Understanding Gossypol Toxicity Problems in Feeding Cotton-By Products to Ruminant Livestock

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INTRODUCTION:

Whole cottonseed (WCS) and cottonseed meal (CSM) are popular by-products of the cottonseed industry. Whole cottonseed is a high source of energy, fiber and proteins in diets of lactating dairy and beef cattle. As much as 7 pounds per cow per day may be fed with excellent results in maintaining high milk production and fat tests. Cottonseed hulls are commonly used to increase the fiber source in rations. After extraction of oil from prepared cottonseed, the resulting cottonseed meal is available for animal feeding (Fig.1). Cottonseed meal, is an excellent and economical source of protein in animal nutrition, particularly in starter and grower rations of dairy calves.

Gossypol is a naturally occurring compound in the cotton plant (Gossypium spp.). Because gossypol has been recognized since the turn of the century to be toxic to animals at high enough levels, a limiting factor of WCS and CSM as feed sources is their gossypol content (Adams and Geissman, 1977). Monogastric species such as swine and poultry have been known to be susceptible to gossypol toxicity. However, despite years of favorable feeding of CSM to pre-ruminant livestock, recently, gossypol toxicity in young calves as well as lambs have been reported (Holmberg et al.,1988; Morgan et al.,1988). These reports have suggested that in calves and lambs the undeveloped rumen (preruminant) function essentially as monogastrics and is unable to detoxify gossypol. Ruminants have been purported to detoxify gossypol in the rumen by binding to soluble proteins (Reiser and Fu, 1962). However, reports of toxicity in mature cattle suggests that the capacity of the rumen to detoxify gossypol can be exceeded.

The effects of gossypol in calves and adult ruminants are covered in this article. In addition, recommendations for safe levels of gossypol consumption are reviewed.

GOSSYPOL PIGMENT

Gossypol, is a yellow polyphenolic pigment found in the glands, stems, and roots of the cotton plant belonging to the genus Gossypium and the Malvaceae family (Adams and Geisman,1977). While gossypol is the major phenolic in cottonseed, there are at least 15 closely related compounds. The phenolic groups on the molecule are

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chemically reactive, so it can bind readily with minerals and amino acids.The major content of gossypol in the plant is found in the seed glands, which appear as small black dots on the cut surface of cottonseed. The amount of gossypol in cottonseed ranges from .16 to 1.61 per cent (Jones, 1991) and is dependent on plant species as well as climatic and soil condition, water supply and amount and composition of fertilizers used (Altschul et al., 1958). The plant species G. barbadense contains more glands and more gossypol when compared to G. hirsutum (Morgan,1989). Gossypol in the plant is related to insect resistance. In experimental conditions, plant varieties bred to contain higher gossypol content appear to be more insect resistant. Although, there are varieties of glandless cotton plants, they make up less than a tenth of one per cent of the acreage of the U.S. cotton crop(Jones,1991).

Gossypol content in feeds is reported in terms of "total", free" and "bound". The biologically active or the toxic form of gossypol is the free form (free gossypol) not the bound form which has complexed with proteins. In whole seed, virtually all the gossypol is in the free form. The processing of WCS into meal complexes gossypol with proteins, primarily the epsilon amino group of lysine and becomes bound, the biologically inactive form. Although, many researchers are concerned about the effect of bound gossypol, evidence is lacking to consider it along with free gossypol in terms of toxicity. This subject is currently under investigation.

The total gossypol content of CSM is not affected by the method used for oil extraction because total gossypol equals free gossypol plus bound gossypol(Jones, 1991). The final free gossypol content in the CSM is dependent on the seed content and method used to extract the oil. Direct solvent extraction yields the highest content of gossypol and screw press the lowest (Berardi and Goldblatt, 1980). The majority of cottonseed mills now use expanders, which is a modified extruder. Expanders introduce some heat and pressure into the process of solvent extraction of cottonseed oil (Jones, 1991). The production of heat in this process binds some of the gossypol (bound gossypol). The different processes used in the U.S. to extract oil have been described (Jones, 1991). They are listed in order of most common used:

1. EXPANDER SOLVENT PROCESS. Prepared seed kernels are run through an expander before using hexane to extract the oil. Yields highest amts of gossypol

2. EXPELLER OR SCREW PRESS PROCESS (OLD PROCESS). Large screw presses are used alone without the use of solvent extraction. Yields the lowest gossypol content.

