Recent Studies on the Vitamin A Research in Animal Feeding

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이 무 환 : 가축사양에 있어서 비타민 A에 관한 최신연구

요 약

최근 가축사양에 있어서 「비타민A」에 관한 연구가 다시 검토되고 있다.
가축체내에서 「캐로틴」이 「비타민 A」로 전화되는 부위는 소장의 벽에서 이루어 지는데 최근에는 이 부위에서 전화되지 못한 「캐로틴」은 몸의 각부위 특히 간에서 이루어 진다고 보고 있다.
새로운 국제 표준으로 「베타캐로틴」이 「비타민 A」로 전화되는 율은 50%로 되어 있다.

가축 체내에서 「나이트레이트」는 「캐로틴」의 「비타민 A」 전화를 억제하며, 고단위 「나이트레이트」나 「나이트라이트」 급여는 축산물 생산을 저해한다. 「나이트레이트」를 농후사료가 적은 사료와 같이 급여하면 증체율이 감소되나 고단위 농후 사료에 보충 급여하면 증체율의 증가된다.

「비타민 A」와 「타이록신」은 길항 작용이 있다. 「타이로프로틴」이나 「타이로유라실」은 약간 높은율의 「비타민 A」 축적을 가져왔고, 갑상선 홀몬은 가축혈액중의 「캐로틴」 함량을 저하 시켰으며, 개에서 「타이록신」은 「캐로틴」 전화를 촉진시켰다. 「타이록신」을 많이 급여했을 때 「비타민 A」의 축적을 증가시키는 경향을 보았다.

「토코페롤」은 쥐에서 「비타민 A」를 절제하는 작용이있다. 인산보충은 「캐로틴」과 「비타민 A」의 체내 이용을 억제한다.

「소디움벤토나이트」는 쥐에서 「비타민 A」결핍을 가져왔으나, 이것이 건조된 알팔파가 함유된 육우의 사료에 함유되었을 때에 「캐로틴」의 이용도는 변함이 없었다.

「아드레나린」 주사는 혈청중에 「비타민 A」 함량을 증가 시켰으며, 이 홀몬은 단위동물의 「비타민 A」 대사작용에 영양을 미쳤으나 반추동물은 예외였다.

「스틸베스트롤」과 「크롤테트리싸이크린」은 육우의「비타민 A」 축적에 영향을 주지 않았다.

「인슈린」은 「비타민 A」 대사작용에 영향을 미친다고 보는 이도 있으나 아직 숙제로 남아있다.

열대지방에서 고단위 「비타민 A」 공급은 소의 「프라스마」의 「비타민 A」 수준을 유지시켰다.

「오레오마이신」 같은 항생물질은 소의 사료중에 적절한 량의 「비타민 A」가 함유되어있지 않으면 효과를 발효할 수 없다.

1, Introduction

Since many researchers focused attention on reevaluation of adequate Vitamin A knowlege, the detailed researches have been reported recently. For further study on Vitamin A in animal feeding, it is necessary to review the new aspects of Vitamin A researches that have ever been worked out by many workers.

Over the past few years a number of very valuable reviews have appeared dealing with various aspects of carotenoid and Vitamin A metabolism. The present review deals with factors influencing the utilzation of carotene, particularly from pasture, which is the main source for most domestic animals, with the conversion of carotene to vitamin A, and with the transfer of this vitamin and of the carotenoids to a animal products.

Other interesting aspects such as Nitrate, Thyroid, Tocopherol, Hormons, Minerals, Antibiotics, Fat and Oils and Environmental Temperatures have been studied on the effects of Vitamin A Metabolism by many workers. But there are still many fields to be fulfilled.

2, Vitamin A

Vitamin A is needed in the feed of all farm and range animals for growth, reproduction bone vision, maintenace of epithelial tissues, and most likely, the cell wall of every cell of the body.

Vitamin A is a complex organic compound that is very susceptible to destruction unless it is artificially protected. Due to the peculiar arrangement in the Vitamin A molecule, there are theoretically 16 different members that would appear alike, however, steric interference very likely prevents occurrence of all but the six members that have been isolated from natural materials.

This presence of these various forms, called isomers would not be so important except only one form is fully biologically potent in preventing vitamin A deficiency symptoms in animals, The presence of large amounts of the lessactive isomers could lead to vitamin failure in the presence of apparent plenty. Only all-trans Vitamin A give the same potency whenmeasured by animals and the ordinary chemico-physical methods.

