9994 P

Insulin Absorption from the Intestine in Normal and in Depancreatized Dogs.*

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Since the isolation of insulin, the subject of the enteral administration of insulin has excited the interest of investigators. The results reported are somewhat confusing and conflicting.

Bollman and Mann[1] found that "Large amounts of insulin may be instilled directly into the duodenum, jejunum or ileum without any appreciable effect on the sugar of the blood of normal dogs except for the slight effects when concentrated insulin was used." Bollman and Mann employed doses varying from 100 to 300 units. Murlin, Tomboulian and Pierce[2] report the absorption of insulin from the Thiry-Vella loops of the jejunum in 4 normal dogs, and in 2 of them after pancreatectomy. These observers found that the absorption was aided by the addition of 0.1% HCl, bile and hexylresorcinol.

In a large series of experiments performed during the past 3 years we have invariably obtained the results reported by Bollman and Mann when insulin in dilute acid solution was introduced into an intestinal loops of normal dogs. More recently we have obtained very definite evidence of absorption in normal and especially in diabetic dogs when the insulin was administered with glycol compounds. The most effective of these substances in our experience has been pinacol or tetramethyl-glycol. This compound is solid at room temperature and melts at 42°C. Our preparations have been prepared in the following manner:

The pinacol was melted at 42°C and added to an equal amount of insulin solution, consisting of 1000 units of insulin dissolved in 1 cc of one-tenth normal HCl. This mixture solidifies rapidly, and after standing for a brief period, it was ground into a powder, and this powder pressed into small tablets containing 50 units of insulin per tablet. In some preparations the insulin pinacol mixture was heated

* I am under deep obligation to Eli Lilly and Company for the supply of insulin which was used in these experiments.

1 Bollman, Jesse L., and Mann, Frank C., *Am. J. M. Sc.*, 1932, **183**, 23.

2 Murlin, John R., Tomboulian, Ruth Latta, and Pierce, H. B., *Am. J. Physiol.*, 1937, **120**, 733.

for one-half hour at a temperature of 110°C and under 10 pounds pressure.

Some of the dogs employed in these experiments had an isolated U-loop of the jejunum, approximately 18 inches long, others a Y-type of loop, which emptied into the mid-portion of the jejunum. After experiments were performed on these normal dogs with U and Y loops, the dogs were depancreatized, and the experiments were

TABLE I.

Dog No. I. Y-loop, weight 7,900 g, pancreas removed March 5, 1938.

Normal Dog—March 1, 1938		Diabetic Dog—March 7, 1938	
Time	Blood Sugar	Time	Blood Sugar
9:30 A.M.	94	9:20 A.M.	193
	Insulin 50 units	10:00 "	Insulin 50 units
11:10 A.M.	100	1:20 P.M.	64
12:45 P.M.	98	2:40 "	49
2:50 "	91	4:00 "	55

Dog No. II. Y-loop, weight 12,050 g, pancreas removed March 24, 1938.

Normal Dog—March 23, 1938		Diabetic Dog—March 25, 1938	
Time	Blood Sugar	Time	Blood Sugar
9:00 A.M.	84	9:30 A.M.	425
9:05 "	Insulin 50 units	9:35 "	Insulin 50 units
10:30 "	93.5	11:00 "	338
12:15 P.M.	87	1:35 P.M.	322
1:30 "	85	2:05 "	384

Dog No. III. Y-loop, weight 5,950 g, pancreas removed March 29, 1938.

Normal Dog—March 25, 1938		Diabetic Dog—March 30, 1938	
Time	Blood Sugar	Time	Blood Sugar
9:00 A.M.	72	8:40 A.M.	172
9:05 "	Insulin 50 units	8:45 "	Insulin 50 units
10:50 "	75	10:30 "	134
12:00 noon	123	12:10 P.M.	159
1:30 P.M.	131	1:35 "	210

Dog No. III. U-loop, weight 10,300 g, pancreas removed March 30, 1938.

Normal Dog—March 25, 1938		Diabetic Dog—April 1, 1938	
Time	Blood Sugar	Time	Blood Sugar
9:00 A.M.	65	9:25 A.M.	425
9:30 "	Insulin 50 units	9:30 "	Insulin 50 units
10:50 "	40	11:15 "	235
12:00 noon	62	1:00 P.M.	167
1:30 P.M.	81	2:40 "	202
		4:30 "	246

Dog No. IV. Y-loop, weight 7,400 g, pancreas removed April 10, 1938.

Normal Dog—April 8, 1938		Diabetic Dog—April 12, 1938	
Time	Blood Sugar	Time	Blood Sugar
9:50 A.M.	79	9:00 A.M.	230
10:00 "	Insulin 50 units	9:30 "	Insulin 50 units
11:30 "	85.5	10:30 "	102
1:00 P.M.	78	12:00 noon	97
2:30 "	82	2:00 P.M.	169

repeated after they had become diabetic. In 37 experiments performed upon 14 dogs before and after pancreatectomy, we obtained definite evidence of the intestinal absorption of insulin in 35% of 14 experiments upon normal dogs and in 92% of 23 experiments upon diabetic dogs. In all experiments the insulin pinacol tablets were inserted into the intestinal loop and the dosage of insulin employed was 50 units. The readings in Table I are typical of the results obtained.

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Use of Phenol in Application of Prebluda-McCollum Reagent for Determining Vitamin B_1.

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Recently Prebluda and McCollum[1] reported that Vitamin B_1 reacts in alkaline solution with diazotized *p*-amino acetophenone to yield a water-insoluble, purple-red compound. Subsequently, we found[2] that xylene quantitatively extracts this pigment and that the xylene layer lends itself to colorimetric evaluation. This procedure, coupled with our adsorption and subsequent elution technics using synthetic zeolite,† appears highly specific for the determination of the vitamin.

Ten cc of a thiamin hydrochloride solution at a pH of 7.0 are pipetted into a 50 cc centrifuge bottle. This is followed by the addition of 20 cc of the Prebluda-McCollum reagent. After 24 hours at room temperature 2 cc of xylene are added and the mixture shaken vigorously for 1½ minutes. After centrifugation the color in the xylene layer is compared in a micro-colorimeter with a standard similarly treated. Subsequently, in studies involving the use of phenol for extracting the vitamin from saturated salt solutions, recoveries greater than 100% were consistently obtained due to the presence of trace quantities of phenol in the final concentrates, which

* Upjohn Fellow in Clinical Research, 1937-1938.

1 Prebluda, H. J., and McCollum, E. V., *Science*, 1936, **84**, 488; *J. Biol. Chem.*, 1938, in press.

2 Melnich, D., and Field, H., Jr., *J. Biol. Chem.*, 1938, Proc., lxxxiii.

† "Decalso," kindly furnished by the Permutit Company, New York, N. Y.