3. PREPRESS SOLVENT PROCESS. Oil is removed using powerful screw presses before using an hexane extractor.

4. DIRECT SOLVENT PROCESS. Uses no expanders and usually results in the highest free gossypol content.

The majority (92%) of the crush capacity of the U.S. cottonseed processing industry is via screw press, prepress solvent or expander solvent processes (Jones,1991 1-18). All of these methods induce considerable heat and pressure in production of CSM, whereby gossypol content is markedly reduced when compared to the solvent extraction method. Furthermore, the direct solvent extraction method is expected to account for none of the 1992-93 crush year, due to a conversion of methodology to expanders (Jones, 1991). In examining these changes in oil extraction methodology, it is this author's opinion that the content of free gossypol in CSM will be lower in the future.

TOXICITY

Factors that predispose the animal to toxicity include age, duration of ingestion, rumen function, protein and mineral content of the ration. It is known that the toxic effect is cumulative in nature, were toxicity occurs after several weeks to months of ingestion. A quantity of gossypol must accumulate to a certain level in order to exert its effects and cause clinical signs or death. Levels in the liver and kidney but not muscle, are elevated in proportion to the amount of free gossypol consumed (Morgan et al. 1988).

It appears that gossypol is cardiotoxic. Death is attributable to heart failure. This accounts for the chronically labored breathing, pendulous abdomen, intermandibular swelling, and jugular distention that are commonly observed in animals with gossypol toxicity prior to death. On post mortem examination, the following findings are usually present; fluid filled lungs, enlarged liver with an nutmeg discoloration, straw color abdominal effusions and edema of the mesentery. The above clinical and post mortem finding are compatible with heart failure. The changes present in the liver may be secondary to heart failure, however a direct effect of gossypol on the liver cannot be ruled out.

In swine and dogs, gossypol content of the liver was related directly to changes in electrical patterns of the heart(Albrecht et al., 1968). Gossypol may bind to phospholipids or epsilon amino group of lysine present in the cytoplasm of cardiac cells, altering cellular permeability of potassium. Changes in intracellular potassium concentration have an affect in cardiac conductivity and function. Gossypol toxicity causing sudden death are attributed to an acute alteration of intra and extracellular potassium content interfering with conduction.

Gossypol may also cause an effect of the red blood cells by increasing hemolysis and affecting their ability to release oxygen from hemoglobin (Morgan, 1989).

TOXICITY IN YOUNG RUMINANTS

Gossypol is detoxified in the rumen by binding to soluble proteins (epsilon amino group of lysine) produced by ruminal microbes and by dilution and slowed absorption (Reiser et al.,1962). Calves and lambs are often fed rations that contain CSM during preweaning (less than 2 months) or after weaning. It is not precisely known when the rumen matures or becomes functional and cannot be entirely determined by age. Therefore, young ruminants with undeveloped rumens appear to function as monogastric animals and gossypol cannot be effectively detoxified.

A 100 % mortality occurred prior to 30 days of age in lambs administered 900 ppm of gossypol acetic acid and myocardial lesions were evident in euthanatized healthy lambs consuming 100 ppm (Morgan et al., 1988) The free gossypol in the study reported above was administered via gelating capsules orally, which could have resulted in a more concentrated , undiluted dose of free gossypol being made available for intestinal absorption. Because death or clinical signs of gossypol toxicity did not occurred to the group consuming 100 ppm, Morgan suggests that up to 100 ppm of free gossypol in lambs is safe.

Death losses from gossypol toxicosis in calves have been reported to range from 350 ppm to 850 ppm (Hollon et al., 1958; Holmberg et al., 1988; Rogers et al., 1975 and Risco et.al., 1992). In the above reports, the variability in calf responses to various levels of gossypol consumption was due to different undefined dietary and management conditions, raising questions about the actual safe concentration of free gossypol in feed. In an attempt to help define at what levels free gossypol is safe in young calves, the author measured the effects of feeding diets containing 0, 100, 200, 400, or 800 ppm of free gossypol to Holstein calves from 1 to 120 days of age (Risco et al., 1992). Clinical evidence of disease was limited to calves fed 400 or 800 ppm free gossypol. We concluded from the study that a ration containing up to 200 ppm of free gossypol is safe, 400 ppm of free gossypol approaches toxicity and 800 ppm causes death losses. In terms of mean daily free gossypol consumption, 2 grams approaches toxicity.

