TABLE 1

"AVIDIN" ACTIVITY OF EGGWHITE LYSOZYME AS COMPARED WITH AN "AVIDIN" CONCENTRATE OF 50 UNITS PER GRAM (S.M.A.)

Tube No.	Biotin (milli-gammas)	S.M.A. Avidin concen. 50 units per g	Lysozyme	Control	Galvanometer reading density
1	50	..	..	√	100
2	50	..	..	√	98
3	50	1 mg	..	..	87.5
4	50	5 mg	..	..	26.00
5	50	..	1 mg	..	56.0
6	50	..	2.5 mg	..	17.5

The data thus show an "avidin" activity of about 100 units per gram for the lysozyme sample. Notice must also be taken of the fact that this sample had been kept for nearly six and a half years at room temperature, which makes it probable that it had lost some of its "avidin" activity, since György *et al.*[10] have observed that whereas the avidin-biotin complex resists the action of digestive enzymes and is also stable to treatment with acid, solutions of "avidin" are slowly destroyed. However, the sample tested had been kept in the form of a dry powder.

The data on the interchangeable activities of "avidin" and lysozyme, along with the data obtained by Meyer[11] strongly suggesting that the lysozyme activity of "avidin" concentrates is due to the avidin-biotin complex, place "avidin" in a new light and promise to provide explanations for certain characteristics that have hitherto appeared paradoxical. Thus, György's observations that "avidin" was "toxic" when given orally, while it was therapeutic when administered parenterally,[12] must now be considered in the light of the present findings, which indicate that "free avidin," rather than being "anti-biotin," more likely serves as a biotin-carrier and thus may be more properly termed a "pro-biotin," its so-called "toxic" effect being due to other reasons, such as molecular size, resulting in its non-absorption from the gastro-intestinal tract.

The data reported here, as well as the data obtained by Meyer, point to the need of a thorough reexamination of the literature on lysozyme from various sources that has appeared since its discovery by Fleming in 1922,[13] and also of the literature of other seemingly related products of bacterial and animal origin, such as the various forms of hyaluronidase and "spreading factor."[14] It may be useful at this time to propose as a working hypothesis that "free avidin" is a member of a group of related substances acting as carriers in a system of enzymes in which biotin serves as the prosthetic group.

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THE TOXICITY OF ORALLY ADMINISTERED TANNIC ACID

SEVERAL reports,[1, 2, 3] inspired by the use of tannic acid in burn therapy, have recently appeared describing the hepatotoxic effects of tannic acid. Baker and Handler[1] observed striking hepatic necrosis in rats within 48 hours after tannic acid was either painted on an area denuded of skin or injected subcutaneously. It seemed of interest to determine the effects, if any, of orally administered tannic acid.

The diets used and the results are summarized in Table 1. Twelve rats of the Vanderbilt strain were employed in each group. All animals weighed between 50 and 60 grams initially and the experiments were conducted for 90 days.

TABLE 1

Group	Diet	Final weight	Hepatic damage
1	Ground Purina Chow	240	0
2	" " "	180	0
3	" " " + 1 per cent. tannic acid	188	0
4	" " " + 2 " " "	169	0
5	Synthetic ration[4]	197	0
6	" "	173	0
7	" " + 1 " " "	169	0

The animals in group 2 were pair-fed with those in group 3 and those in group 6 with group 7. The deleterious effect of tannic acid on rat growth appeared to be only due to the animal's dislike for the diet. After 90 days the animals were sacrificed by decapitation and liver specimens from each group were taken for histological examination. In no instance was there evidence of the hepatic necrosis described previously. The gastrointestinal tract appears to be completely impermeable to tannic acid since during the course of the experiment the animals in groups 3 and 7 ingested 100 times the amount of tannic acid which, given subcutaneously, invariably produced hepatic necrosis. The innocuous results of tea drinking, by man, are in accord with these findings.

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[1] Roger D. Baker and Philip Handler, *Ann. Surg.*, 118: 417, 1943.

[2] F. W. Hartman and H. L. Romence, *Ann. Surg.*, 118: 402, 1943.

[3] D. B. Wells, H. D. Humphrey and J. J. Coll, *New Eng. Jour. Med.*, 226: 629, 1942.

[4] The synthetic ration was casein 20, cottonseed oil 15, cod liver oil 5, salt mixture 5, sucrose 55. To each kilogram of this diet were added thiamine 2.5 mg, riboflavin 5 mg, pyridoxine 2.5 mg, calcium pantothenate 40 mg, choline chloride 200 mg.