

I have used the figure 238, which is based upon an analysis by Dean and Hilditch.³

Altogether, I have performed about 200 digestions of various durations on lard. In any one digestion test, the percentages of hydrolysis in the separate samples do not differ by more than 0.5% and are usually much closer.

Bile salts alone will not hydrolyse fats at all, but that they are a definite aid to lipase action is shown in a 6-hour digestion test in which lipase alone produced 14.5% hydrolysis of lard, whereas lipase with bile salts produced 16.1% hydrolysis.

Summary. A method is presented for the *in vitro* hydrolysis of fats by bile salts and lipase. In this method an attempt is made to simulate body conditions of temperature, enzyme action, gut motility, and emulsification. The hydrolysis reaches an equilibrium point after about 24 hours, when about 24% of the fat has been broken down.

8790 C

Insulin Absorption from Application to the Skin.

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Soon after the discovery of insulin there were several reports in the literature of attempts to introduce insulin into the blood stream by methods other than those of intravenous and subcutaneous administration. Telfer¹ reported that insulin in an inunction when rubbed on the skin of rabbits produced a fall in blood sugar. Harrison² repeated this work and found that the inunction of insulin under these conditions had no effect even when introduced in very large amounts. More recently Hermann³ and Hermann and Kassowitz⁴ have reported a marked fall of blood sugar in both animals and patients following the application of an insulin salve on the skin.

³ Dean, H. K., and Hilditch, T. P., *Biochem. J.*, 1933, **27**, 889.

¹ Telfer, S. V., *Brit. M. J.*, 1923, **1**, 715.

² Harrison, G. A., *Quart. J. Med.*, 1926-27, **20**, 187.

³ Hermann, Siegwart, *Arch. f. exp. Path. u. Pharm.*, 1935, **179**, 529.

⁴ Hermann, Siegwart, und Kassowitz, Heinz, *Arch. f. exp. Path. u. Pharm.*, 1935, **179**, 524.

TABLE I.

Date	Rabbit No.	Time	Blood Sugar, mg.
4/7/36	1	8:40 a.m.	100.5
		9:10 "	25 units insulin.
		10:50 "	68
		12:35 p.m.	90.5
		1:50 "	104.5
4/7/36	2	8:55 a.m.	105
		9:55 "	25 units insulin.
		11:05 "	59
		12:40 p.m.	71
		1:55 "	93
4/9/36	3	3:20 "	94
		9:10 a.m.	127
		9:40 "	25 units insulin.
		11:55 "	69
		1:30 p.m.	88
4/11/36	4	2:50 "	121
		9:20 a.m.	114
		10:00 "	25 units insulin.
		11:45 "	62
		1:15 p.m.	69
4/11/36	5	2:45 "	121
		9:00 a.m.	112
		9:25 "	25 units insulin.
		10:35 "	50.5
		12:10 p.m.	Convulsions.
4/11/36	6	12:15 "	25
		12:25 "	10 cc. 50% glucose intravenously. Animal recovered.
		1:55 "	46
		9:20 a.m.	124.5
		9:40 "	25 units insulin.
4/11/36	7	11:55 "	78
		12:30 p.m.	22.5
		1:30 "	In shock.
		1:40 "	24
		1:45 "	10 cc. 50% glucose intravenously. Animal recovered.
4/11/36	8	9:25 a.m.	118
		9:30 "	25 units insulin.
		11:15 "	52
		12:40 p.m.	33
		2:00 "	49
4/21/36	9	9:15 a.m.	124
		10:05 "	25 units insulin.
		11:35 "	65
		1:05 p.m.	51.5
		2:45 "	61
4/21/36	9	9:20 a.m.	128
		10:00 "	25 units insulin.
		11:50 "	52
		1:15 p.m.	16
		1:15 "	Convulsions. 10 cc. 50% glucose in- travenously. Animal recovered.
		3:00 "	138

4/24/36	10	9:15 a.m.	118
		9:50 "	25 units insulin.
		12:05 p.m.	37.5
		1:10 "	28.5
		1:10 "	Convulsions. 10 cc. glucose intra- venously. Animal recovered.

Details regarding the preparation and composition of this salve are not given.