RUMINANTS

In ruminants, the protein binding detoxifying mechanism can be overwhelmed if the free gossypol content is excessive, or a low protein content is present in the rumen. The symptoms of gossypol toxicity seen in ruminants include sudden death as in monogastrics, physiological and reproductive effects without death (Smalley and Bicknell, 1982).

Physiological changes occurred and gossypol was found in tissues in 24 lactating dairy cattle fed a diet containing 45% direct solvent extracted CSM (.225% free gossypol) for 14 weeks (Lindsey et al., 1980). Free gossypol intake averaged 24.2g/day or 19.4mg/lb, and the concentration of free gossypol in the ration as fed was .1012 ppm. The clinical signs observed by Lindsey, were limited to reduced milk production and respiratory stress. Physiological changes were a decrease in hemoglobin content and an increase in erythrocyte fragility, which appeared to be detrimental only in periods of heat or nutritional stress.

A ten per cent mortality rate was reported in lactating dairy cattle fed 6 to 10lbs/head/day of whole seed for a 6-8 month period (Smalley and Bicknell, 1982). The level of free gossypol in the whole seed ranged from .17 to .68 per cent. Milk production was not affected and death was preceded by minimal signs of toxicity. Lesions found on post mortem examination resembled those seen in swine with gossypol toxicity. Gossypol was not found in the milk.

It should be kept in mind that in the reports cited above cows were fed high levels of cottonseed which contained a high concentration of free gossypol. There has been a paucity of research evaluating at what level free gossypol is safe for ruminants. It is generally accepted that the period from about three to eight weeks of age is considered a transitional period during which the rumen becomes functional. From three to eight weeks of age the ability to detoxify dietary free gossypol increase and 200 ppm is safe. From 8 to 24 wks of age 200 ppm is considered safe whereas mature ruminants (older than 24 wks) can tolerate up to 600 ppm in their diets without adverse effects (Calhoun and Holmberg, 1991).

Because gossypol intake has been associated with infertility in men in China (Liu et al., 1985), considerable interest in the role of this compound as a male contraceptive has occurred. Research in this area over the past years has created some concern about the safety of cottonseed products to breeding age cattle. The reproductive effects of gossypol in ruminants has been reviewed by Randel et al., (1992).

The ruminant female appears to be more resistant to gossypol when compared to the male. In vitro studies have shown some inhibition of embryonic development and ovarian steroidogenesis. However, in a commercial operation it appears unlikely that gossypol intake affects reproduction in females. In a study involving post pubertal beef heifers direct solvent CSM and WCS were fed to provide intakes of 0, .4, 1.7, 3.3 and 8.2 g/day of free gossypol for 62 days. Cumulative 30 day pregnancy rates were not different among treatment group (Gray et al., 1990).

Gossypol appears to exert unique and selective effects upon the male reproductive system. These include reduced spermatogenesis and impaired sperm motility; the latter associated with morphological aberrations of the sperm midpiece. Feeding gossypol containing feedstuffs to bulls and rams has been shown to damage the spermatogenic epithelium (Randel et al., 1992). In addition, feeding WCS but not CSM delayed puberty in Brahman bulls. The author (unpublished information) has observed an increase in sperm cell midpiece abnormality and erythrocyte fragility in Brahman bulls fed 6 kg of CSM (8.2 g/day of free gossypol). The type of cottonseed product (CSM vs WCS), total vs free gossypol and amount of gossypol fed may determine whether or not changes in spermatozoal morphology occur. When WCS was used to provide up to 27 g/d of FG to bulls no changes in sperm morphology were detected (Chase et al., 1989). It has been suggested that detoxification of gossypol in the rumen is more efficient with WCS diets than with CSM diets. In a study by Jimenez et al., (1989) a CSM ration that provided 13.5 g/d of total gossypol, was fed for 42 days without changes in sperm morphology noted.

Collectively the studies cited above suggest that gossypol can escape complete detoxification in the rumen and have an effect on erythrocyte fragility and testicular tissue. However, the relevance of these studies to commercial cattle operations needs to be brought into its proper perspective. First, the levels of CSM or WCS fed in the study rations were high and exceeded commercial ration recommendations. Second, the free gossypol content in the CSM study rations was obtained from solvent extraction methods. Finally, males in the above cited studies were not subjected to a breeding or fertility study. Further studies are warranted in order to determine whether or not these changes observed affect breeding performance in bulls.

