Chronic Toxicity of Gossypol[1]

Edward Eagle

Swift & Company, Research Laboratories, Chicago

The widespread publicity attained by gossypol as an appetite depressant, since the report (*3*) that highly purified preparations of gossypol act by delaying the passage of food from the stomach to the duodenum in the rat, has led to repeated requests for the use of this material for clinical trial in the treatment and control of obesity. Gossypol, a polyphenolic yellow pigment, is the principal component found in the pigment glands of cottonseed (*1*). Its acute oral toxicity and that of cottonseed pigment glands for rats, mice, rabbits, and guinea pigs have been reported (*2*).

To determine the effects of repeated oral doses of gossypol on the food intake and body weight, four young, litter-mate male dogs (5.0 to 5.4 kg) were given daily doses of 0, 50, 100 and 200 mg/kg body wt of the material, respectively, during three different experimental periods according to the following schedule: 55-day control period, 5-day experimental period (gossypol by capsule), 9-day control (rest) period, 5-day experimental period (gossypol by stomach tube), 9-day control period, 9-day experimental period (gossypol by stomach tube). From the first administration to the last, each of the three experimental dogs received a total of 19 daily doses of gossypol within a period of 37 days, which resulted in the death of all three dogs within 5 days after the last dose (one on the fourth and two on the fifth day).

The consistent effects of repeated doses of gossypol in the dogs were nausea, vomiting, diarrhea, anorexia, and marked weight loss. During the final period of gossypol administration the average food intake (dry basis) of each of the experimental dogs fell to 6.0, 0.4, and 3.0 g/kg body wt/day, respectively, while the control dog ate 28.0 g/kg body wt/day, and they lost 20, 26 and 25% of their body weight (the control dog lost 0.7%) within a period of 9 days. Post-mortem examination showed essentially the pathological findings reported for the rat, mouse, rabbit, and guinea pig (*2*), with marked lesions of focal necrosis involving the cecum, ileo-cecal valve, and adjacent portions of the large intestine. Further experiments are in progress.

It is suggested that the use of gossypol in human subjects be withheld until more data on its pharmacology and toxicology are available.

References

1. Boatner, C. H., Hall, C. M., O'Connor, R. T., and Castillon, L. E. *Bot. Gaz.*, 1947, **109**, 108–120.
2. Eagle, E., Castillon, L. E., Hall, C. M., and Boatner, C. H. *Arch. Biochem.*, 1948, **18**, 271–7.
3. Zucker, T. F., and Zucker, L. M. Abstracts of Papers. Amer. Chem. Soc., April, 1947, p. 47B.

[1] The samples of gossypol used in this study were supplied by the Southern Regional Research Laboratory, U.S.D.A., New Orleans, Louisiana, one of the laboratories of the Bureau of Agricultural and Industrial Chemistry, Agricultural Research Administration.

Application of Chromatography to the Separation of Subcellular, Enzymatically Active Granules

Vernon T. Riley, Marie L. Hesselbach, Silvio Fiala, M. W. Woods, and Dean Burk

National Cancer Institute, National Institutes of Health, Bethesda, Maryland

It has recently been shown (*3*) that the chromatographic columnar adsorption method (*4, 6*) can be applied to the partial separation of biologically active particulates of virus dimensions from a chicken tumor extract. The present communication extends this chromatographic application to larger subcellular components, in the microscopically visible range, as found in pigmented mammalian tumors.

It has been found that melanized granules, varying in size from 0.2 to 0.6 μ or more, of the Cloudman S91 and Harding-Passey mouse melanomas, can be reversibly adsorbed on Celite columns (Fig. 1) and are thus subject to chromatographic manipulation. As a consequence, certain other constituents of the tumor homogenates employed as starting material can be readily separated from the granules, thereby providing a basis for noncentrifugal segregation of a substantial portion of the other tissue components. The particulate elements (*1, 2, 5*) separated by chromatography were found to possess high dopa oxidase and succinoxidase activities. As indicated by the

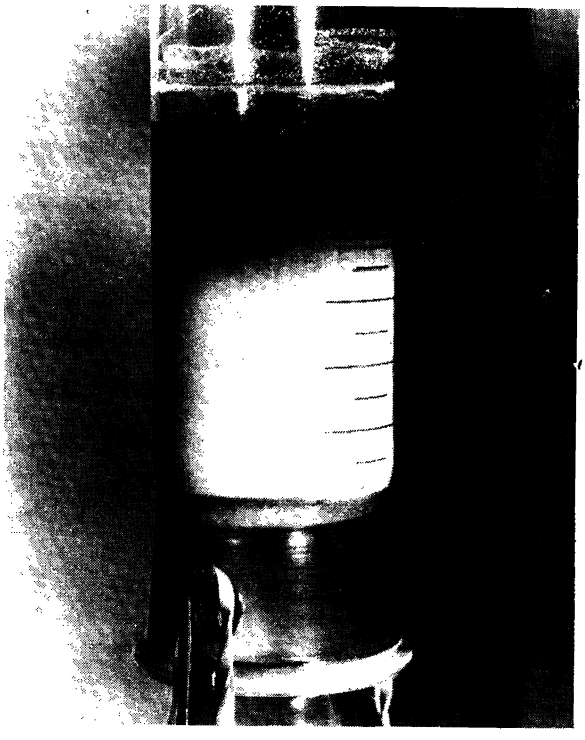

Fig. 1.—Adsorbed melanin granules on the developed chromatographic column prior to extrusion and segmentation.