The Status of the Cottonseed Meal Injury Problem*

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THE author proposes to give briefly the status of the problem involved in the feeding of cottonseed meal, a product which is of great economic importance to the country.

Feeders have long been aware that the *seed* of the cotton plant, unlike that of the wheat plant, could not be fed in large amounts with impunity. Later when the meal was fed in the larger amounts, trouble was encountered also.

Finally, in 1915 Withers and Carruth[1] announced the rediscovery, in cottonseed, of a toxic phenol-like substance, gossypol. This was obtained from the seed, where it occurs in relatively large amounts. It was later obtained, also, from the meal together with another form, D-gossypol, which differed in solubility.[2]

Withers and Carruth fed gossypol to rats, rabbits, pigs and chickens with varying effects.

The effect or toxicity of the gossypol added to the food or of the cotton seed meal itself was based upon growth and well-being of the animal. Feeding experiments were carried on for some time. When no untoward results, or at most only slight effects, were obtained, this was spoken of as a tolerance to gossypol. This occurs with the albino rat, likewise with chickens.

Later Schwartze[3] carried on extensive investigations on the distribution and extent of gossypol in various cottonseeds over the cotton belt. This investigator also studied the toxicity and pharmacology of gossypol on rats, rabbits, mice and guinea pigs. His measuring stick of the severity of the toxic effects on rats (with which most of the pharmacological work was done) was loss of appetite and loss of weight.[4] It was found that the threshold value of toxicity for the rat is 67.5 mgs. per kilogram weight. The minimum lethal dose is 30 to 50 mgs. per kilo when dissolved in oil and injected intraperitoneally or intravenously.

Shortly after this Jones and Waterman[5] showed that gossypol added to a pepsin-trypsin digestion in vitro affected the rate of digestion by retarding the enzymatic action. They fed a low concentration of gossypol containing approximately one-fifth as much gossypol as the amount contained in the daily consumption of cottonseed meal per head of cattle at our station. They obtained marked inhibition, both of digestion of the cotton seed globulin and of the casein to which the one per cent was added. They advance this inhibitory effect of gossypol upon digestion as a tentative explanation for the low coefficient of digestion (83 per cent) of cottonseed meal with animals.

The work reviewed above and that of others lead to the conclusion or belief that the toxic prin-

[1] The numbers refer to references at the conclusion of the article.

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ciple in cotton seed was an explanation of the injurious results which were obtained when large amounts of cotton seed meal were fed. It should be noted that most of this work was done by feeding the seed or the gossypol isolated from the seed.

Another series of investigations on the nutritive value of cotton seed meal gave somewhat different results and interpretations. These will be reviewed briefly.

Rommel and Veddar[6] in 1915 published preliminary results of feeding cottonseed meal to pigs. Veddar had studied the effects of Beri beri in the Philippines and noted the marked similarity of symptoms. His conclusion was that the symptoms produced by feeding cotton seed meal to rapidly growing pigs was probably due to a deficiency of Vitamin B in the ration.

In 1916, Wells and Ewing[7] of the Georgia Station, feeding cottonseed meal to steers, produced certain effects from which they concluded that the problem resolved itself into one of an incomplete food.

Richardson and Green,[8] of the University of Texas in 1917, published results of extensive studies on the nutritive value of cottonseed meal. They were unable to demonstrate any effect of toxicity on the white rat. Upon the diets fed their rats reproduced several generations of young. Only when gossypol itself was added to the ration were any effects observed.

Recently in 1924, McGowan and Crichton[9] in Aberdeen, Scotland, have obtained injurious results when feeding cottonseed cake to young pigs. They corrected these results by adding iron oxide to the ration. They were able to simulate the symptoms by substituting peanut meal without the iron oxide. This produced similar lesions of the kidney. These investigators think that Withers and Carruth's results are due to deficiency. Their results, based upon a series of investigations, cause them to reject Withers and Carruth's interpretation that it is the toxic effect of D-gossypol[10] which produces injurious results in pigs.

From the above studies on the nutritive value of cotton seed meal were obtained different results from those obtained when isolated gossypol was added directly to the ration. In most of these experiments the amount of gossypol or D-gossypol, present in the cotton seed meal which was used, is not known. Some light is thrown upon these conflicting results by a recent publication—Studies in Gossypol: The Gossypol and D-gossypol content of some North Carolina Meals.[11] Of the 40 meals examined, it was found that 75 per cent of the gossypol in the seed is destroyed in the process of manufacture and that the amount of gossypol left in the meal is quite different from that found by Schwartze in the seed. Using the tolerance or threshold value of gossypol in the rat, the conclusion was reached that when cotton seed meal consituted 50 per cent of a balanced ration, that of the 40 meals examined the gossypol in only five of them (12½ per cent) would produce any toxic effect.

If there is a threshold value of toxicity, such an explanation may, in some measure, explain why cottonseed meal can at times be fed to farm animals in considerable amounts without apparent injury.