DIAGNOSIS

When suspecting or investigating a gossypol toxicity problem the following factors must be considered:

HISTORY OF FEEDING COTTONSEED PRODUCTS

1. Young calves - Cottoseed meal or cottonseed hulls in starter or grower rations.
2. Ruminants - Whole cottonseed or cottonseed meal fed above recommended levels.

GOSSYPOL CONTENT IN FEED

1. Determine what method was used for oil extraction in the cottonseed meal source. Direct solvent vs. Mechanical press.
2. Have feed tested at official gossypol testing laboratories.
3. Analyze the cottonseed feedstuff(whole seed, cottonseed meal or hulls) in the mixed ration separately. Analysis for total and free gossypol concentration in mixed rations is unsatisfactory.
4. From the levels of free gossypol in the WCS, CSM or hulls calculate the content that would be present in the diet. For example: The pellet content in a starter ration for calves is 25%. The free gossypol content in that pellet (composed of CSM and hulls) is 800ppm. Therefore, the total free gossypol content for the starter ration is 200 ppm (.25 x 800 ppm).
5. To estimate free gossypol in whole seed from that level reported in kernels multiply by a factor of 0.68.

WCS Free gossypol = 6000 ppm

CSM " ≈ 400-600 ppm

CSH " as high as 100 ppm

CLINICAL PICTURE

1. Multiple animals involved.
2. Sudden death syndrome.
3. Chronic respiratory problems, unresponsive to antibiotics.
4. Animals not doing well, depress.
5. History of infertility.

GROSS NECROPSY FINDINGS

1. Perform by a veterinarian familiar with this toxicity.
2. Lesions compatible with failure of the cardiovascular and respiratory system as reported in swine.
3. Histopathology should be performed and interpreted by a pathologist familiar with this toxicity.

CLINICAL PATHOLOGY

There are minimal changes in blood chemistry and erythrocytes parameters during toxicity. Changes that have been consistently reported are as follow: An increase in erythrocyte fragility, hemoglobinuria, anemia and a decrease in hemoglobin content.

DIFFERENTIAL DIAGNOSIS

The following disease processes must be ruled out (Morgan, 1989).
1. Monensin toxicity.
2. Vitamin E and Selenium toxicity.
3. Toxic plants such as: Coffee senna, bracken fern, white snakeroot, Lantana and milk weed.

PREVENTION/RECOMMENDATIONS

As discussed earlier the stage of rumen development is critical in detoxifying gossypol. While the young ruminant is being fed milk, rumen development and function is minimal. During this time the animal functions essentially as a pre-ruminant and tolerable levels of free gossypol in the diet are similar to non-ruminant species. In poultry and swine this level is 100 ppm. However, acceptable weight gains and no illness was found in calves consuming up to 200 ppm of free gossypol (Risco et al., 1992). In the above study a 31% CSM diet was fed for the first 120 days of life. Free gossypol intake was less than 1 g/day/.

Calhoun and Holmberg (1991) have recommended that adult cattle be fed a diet that contains no more than 600 ppm or 6.8 mg/lb LW/day of free gossypol. Consumption of free gossypol at this level in commercial operations should not adversely affect reproduction in females (Grey et.al., 1990). In ruminant males use for breeding the recommendation is 200 ppm free gossypol in the complete diet. It is this authors opinion that consumption of up to 2 g/day of free gossypol in ruminant males is safe in terms of reproductive performance. When considering toxicity levels of free gossypol in ruminants the source, WCS vs CSM should be considered. As stated earlier detoxification of free gossypol in the rumen appears to be more efficient with WCS.

In poultry and swine diets, iron is added to rations in the form of ferrous sulfate at a ratio of 1:1 iron to free gossypol in order to help prevent toxicity. An insoluble complex is formed between the iron and gossypol which prevents absorption. In addition, high intake of protein and calcium appears to have a protective effect. The mitigating role of minerals and vitamins supplementation on free gossypol absorption warrants further research.

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FIGURE 1. PROCESSING STEPS FROM HARVEST TO PRODUCTS OF COTTONSEED.