and it was the hope of the founder that his gift would be the nucleus of a large endowment fund contributed by many persons and many organizations, thus making available ample income to support worth-while investigations which would advance science, the profession of engineering and the good of mankind."

The following general policy has been adopted by the Engineering Foundation Board: "The Foundation will concern itself with human as well as technical aspects of engineering problems of wide interest. Activities which will have as their main objectives 'the advancement of the profession of engineering,' whether by research or other means, will be given preference. The foundation will initiate new projects or will select from time to time projects presented to it which are deemed most likely to attain its objectives."

SPECIAL ARTICLES

ANTHELMINTIC ACTIVITY OF CRYSTALLINE PAPAIN

THE anthelmintic properties of certain plant extracts were recognized and made use of by some physicians as early as 1802, but the use of such extracts seems to have been neglected in recent years. Possible reasons for this were the inconvenience of handling the relatively unstable fresh juices and the ignorance of the fact that the anthelmintic properties were associated with labile enzymes. It was reported in 1802,[1] 1879[2] and 1881[3] that many physicians had successfully used the crude latex of *Carica papaya* or the papain obtained from it against ascarids, tapeworms, trichuris and hookworm lodged in the intestinal canal. The effectiveness of the enzyme was demonstrated beyond doubt. Although the anthelmintic value of ficin has been reinvestigated recently,[4, 5] the use of papain appears to have been completely forgotten. That large amounts of dried preparations of this enzyme are available is shown by the fact that in 1938 the United States imported 222,675 pounds of papain, according to the Chemical Division, Department of Commerce.

The present authors have reported[6] that bromelin of fresh pineapple juice can digest live Ascaris worms *in vitro*. In a search for other active plant proteases, it was found that a commercial preparation of papain (Merck) possessed strong worm-digesting activity. This finding is a confirmation of certain claims made in 1879.[2] A 0.7 per cent. solution of dried preparation in M/18 phosphate-phthalate buffer pH 5 digested *Ascaris lumbricoides* (obtained from hog intestines) almost completely in 17 hours, while a 0.07 per cent. solution also showed some activity. Since this preparation had been on hand several years, a fresh sample was analyzed and found to have approximately the same activity. *Macracanthorynchus hirudinaceus* (from hog intestine) was not digested by a 0.7 per cent. solution of either of these papain preparations, but was digested by fresh pineapple juice.[7]

It has frequently been suggested[8] that crude papain contains more than a single protease. It was therefore desirable to determine whether the worm-digesting activity of crude papain was attributable to papain itself or to some accompanying enzyme. To settle this question, pure crystalline papain[9] was tested on *Ascaris lumbricoides*. As may be seen from Table 1, rapid ulceration, followed by digestion of worm tissue, occurred in tubes containing 0.11 per cent. of crystalline papain, while digestion took place more slowly in weaker concentrations of enzyme. The crystalline enzyme was 14 times as active as the commercial preparations in worm-digesting ability.

TABLE 1

WORM-DIGESTING ACTIVITY OF CRYSTALLINE PAPAIN

Concentration of enzyme[1]	Observations on worms after		
	2 hours	7 hours	16 hours
Per cent.			
0	No change	No change	No change
0.005	" "	1 worm ulcerated, other 2 unaffected.	2 worms ulcerated, other unaffected.
0.02	" "	6–12 ulcers per worm.	All 3 worms badly ulcerated and partly digested.
0.11	Numerous ulcers on 3 worms; some digestion begun.	Worms badly ulcerated and partly digested.	All 3 worms completely disintegrated and well-digested.

[1] The enzyme was dissolved in 12.5 cc of 0.067 M phosphate-phthalate buffer, pH 5. One worm was placed in each test-tube (15 x 150 mm.) and the tube incubated at 40° C. All determinations were made in triplicate. The enzyme crystals had an activity of 11 units per mg. of protein N, determined by milk clotting (private communication from Dr. A. K. Balls).

Walti[5] has reported that crystalline ficin can also digest live ascarids *in vitro*. It therefore appears that the anthelmintic properties of the latex of Ficus spe-

[1] R. Sprengel, *Medicinisch chirurgische Zeitung*, 1: 353, 1802.

[2] A. Wurtz and E. Bouchut, *Paris Médical*, pp. 5–35, 1879.

[3] Anonymous, *Paris Médical*, No. 30, July 28, 1881.

[4] F. C. Caldwell and F. L. Caldwell, *Am. Jour. Trop. Med.*, 9: 471, 1929.

[5] A. Walti, *Jour. Amer. Chem. Soc.*, 60: 493, 1938.

[6] J. Berger and C. F. Asenjo, SCIENCE, 90: 299, 1939.