During the past year in connection with other experiments on insulin absorption^{5, 6} we have made numerous attempts to lower the blood sugar by means of dermal applications. Finding that certain glycol compounds aided the absorption of insulin through the mucous membrane, we have employed these and similar compounds as vehicles for the insulin when applied to the skin.

In the course of our experiments we have used a variety of substances as vehicles, including glycerin, triethanolamin, glycocon, deramin, polycol, propylene glycol, diethylene glycol, glycol laurate, pinacol, di-nitro-benzine, triethylene glycol, decamethylene glycol, and diethylene glycol monoethyl ether. All of these substances are well known chemical compounds except glycocon, polycol and deramin, which are proprietary preparations containing glycols. In addition to these substances salves made of lecithin with methyl salicylate, cantharides, guaicol and menthol were employed. Frankly negative or doubtful results were obtained with all of these combinations with the exception of a mixture of pinacol and insulin and diethylene glycol monoethyl ether and insulin. The results obtained with the latter substance were apparently more striking than those obtained with pinacol.

Recently we have adopted a procedure which on application to the skin of a rabbit has shown an insulin effect. The animal was not fed for 24 hours before the test and the skin of the abdomen having been shaved was rubbed for a few minutes with 3 to 4 drops of glycerin. Ten to 15 minutes later the insulin in diethylene glycol monoethyl ether was applied. This solution was made by mixing one part of an insulin solution with 3 parts of diethylene glycol monoethyl ether. The insulin solution was prepared by dissolving powdered insulin in N/10 HCl. The solution of insulin and diethylene glycol monoethyl ether employed in the tests contained 25 units per 0.1 cc. After application, the solution was rubbed in gently with a glass rod, great care being taken to cause no abrasions

⁵ Major, Ralph H., *J. Lab. and Clin. Med.*, 1935, **21**, 278.

⁶ Major, Ralph H., *Am. J. M. Sc.* (in press).

of the skin. A few typical protocols of such experiments on rabbits are given in Table I.

In the course of repeated experiments on the same animals, some rabbits apparently became refractory after the insulin had been applied to the skin of the abdomen 3 or 4 times. It was found, however, that such animals were not refractory if the hair was shaved off the back or the thigh and the insulin applied on this fresh area.

The above observations on normal rabbits indicate that under the proper conditions insulin may be absorbed through the skin and produce a definite and marked fall in blood sugar.

8791 C

Capillary Fragility and Vitamin C.

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It has recently been suggested that tests of capillary resistance may be used as an index of the presence of mild states of vitamin C deficiency or subclinical scurvy.¹⁻⁴ Attempts to correlate the capillary resistance with other laboratory and clinical manifestations of scurvy have resulted in conflicting opinions.⁵⁻¹³

Two methods, fundamentally different in principle, have been used to determine capillary strength. Both depend on the produc-

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¹ Göthlin, Gustaf F., *Skand. Arch. f. Physiol.*, 1931, **61**, 225.

² Göthlin, Gustaf F., *J. Lab. and Clin. Med.*, 1933, **18**, 484.

³ Dalldorf, Gilbert, *Am. J. Dis. Child.*, 1933, **46**, 797.

⁴ Stocking, Ruth E., *Arch. Ped.*, 1933, **50**, 823.

⁵ Hess, Alfred, *J. A. M. A.*, 1932, **98**, 1429.

⁶ Greene, David, *J. A. M. A.*, 1934, **103**, 4.

⁷ Perry, C. B., *Lancet*, 1935, **2**, 426.

⁸ Schultzer, P., and Grüs, O., *Acta Med. Scand.*, 1935, **85**, 563.

⁹ Abt, A. F., Farmer, C. J., and Epstein, I. M., *J. Ped.*, 1936, **8**, 1.

¹⁰ Wright, I. S., *Proc. Soc. Exp. Biol. and Med.*, 1934, **32**, 475.

¹¹ Rinehart, James F., *Ann. Int. Med.*, 1935, **9**, 671.

¹² Harris, L. J., and Ray, S. N., *Lancet*, 1935, **1**, 71.

¹³ Molitsch, M., *J. Lab. and Clin. Med.*, 1935, **21**, 43.