TABLE II

Toxicity Studies on Various Samples of Gossypol

Sample	LD_{50} value	Number rats used
	mg./kg.	
A	> 600	40
B	>1,600	20
C	3,340	36
D	2,600	27
E	2,800	20
F	2,800	24
All	2,720	167

dogs (12, 13). The effects of small, single, and repeated doses of these same samples of gossypol on the body weight of rats (14) were less marked than was the case for dogs. The symptoms in the rat of intoxication from oral administration of cottonseed pigment glands (and of gossypol in large doses) were immediate diarrhea, anorexia, severe weight loss, prostration, nasal exudation, and hair loss and ulceration at the base of the tail. Post-mortem examination of the rats showed hemorrhagic involvement of the entire gastro-intestinal tract, congestion of the splanchnic organs, distention of the stomach with food, fluid in the abdomen, and pulmonary edema.

All of the foregoing results confirm the original conclusion from acute oral toxicity studies on rats, mice, rabbits, and guinea pigs (1) that the toxicity of cottonseed pigment glands is attributable either to some component or components of the glands other than, or in addition to, gossypol and gossypurpurin, or to some material in the glands which enhances the physiological activity of gossypol.

Summary

Twenty-one preparations from cottonseed pigment glands were tested for their acute oral toxicity in 1,208 fasted rats and for their content of extractable gossypol and gossypurpurin. LD_{50} studies on six samples of pure gossypol were performed on 167 fasted rats. There was no correlation between the toxicity of the various samples of cottonseed pigment glands and their extractable gossypol or gossypurpurin content. Samples containing very large amounts of extractable gossypol were less toxic than many samples with considerably lower extractable gossypol content.

Various fractionation procedures carried out on the same lot of cottonseed pigment glands caused wide alterations in their toxicity, from the extreme of very marked toxicity for the water-soluble, acetone-soluble fraction (LD_{50} ca. 700 mg./kg.) to no detectable toxicity for the acetone-insoluble residue (LD_{50} > 6,000 mg./kg.).

There was a decreased toxicity of subsequently prepared pigment glands with increased time of storage of the cottonseed in a silo. Storage of the pigment glands themselves at 7°C. however had little effect on their toxicity even after 26 and 32 months.

The procedures causing greatest detoxification of cottonseed pigment glands, given in the order of increasing effectiveness, were: heating in the presence of water < extraction with ethanol < extraction with acetone.

In the fasted rat the acute oral toxicity of pure gossypol was less than that of 17 preparations from cottonseed pigment glands having extractable gossypol contents ranging from as little as 24 to as much as 90%.

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Report of the Gossypol Committee April, 1950

During the year nine samples of cottonseed meal were sent out to the committee, and herewith are the results on the work:

	No. 1	No. 2	No. 3	No. 4
T. H. Hopper	0.625	0.077	0.119	0.423
T. L. Rettger	0.630	0.070	0.120	0.355
W. T. Coleman	0.717	0.073	0.137	0.420
V. C. Mehlenbacher	0.630	0.080	0.125	0.430
K. Kuiken	0.600	0.069	0.115	0.375
H. L. Craig	0.613	0.067	0.109	0.368
E. H. Tenent	0.625	0.075	0.119	0.378
Averages	0.634	0.073	0.121	0.393

It is the unanimous opinion of the committee that the present A.O.C.S. tentative method for the determination of free gossypol be made the official method

	No. 5	No. 6	No. 7	No. 8	No. 9
T. H. Hopper	0.072	0.028	0.036	0.058	0.037
T. L. Rettger	0.065	0.030	0.040	0.060	0.042
W. T. Coleman	0.068	0.023	0.024	0.044	0.025
V. C. Mehlenbacher	0.070	0.023	0.032	0.056	0.033
K. Kuiken	0.063	0.026	0.026	0.041	0.028
H. L. Craig	0.060	0.028	0.033	0.054	0.034
E. H. Tenent	0.070	0.031	0.039	0.053	0.039
Averages	0.067	0.027	0.033	0.052	0.031

of the American Oil Chemists' Society and that the committee now be discharged.

W. T. COLEMAN
V. C. MEHLENBACHER
T. L. RETTGER
K. A. KUIKEN
H. L. CRAIG
T. H. HOPPER
E. H. TENENT, chairman