[7] Puerto Rican pineapples were used here.

[8] A. K. Balls and H. Lineweaver, *Jour. Biol. Chem.*, 130: 669, 1939.

[9] The authors are particularly grateful to Dr. A. K. Balls, of the United States Department of Agriculture, for a generous gift of crystalline papain.

cies and of *Carica papaya* are to be attributed to the proteinases of these plants. However, there is some evidence on hand that certain other plant proteinases which are as proteolytically active as papain do not possess this peculiar ability to digest live worms.

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CONVERSION OF ESTRADIOL TO ESTRONE IN VIVO[1,2]

WESTERFELD and Doisy measured the estrogenic activity of the phenolic fraction of the urine of monkeys injected with estradiol.[3] They found that 30 to 45 per cent. of the activity of the excreted estrogens was present in the ketonic fraction. After the administration of estradiol to estrous, hysterectomized estrous, or pregnant rabbits, Pincus showed the possible presence of estrone in the urine.[4] He was unable, however, to find any evidence for estrone in the urine of ovariectomized animals injected with estradiol. Neither the work of Westerfeld and Doisy nor that of Pincus was supported by chemical isolation and identification of metabolic products. This communication deals with the isolation and identification of estrone from the urine of long-time ovariectomized guinea pigs to which estradiol had been administered.

Ten mg of estradiol dipropionate in oil solution were administered by subcutaneous injection daily for 5 days to each of 5 adult guinea pigs which had been ovariectomized for at least one year. The urine was quantitatively collected during the injection period and for the following 5 days. After acidification with 10 per cent. of concentrated hydrochloric acid, the mixture was refluxed for 15 minutes and thoroughly extracted with benzene. That portion of the extract representing the phenolic compounds was separated by the Girard-Sandulesco reagent into ketonic and non-ketonic fractions.

The ketonic fraction contained more than 50,000 I. U. of estrogenic material when assayed by the vaginal smear test on the spayed adult mouse. The ketonic substances were subjected to high vacuum sublimation and the fraction subliming at 150° C. and 3 micra of mercury was collected. This semicrystalline material was crystallized from methanol and a crop of approximately 5 mg of crystals, m. p. 242–245° C., was recovered. After recrystallization from methanol, the melting-point was raised to 245–246° C. The melting-point of a mixture of this compound with an authentic sample of estrone (m. p. 255–258° C.) was 247–249° C. The benzoate melted at 211–214° C. When mixed with a sample of estrone benzoate (m. p. 215–217° C.), the melting-point was 211–214° C. All melting-points are uncorrected.

In a second experiment 50 mg of estradiol dipropionate were administered orally for 2 days to each of 5 adult guinea pigs spayed for at least one year. A procedure similar to that outlined above was used with the following modification: The phenolic compounds were fractionated between 0.1 N sodium hydroxide and 10 per cent. sodium hydroxide and the material soluble in the latter solvent separated into ketonic and non-ketonic portions by the Girard-Sandulesco reagent. About 12 mg of crystalline estrone, m. p. 256–257° C., were obtained from the ketonic fraction without resorting to high vacuum sublimation. It did not depress the melting-point of an authentic sample of estrone.

Thus it appears from this work that, at least in the guinea pig, estradiol may be converted to estrone even in the absence of the ovary. This and further work on the metabolism of the estrogenic hormones will be reported in detail.

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TOMATO POMACE IN THE DIET

TOMATO pomace is the term applied to the dried residues that remain after the preparation of tomato juice. These residues contain the seeds, skin and some of the original pulp. The composition of the material[1] used in our studies was the following: Protein, 24 per cent.; ether soluble, 14 per cent.; fiber, 33 per cent.; ash, 4 per cent., and moisture, 7 per cent. An analysis for pectin by Z. I. Kertesz, of Geneva, N. Y., showed 3.8 per cent. of this substance.

Three properties of this tomato pomace attracted our attention while improved feeding mixtures were being developed for dogs, foxes and minks. A sample of tomato pomace was ground for a rat assay and for a carotene determination. After these were made the material was left in a mason jar without a rubber for a year in a warm laboratory. At the end of this time

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[2] From the Laboratories of Physiological Chemistry and Primate Biology and the Adolescence Study Unit, Yale University School of Medicine, New Haven.

[3] W. W. Westerfeld and E. A. Doisy, *Ann. Int. Med.*, 11: 267, 1937.

[4] G. Pincus, *Cold Spring Harbor Symposia on Quant. Biol.*, 5: 44, 1937.

[1] C. M. McCay, "The Nutritional Requirements of Dogs," p. 27. Ithaca, 1939.