The various isomers have biological potencies as follows;

Isomers	Biopotency per equal weight
7, 9, 11, 13-tetratrans(all trans)	100%
neo a(13-cis)	75%
neo b(11-cis)	24%
neo c(11, 13-dicis)	15%
iso a(9-cis)	21%
iso b(9, 13-dicis)	24%

There are several carotenes, but the one with highest biological activity is beta-carotene. Theoretically, this Vitamin A precursor should be slightly more potent than Vitamin A itself, as each molecule of beta-carotene is composed of Vitamin A. However, animals are wasteful in using beta-carotene and we find the following ralationship;

1 gram beta-carotene=1,670,000 I.U. of A

1 gram Vitamin A =3,330,000 I.U. of A

These values are determined with the rat and represent relative biopotencies for that animal. The rat then secures only about 1/2 (50.1%) of the theoretical Vitamin A value of carotene.

3, Conversion of Carotenoids to Vitamin A

Even 30 years after the discovery of the conversion, however, the mechanism by which carotene is converted to Vitamin A must be regarded as one of the major unsolved problems in the Vitamin A field. The problems remain to be solved concerning tha site of the conversion are;

1) For many years it was thought that the conversion was effeceted in the liver.

2) The application of modern chromatographic methods demonstrated that conversion takes place in the intestinal walls.

3) Recent evidence has suggested that various parts of the body, and particulary the liver, may be capable of converting any carotene which escapes conversion in the intestines.

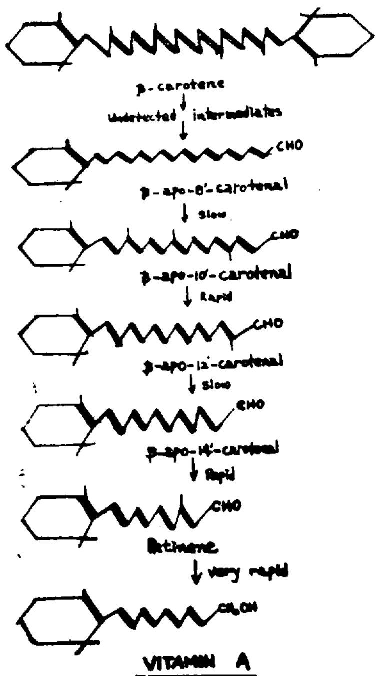
a) Mechanism of Conversion

Hunter (1946) has suggested oxidative attack at the central double bond of beta-carotene to yield two molecules of Vitamin A aldehyde, which are then reduced to Vitamin A.

Glover and Redfern (1954) have shown that the initial attack is at a terminal, rather than the central, double bond.

A somewhat similar attack in vivo would produce a series of aldehydic intermediates of decreasing chain length. They suggest a type of beta-oxidation of the carotene molecule to form Vitamin A aldehyde. Carter at al (1939) found that branched chain fatty acids are oxidized in vivo when the methyl group is in the alpaposition, but not when it is in the beta-position, to the carboxyl group. Redfearn (1957) has shown that bata-methyl groups in higher homologues of Vitamin A do not appear to inhibit further oxidation.

The following is the possible mechanism, as proposed by Glover and Redfearn (1956) for the conversion of beta-carotene to Vitamin A by a process of beta-oxidation.



It would seem that protamins are first transformed into Vitamin A aldehyde by stepwise oxidation from one end of the molecule, and then reduced to Vitamin A. Other carotenes, such as and carotene cannot yield more than one molecule of the Vitamin on oxidative scission. This is because beta-ionone ring is an essential part of the Vitamin A molecule (Vit. A_1), and while beta-carotene contains two such rings, alpa- and gama-carotene each have but one beta-ionone ring. (West and Todd, Text book of Biochem.)

b) Site of Conversion

Glover and Redfearn reported that the ability to convert carotene to Vitamin A would not be restricted to the intestinal wall. Sexton, Mehl and Deuel injected carotene intravenously into rats, carotene but not Vitamin A was deposited in the liver. When carotene was given orally, Vitamin A was found in the liver. These workers pointed out that the conversion of carotene to Vitamin A is an extrahepatic (outside of liver) function in the rat and suggested the wall of the intestine as a possible site for this transformation.

4, Influences of Nitrates on Vitamin A Metabolism

Recently, Nitrates and it's function on the Vitamin A metabolism especially relating to animal feeding, has appeared attractive to many researchers. Some investigators think that the use of higher levels of N_2 fertlization is partially responsible.

