin A intake in beef cattle, NASEM (2000) and NASEM (2016)

<table>
<thead>
<tr>
<th>Committee</th>
<th>Adequate intake of vitamin A, IU/kg BW</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Growing and finishing</td>
</tr>
<tr>
<td>NASEM 2000</td>
<td>2200</td>
</tr>
<tr>
<td>NASEM 2016</td>
<td>2200</td>
</tr>
</tbody>
</table>

Ultimately, balancing vitamin A supply for ruminants involves formulating a diet that provides sufficient vitamin A to meet the animal’s requirements, without exceeding safe levels. To ensure the safe and appropriate use of retinyl esters in cattle farming, it is essential to follow specific guidelines that limit the supplemental levels of vitamin A to the recommended intake levels as established by relevant authorities such as EC in the EU or CFIA in Canada. Any use of vitamin A in ruminants should be carried out within the framework of legal provisions and guidelines to prevent over-supplementation and potential negative impacts on animal health and welfare. Adherence to these guidelines is crucial to ensure that vitamin A supplementation in cattle farming is sound and effective in promoting optimal health and productivity. Hypervitaminosis A is highly unlikely to occur in cattle due to the strict regulation of vitamin A levels in animal feed, and it has not been reported in practical farming or husbandry scenarios, although it can be induced in certain experimental conditions.
Conclusion

Cattle require retinol as a key vitamin. It is common for ruminant feeds to be deficient in vitamin A. Therefore, synthetic retinyl acetate supplementation is given to the animals to meet their dietary requirements. The positive effects of retinol supplementation and injection have been demonstrated on cattle reproduction, performance, immunity, and health. Balanced cattle diets can maximize performance under specific conditions, if we know when it is appropriate, or best, to administer greater retinol supplementation or injection during production, and consider its effects on other vitamins, especially vitamins E and D. Therefore, further research is needed on the interaction of retinol with other fat-soluble bioactive agents. Additionally, we advocate establishing retinol requirements which take into account the function of vitamin A, genetics, and cattle farming methods based on the current state of science.

Acknowledgments

Thanks to Ute Obermueller-Jevic, PhD for her constructive comments on the draft manuscript.

Disclaimer

None.

Conflicts of Interest

The authors have no conflicts of interest to declare.

Declaration of Funding

The authors reported there is no funding associated with the work featured in this article.
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