TABLE IV.
Initial Rise, Followed by Drop of Postabsorptive Blood Sugar Level of Diabetics after Changing from High Fat to Low Fat Diet.

No.	Patient	Date	Blood sugar mg %
1.	E.S.♀	April 22, 1936	325
		" 24	335
		May 8	276
		" 19	170
2.	P.R.♂	June 14, 1939	108
		" 15	124
		" 16	107
3.	G.L.♂	Jan. 8, 1940	187
		" 12	232
		" 16	190
		" 19	171
4.	M.S.♂	Aug. 22	151
		" 23	168
		" 26	140
		" 30	108
5.	M.Se.♂	Dec. 8, 1942	121
		" 9	147
		" 11	127
		" 12	109

vails and the blood sugar follows the usual declining course. Thus the initial rise can be misleading if one observes the changes of the blood sugar only for a few days after the change in diet. In Table IV are recorded a few cases which illustrate this phenomenon. The changes of the postabsorptive blood sugar level under the influence of diet are reversible in diabetic patients in the same way as in the normal: high fat rations, associated with restrictions of carbohydrates, augment the hyperglycemia, while low fat, liberal carbohydrate diets lead to a decrease of the blood sugar.

Summary. 1. Diets containing high fat rations and restricted amounts of carbohydrates increase the postabsorptive (fasting) blood sugar level. 2. This change takes place in healthy and diabetic individuals alike, with the difference that it is much more accentuated and obvious in the diabetic organism. Thus, the physiologic processes in the healthy and in the diabetic individual are qualitatively identical, but in the diabetic they are greatly exaggerated (Claude Bernard); in other words, the difference between the normal and the diabetic individual, in regard to the physiologic process described, is only of degree but not of kind.

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Effect of Rutin on Induced Proteinuria in Albino Rats.*

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Various reports have appeared in the recent literature concerning the ability of the flavone, rutin, to decrease capillary permeability. These publications are somewhat at variance with one another, and many of them deal with qualitative data. Since the permeability of the glomerular capillaries is one of the factors which influence the rate of protein excretion in the urine, and since it has been claimed that rutin changes capillary permeability, a quantitative study was undertaken to determine the effect of large doses of rutin on the rate of protein excretion following parenteral administration of bovine albumin to albino rats.

A total of 84 healthy albino rats, of both sexes, was selected at body weights of approximately 150 g each. These were separated into 4 groups, rats within each group being of the same sex. During the 72 hours of the experimental period following the initial administration of albumin all rats were kept in urine collection cages and were fed 10% dextrose in water containing 0.4% sodium chloride and vitamins of the B com-

* The bovine albumin used in these experiments was obtained through the courtesy of Dr. J. D. Porsche from the Armour Laboratories.

The rutin used was supplied by the Abbott Laboratories.

TABLE I.
Average Autopsy Findings (per rat).

	Control rats				Rutin-treated rats			
	Group II	Group III	Group IV	Mean	Group II	Group III	Group IV	Mean
No. and sex	11 ♂	12 ♀	11 ♀	—	11 ♂	12 ♀	12 ♀	—
Body wt, g	145	146	143	145	145	147	141	144
Carcass wt, g	110	108	107	108	109	110	106	108
Kidney wt, mg	1159	1106	1129	1131	1267	1225	1147	1213
Kidney protein content, mg	191	176	172	179	196	187	178	187
Liver wt, mg	6318	7137	6845	6767	6840	7950	7222	7337
Heart wt, mg	611	597	613	607	604	619	607	610
Serum protein, g %	5.63	6.21	5.98	5.94	5.06	5.19	5.06	5.11
Serum creatinine, mg %	0.72	0.84	0.67	0.74	0.61	0.64	0.84	0.70
Creatinine excret., mg/rat/24 hr	4.73	5.22	4.99	4.98	4.62	5.34	5.04	5.00

plex. Each of the 4 groups was subdivided into equal numbers of control rats and rats to be treated with rutin. Equivalent body weights and normal proteinuria,[1] the latter having been determined one day prior to the start of the experimental period, served as the criteria. The normal proteinuria for the rats in these experiments, expressed as mg of proteinuria per rat per 24 hours, averaged 5.3 mg for the males and 3.2 mg for the females.

Sixteen cc of 6.2% bovine albumin in normal saline were administered intraperitoneally to each rat 3 times: at the start of the experimental period and 8 and 24 hours later. The controls were given subcutaneous injections of 1 cc of normal saline at the 24th, 26th, 28th, and 30th hours, and the experimental rats were injected similarly and at the same time intervals with 1 cc doses of a preparation of rutin in normal saline. The rutin concentration was 45 mg per cc, each dose being equivalent to 300 mg of rutin per kg of body weight.

Urine collections were made at 8, 24, 26, 28, 30, 32, 48, 56, and 72 hours. The urinary output from each rat was first measured and charted. Then the specimens were combined to make one urine pool for each collection period for the control animals and one for those rats receiving rutin. The animals were killed on the 72nd hour and various autopsy measurements were made. As Group I, consisting of 12 female rats, was intended to be an exploratory group, no autopsy data were obtained.