This results in higher levels of Nitrates in the plants, since they cannot convert as much of the Nitrogen into plant protein. In the rumen these Nitrates are changed into Nitrites(NO_2)which in some way either interfere with carotene conversion to Vitamin A by the animal. At the same time, there are others who are not sure that Nitrates are as important in increasing Vitamin A needs as was thought to be the case a year or so ago. This may be due to the fact that Nitrates will not affect the Vitamin A status under all dietary and environmental conditions.

Weichenthal et al (1961) reported that the feeding $NaNO_3$ to fattening cattle reduced feed consumption and weight gains but resulted in the formation of relatively small quantities of methemoglobin. The feeding of $NaNO_3$ appeared to have no effect on plasma Vitamin A levels.

Hale et al of University of Arizona in 1961 worked with 12 fattening steers on the effect of concentrate level (71.3 and 54 TDN) and KNO_3 addition to the ration (none and 1% KNO_3 on hepatic Vitamin A stores and performance of fattening steers.

The high concentrate ration caused a significantly larger depletion of liver Vitamin A than did the low concentrate ration. The same trend occured with the Nitrate addition, however, the difference was not significant. Although there was no treatmen effect upon average daily gains, there was a significant interaction between the concentrate level and Nitrate addition. This was due to the reduction in daily gains when Nitrate was fed with the low-concentration and an increase in gains due to Nitrate with the high concentrate ration. Both concentrate level and Nitrate addition reduced feed intake.

Neumann indicated that cattle with medium liver stores of Vitamin A lost this Vitamin A in direct relation to the amount of Nitrates in their ration. The rapid rate of depletion of Vitamin A from the livers suggested that the carotene in the ration was not being utilized at all.

Nitrate problem is also being reviewed in relation to other species as well. Under experimental conditions at the University of Missori, Pfander reported high Nitrate or Nitrite feeding to beef cattle, dairy cattle, sheep and swine has caused abortion, lowered milk production, reducedgains, produced unthriftiness, reduced Vitamin A in blood and liver and caused diarrhea. Nitrates in the water can also interfere with conversion of carotene to Vitamin A. It was reported that southern Minnesota wells with as much as 190 parts per million of Nitrates in the water. The report cites a number of cases in which direct results were obtained when high Nitrates were eliminated from wells. Feeding higher levels of true Vitamin A also has helped to offset the effects of Nitrate interference from the water supply in carotene conversion.

5. Vitamin A and the Thyroid

Many workers have studied on the relationship between Vitamin A and the Thyroid gland. Up until now, these workers have found the following evidences for an interrelationship between these two;

1) In various ways Vitamin A and thyroxine are antagonistic in their action.

2) Thyroxine is concerned in the conversion of carotene to Vitamin A.

3) Thyroxine influences the storage of Vitamin A, and the rate at which the Vitamin is used up.

1) The Antagonism between Vitamin A and Thyroxine.

(1) The Thyroid in relation to Vitamin A deficiency.

In 1932, Von Euler and Klussman suggested an antagonism between thyroxine and carotene. They found that the two substances had opposite action on the growth of rats deficient in Vitamin A. Thus doing with carotene promoted growth, but thyroxine accelerated the decline of the animals. The effect of thyroxine in inducing Vitamin A deficiency was confirmed by many workers.

In the reverse direction thyroidectomy, or dosing with thyroid inhibitors, ameliorated the effects of Vitamin A dediciency .

Cooper, March and Biely(1950) found that thiouracil could also improve the growth rate of chicks given small doeses of Vitamin A.

(2) Influence of Vitamin A on the condition of the thyroid gland.

Further evidence of antagonism between vitamin A and thyroxine, or at least of some form of interaction, may also be seen in the influence of the Vitamin A status on the size and histological condition of the Thyroid gland. Changes have been reported to occur both in deficiency of Vitamin A and in excess. Opposition to the action of the thyrotrophic hormone of the pituitary by large doses of Vitamin A was reported by Shneide and by Fellinger.

2) The influence of Thyroxine on the conversion of Carotene.

In 1933, Fasold and Heidemann indicated that the Thyroid is concerned in the conversion of carotene. The milk fat of the goat is usually white, like that of the sheep, but after thyroidectomy it became yellow. In the reverse direction Parhon and Werner found that thyroxine lowered the level of carotenoids in the blood of drakes. Inpigs which had been dosed with carotene Swick, Grummer and Baumann(1952) found slightly higher stores of Vitamin A in animals which had been treated either with thyroprotein or thiouracil than in control animals.

Kowalewski et al reported that there was accelerated effect on carotene conversion by thyroxine in normal dogs.