In 1926, Schwartze,[12] at The Tulsa Meeting of the American

Chemical Society, reviewed his previous work and attempted to apply his results, which were obtained from the analysis of the seed, to that of the meal. It is probable that this may not hold in view of the relatively great differences in the amount of gossypol in the seed compared to that in the meal. Bearing upon this point are several other facts. Schwartze found that the seed grown in the Southeastern States contained the greatest amount of gossypol and thus such meals themselves should contain a larger amount of the gossypol if this has not been destroyed in the process of manufacture. The amount of gossypol that meals contain in other sections of the Cotton Belt has not been determined. In this State 75 per cent of the gossypol in the seed is changed in the manufacture of meal to a less soluble form. Of the meals analyzed for gossypol, very few would produce any gossypol symptoms as shown by retardation of growth of the rat when ordinary or inconsiderable amounts constituted the ration (based upon the tolerance of the rat to gossypol). If, however, this substance cumulates in the body and is not eliminated as rapidly as ingested, then the effects of the smaller amounts of gossypol in the meal would depend upon the amount and length of time that the meal was fed.

Reference has been made above to the great reduction in the amount of gossypol in meal made from seed high in gossypol. It is not known what amount of gossypol remains in the meals made from seed relatively low in gossypol. Schwartze found that the different lots of seed varied greatly in the amount of gossypol which they contained. This substance would perhaps also vary still more in such meals after being subjected to heat and moisture in the process of oil extraction.

A changed form of gossypol, D-gossypol, is present in the meal, which in the hands of Withers and Carruth[13] was considered to be "of very slight toxicity for rats" or that it constituted a "far less toxic material." The toxicity of this substance has not been experimentally determined by feeding tests or by other means.

That gossypol itself is toxic there can no longer be any doubt. It causes at least two syndromes of symptoms, digestive and respiratory disturbances.

The quantity necessary to produce toxic or retardation-of-growth effects, with the exception of the rat, rabbit and cat, is not known. This applies to farm animals where the per cent of gossypol present in the meals fed, has not been estimated. Schwartze found 45 to 50 mgs. per kilo weight the largest survival dose for the rat when using intraperitoneal injections. This is 20.4 to 22.5 mgs. per pound live weight equivalent to 10.2 to 11.25 grams per 500 pounds (the weight of a heifer or steer).

The same investigator found 67.5 mgs. of gossypol per 100 gms. of food the threshold value of toxicity for the rat. These amounts are quite high when compared with the amounts ingested in the heavy feeding of cotton seed meal to dairy cattle at our station which are 45.3 mgs. gossypol per 100 pounds live weight.* (Approximate average of 10 head, or 0.3893 gram gossypol consumed per head per day.)

Recently we have fed 12.43 per cent cotton seed meal in the ration to growing swine with an average intake estimated at 35.3 mgs. gos-

* Soft Pork Studies by E. H. Hostetler and J. O. Halverson.

sypol* per day extending over 70 days to marketable weight with no apparent injury or arrest of gain in weight.

From this it appears that the amount of gossypol ingested in the meal by swine and dairy cattle is considerably less than the amounts experimentally found necessary to produce toxic effects on small laboratory animals. Gossypol is absorbed slowly when fed by mouth and is then apparently of a low degree of toxicity.

Icie G. Macy and Julia Outhouse[14] have recently summarized the effect of feeding cottonseed meal upon farm and small animals as follows:

Calves of 8 to 12 months are very susceptible.

Lactating cows are relatively immune.

Swine are particularly susceptible to cottonseed poisoning.

Guinea pigs and rabbits are affected.

Dogs show no effects in 120 days.

Sheep show no apparent symptoms.

The rat is more resistant.

The statements above as to calves and swine need, perhaps, in view of later work, some qualifications.

The results given in the literature on Gossypol Poisoning of Animals are chaotic.

One set of investigators fed seed comparatively high in gossypol and "isolated gossypol" in rather large amounts, in which the gossypol was injected intraveneously or added to the ration. In another series of experiments cottonseed meal comparatively low in gossypol was used in which the actual amounts present have not been determined. Doubtless the order of magnitude of gossypol ingested was not the same. The experimental work in feeding cottonseed meal gave results which might as readily be interpreted as being due to a deficiency as to toxicity. It is not improbable that rations containing large amounts of cottonseed meal may have been nutritively deficient in some respects where the animals were closely confined for long experimental periods. Factors such as these may have produced different results.

For farm animals the threshold value of toxicity of the gossypol present in cottonseed meal is not known. Apparently this is somewhat high, relatively speaking, thus enabling considerable cottonseed meal to be fed. Also the relatively low amount of gossypol left in the meal makes it possible to feed more meal with impunity. The D-gossypol in the meal seems to be held in a "bound" state and together with the gossypol does not appear to be actively toxic for farm animals in the sense of causing sudden deaths after short periods of feeding. Usually sudden deaths occur after somewhat longer periods of feeding or are preceded by swollen limbs, "fits" and a gradual decline and loss in weight. It is not known whether these two substances in cottonseed meal as ordinarily fed, exert a low order of toxicity on farm animals. Cattle and young stock fed a ration of which cottonseed meal constitutes a large part, get along fairly well for a considerable period of feeding.

In this problem are involved other factors among which are the condition of the animal and nutritive deficiencies in the ration. These deficiencies in the ration may be those due to the cottonseed meal itself and which are usually not

* Approximate figures obtained from the projects "Studies on Cottonseed Meal Feeding to Dairy Cattle" by R. S. Curtis, J. O. Halverson, and C. D. Grinnells.

properly supplemented in practical feeding of animals on farms.

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Correction

Under "Standardization of Lovibond Glasses, Report for January, 1928," OIL AND FAT INDUSTRIES, March, 1928, page 93, first column, last line under Section I, for ".... glasses in questionable" read ".... glasses is questionable"