Findings are presented in Table I as average figures for the rats within each group. Gravimetric determinations of kidney protein content were made on pooled kidneys.[2] Serum protein and creatinine were measured from pooled blood specimens, the creatinine being determined by the method of Addis *et al.*[3] The protein content of the urine and serum pools was measured by a modification of the biuret method of Kingsley.[4] Addition of rutin in high concentration to specimens of known protein content did not effect the protein determinations. All biochemical measurements were made in duplicate.

Fig. 1 shows that rutin was ineffective in altering the proteinuria induced by the administration of bovine albumin. Differences in proteinuria between control animals and rats treated with rutin were no greater than those between separate control groups. We have no reason to believe that average autopsy values (Table I) revealed significant dissimilarity between control animals and those treated with rutin in regard to body, carcass, or organ weights, kidney protein content, or serum protein values. The concentration of creatinine in the serum and the rate of excretion of creatinine in the urine did not appear to be changed by the administration of rutin. No evidence of toxicity was observed,

[1] Shih, H. E., *Am. J. Physiol.*, 1935, **113**, 120.

[2] Addis, T., Poo, L., Lew, L., and Yuen, D., *J. Biol. Chem.*, 1936, **113**, 497.

[3] Addis, T., Barrett, E., and Menzies, J. T., *J. Clin. Invest.*, 1947, in press.

[4] Kingsley, G., *J. Biol. Chem.*, 1939, **131**, 197.

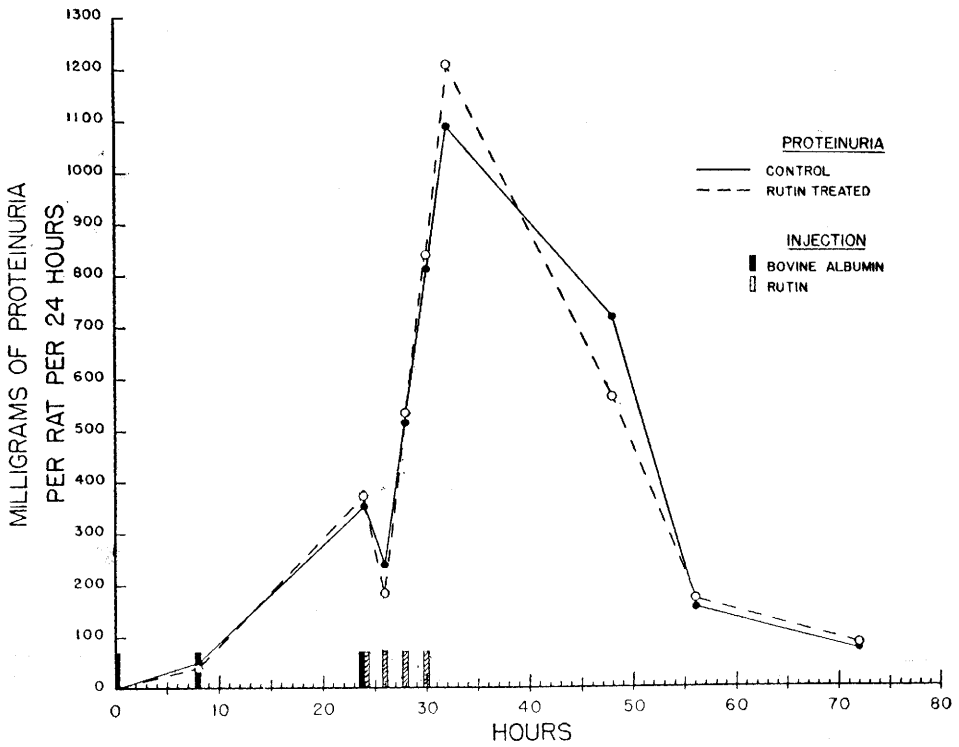

Fig. 1.
Average values for Groups I-IV, expressed as mg of proteinuria per rat per 24 hours.

despite the high dosage of rutin employed.

The urines of the rats given rutin became tinged with the yellow color of rutin in an alkaline medium one hour after the first injection of rutin, and this coloration persisted through the last collection of urine 48 hours later. When such urines were acidified, the yellow color disappeared. No such color change was noted in the blood sera, even when made strongly alkaline. These observations are similar to those described by Wawra and Webb[5] for another related flavone, hesperidin.

Summary. In albino rats with proteinuria induced by the administration of bovine albumin, rutin in high dosage did not appear to alter significantly (1) the degree of proteinuria, (2) the organ or body weights, (3) the total serum protein content, (4) kidney protein content, (5) the serum creatinine concentration, or (6) the rate of excretion of creatinine in the urine. No toxic manifestations attributable to rutin were observed. A color change in rutin solution, from yellow in alkaline medium to colorless in acid medium was noted.

[5] Wawra, C., and Webb, J., *Science*, 1942, **96**, 302.