3) The Influence of Thyroxine on the Storage and Expenditure of Preformed Vitamin A

a) Storage

Less evidence is available on the effect of the thyroid status on the storage of Vitamin A than on the conversion of carotene. In most experiments little difference has been found between the storage in normal animals and others in the hypo or hyperthyroid state. There are some indications, howaver, that excess of thyroxine may tend to increase the storage of the vitamin.

In rats given daily doses of 3,000 i.u. of Vitamin A Logaras and Drummond found that treatment with either thyroxine or dinitro or dinitrophenol increased the average storage of the vitamin by 15~20% over the level found in untreated animals.

Johnson and Baumann (1947), who gave 130 i.u. daily, found little difference in storage by normal, hyper and hypothyroidal rats.

Morgan and White (1950) found that the stores accumulated by rats, given about 100 i.u. of the vitamin daily for six weeks, were the same in controls and in animals given thyroid. The equality in the total stores was maintained even although the livers were enlarge by the treatment with thyroid.

b) The Expenditure of Vitamin A

Johnson and Baumann indicated that thyroxine increases the expenditure of the Vitamin A reserves during restriction to a deficient diet. In their experiments on rats both normal and thyroid-treated rats the expenditure of vitamin could be reduced by restricting the food intake, which inturn restricted growth.

It was concluded that a three-fold increase in the metabolic rate could be more than counter-balanced by a decrease in the growth rate by 50%.

6. Other Factors Influencing on Vitamin A Metabolism

a. Tocopherols

It has recently been shown that tocopherols exert prenounced Vitamin A sparing action in the rat, especially when Vitamin A is fed at near minimum levels (Moore, 1940; Hickman etal., 1942, 1944; Harris et al., 1944; Lemley et al , 1947; and others).

However, even at higher levels of Vitamin A intake there is still some sparing action (Guggenheim, 1944; Moore 1940).

Whiting and coworkers (1949) worked on the influence of Tocopherols upon the mammary and placental transfer of Vitamin A in the sheep, goat and pig. And they reported that the Vitamin A and Tocopherol supplementation did not increase the Vitamin A content of the blood plasma of these animals. Spielman et al (1946) found that even when high levels of carotene (1,000,000 I.U. daily) were fed to dairy cows there was a considerable drop in the blood plasma.

b. Phosphorus (soft) and Sodium Benonite

The possibility that phosphorus affects the utilization of carotene was suggested by an observed inverse relationship between the inorganic phosphorus and carotene content of the blood plasma of Hereford cows maintained on adequate-and low-phosphorus rations (Ross and Gallup, 1949). Although inefficient in the results with steers, supporting evidence was not obtained in similar studies conducted with lambs(Thimas, 1951): Viamin A levels in the blood and liver of lambs fed nine times their minimum requirement of carotene were unaffected by phosphorus deficiency.

In studies of the effect of phosphorus deficiency on carotene and Vitamin A metabolism, increases in plasma carotene levels were observed in seperate experiments with phosphorus -deficient steers (Thomas, Gollup and Whitehair, 1953). Although these increase were relatively small, they were believed to indicate inefficient conversion to Vitamin A during phosphorus deficiency.

Thomas and Coworkers (1953) reported that with respect to phosphorus intake and plasma Vitamin A levels, the results reveal no definite relationship or trend and that milk from the phosphorus deficient cows contained more carotene but less Vitamin A than that from the cows fed adequate phosphorus.

Studies with rats and sheep by Klosterman et al. (1952) indicated that phosphorus supplementation depressed carotene and Vitamin A utilization. However, Erwin and Page (1958) found that supplementation with soft phosphate resulted in a significantly greater loss of Vitamin A from the liver of the lamb than did supplementation with either bone meal or dicalcium phosphate.

The incorporation of sodium bentonite, acolloidal clay, into purified rations has resulted in a Vitamin A deficiency in rats, as reported by Laughland and Phillips(1954), and in chicks, by Briggs and Spivey(1954). Erwin et al. (1957) reported that colloidal clay not only absorbed carotene but also other pigments found in alfalfa. However, when bentonite was added to a steer ration that contained dehydrated alfalfa, carotene utilization was not altered.

c. Hormons:

1) Adrenaline

With rats, Klopp et al (1951)found that Adrenaline injections resulted in an increased serum Vitamin A content.

Further, Adrenalectomized dogs and rats exhibited a marked reduction of serum Vitamin A. With rabbits and rats, Goodwinet al, (1949) repoted that there was evidence that Adrenaline influenced Vitamin A metabolism. Gleye et al. (1954) have shown that Adrenaline markedly reduced serum albumin in the guinea pig.

The effect of Adrenaline on the alternation of Vitamin A in the blood of man and monogastric animals reported by Hillman(1949) and Klopp et al. (1951) was predisposed by changes in serum protein fractions.

Vernell and Erwin(1959) worked on the effect of Adrenaline on Vitamin A metabolism in cattle and sheep. And found that Adrenaline injections altered neither the ratio of serum proteins in cattle nor plasma carotene and Vitamin A livels of cattle and sheep. Further, the hormone did not influence the content of carotene and Vitamin A in the bovine livers even though adrenaline markedly altered the physical activity of the calves. These results suggest that fac tors regula ting Vitamin A metabolism may be different in the ruminant from those in certain monogastric animals.

2) There is a report on Stilbestrol and Chlortetracycline;

Erwin and Goworkers (1958) reported that neither stilbbestrol nor chlortetracycline influenced liver carotene or Vitamin A storage in beef steers.

3) Insulin

The relationship of insulin to Vitamin A metabolism is unclear. It has been felt by various workers that diabetic individuals have impaired efficiency of carotene conversion into VItamin A.

Soble and others(1953) showed definitely that the conversion was markedly lowered in alloxan diabetic rats. In isolated intestinal loops from such rats Rosenberg and Sobel demonstrated a marked diminution in the conversion process.

d. Temperature

Purdue workers showed that during the hot summer months there was a greater difference between the control lot and the steers fed the higher levels of supplemental vitamin A than was apparent after the onset of cooler weather. There was less decline in appetite during the hot weather and also less panting with the steers fed Vitamin A.

During the hotest weather in August, the level of plasma Vitamin A in the control cattle decreased 50%, but the group fed 3,2000 I. U. of supplemental Vitamin A showed a drop of only 15% in the level of plasma vitamin A. Recent Florida data with sheep kept in temperature controlled chambers showed that sheep kept at 90° F. had a lower feed intake and lower blood vitamin A level than sheep kept at 55° F.

These data substantiate the Purdue data showing that hot weather decreases feed intake and blood vitamin A level. More research is needded along this line, however, to more adequately substantiate these two studies. John Algeo reported that Vitamin A is helpful to cattle feeders in his area of the country in alleviating some of the effects of hot weather. He also feels that Vttamin A will help in alleviating some of the effects of cold weather.

e. Antibiotics

Reports by Coates et al. (1952) and Burgers et al. (1951) with chicks fed antibiotics indicate an increased liver content of Vitamin A, but Coates et al. (1952) indicated an increase in Vitamin A only in the presence of increased growth.

Purdue researchers have shown a very important interrelationship between Aureomycin and Vitamin A. The control cattle receiving no supplemental vitamin A showed a growth depression from Aureomycin. All steers whichreceived Vitamin A, however showed a significant incresae in daily gain from Aureomycin. This findingneeOs follow-up study, since it may indicate that antibiotics may not give their optimum response unless the cattle ration is adequate in vitamin A.

7. Summary

These few years, adequate Vitamin A knowlege have been re-evaluated.

Conversion of Carotene to Vitamin A takes place in the intestinal walls. Recent evidence has suggested that various parts of the body, and particulary the liver may be capable of converting and Carotene which escapes conversion in the intestines.

The new international standard for Vitamin A is based on 50 per cent conversion of beta-carotene to Vitamin A.

Nitrates interfere with carotene convesion to Vitamin A by the animals. High Nitrate or Nitrite feeding was reported to be harmful for animal production.

When Nitrate was fed with the low-conctrate ration, daily gain was decreased and increased when Nitrate fed with the high-concentrate ration.

Vitamin A and Thyroxine are antagonistic in their action. Thyroprotein or Thiouracli resulted slightly higher stores of Vitamin A. Thyroxine lowered the level of carotenoids in the blood of animal. There was accelaerated effect on carotene conversion by Thyroxine in normal dogs. The excess of Thyroxine may tend to increase the storage of Vitamin A.

Tocopherols has Vitamin A sparing action in the rat.

Phosphorus supplementation depressed carotene and Vitamin A utilization.

Sodium benetonite resulted Vitamin A deficiency in rats, but when it was added to a steer rátion that contained dehydrated alfalfa, carotcne utilization was not altered.

Adrenaline injection resulted in an increased serum Vitamin A content. Adrenaline influenced Vitamin A metabolism, in mono-gastric animals, but not in ruminant.

Stilbestrol and Chlortetracycline did not influenced Vitamin A storage in beef steers.

Insulin may effect Vitamin A metabolism but it remains unclear.

Antibiotic (Aureomycin) may not give their optimum respons unless the cattle ration is adequate in Vitamin A.

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