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Some favorable effects from the alimentary administration of insulin.*

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Since July, 1922, when absorption of insulin from the alimentary tract was first observed by us [1,2] various attempts have been made to devise a practicable method for oral administration. No difficulty was experienced in demonstrating absorption of simple extracts by depancreatized dogs proving that insulin can survive the destructive action of the stomach.[3] With normal animals, normal human subjects and diabetic patients having an efficient supply of trypsin the insulin was almost always destroyed.[4,5] Nevertheless a few instances of obvious absorption were encountered in human diabetics. These were reported in brief at the 11th International Congress[6] of Physiologists at Edinburgh, July, 1923. In this same month attempts were made to delay the destructive action of trypsin by combining with insulin certain weak organic acids and enclosing the combination in enteric coated capsules. Later enteric coated tablets were prepared for us by reputable pharmaceutical houses. Several cases have now been treated for different lengths of time with these tablets. Not all reacted favorably.

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[1] Sutter, C. C., and Murlin, J. R., PROC. SOC. EXP. BIOL. AND MED., 1922, xx, 68.

[2] Murlin, J. R., *Endocrinology*, 1923, vii, 519.

[3] Murlin, J. R., Clough, H. D., Gibbs, C. B. F., and Stokes, A. M., *J. Biol. Chem.*, 1923, lvi, 253.

[4] Dudley, H. W., *Biochem. J.*, 1923, xvii, 376.

[5] Witzemann, E. J., and Livshis, L., *J. Biol. Chem.*, 1923, lvii, 425.

[6] No abstract of this report was published because it was received too late.

TABLE I. Tests on Human Cases.

Patient	Date	Amt. and No. of Extract.		Drop in blood sugar mg.	Hrs.	Drop in urine sugar in 24 hrs. gm.	Remarks
		Duodenal Administration. 1st blood before breakfast.					
Bu[1]	1922 July 6-7	360 cc. No. 25 (2) + 0.1 per cent HCl		61	11	22	
	8-9	400 cc. No. 33 + 0.2 per cent HCl		40	2⅓	20	
	15-16	250 cc. No. 39 (1) + 0.1 per cent HCl		40	2	34	Following 250 cc. 0.3 per cent Na_2CO_3
	18-19	500 cc. No. 41 (2) with 6 per cent alc.		60	4	8	
	20-21	1000 cc. No. 49 (1) with 6 per cent alc.		60	4¾	34	2 doses 3½ hrs. apart
B1	18-19	500 cc No. 45 (2) with 8 per cent alc.		101	6	16	Patient intoxicated
	22-23	500 cc. 5 per cent alc. alone		36	3	7	A. M.
		500 cc. No. 48 (2) with 5 per cent alc.		42	5½	13	P. M.
	25-26	700 cc. No. 46 (1) with 5 per cent alc.		53	8½	6	
	27-28	1000 cc. 5 per cent alc. alone		34	8½	1.1	
	29-30	800 cc. No. 46 (1) no alc.		42	9¼	5.0	
		Stomach Administration of Enteric Coated Tablets—constant diet.					
	1923			Blood sugar level mg.			
E. V.	Nov. 8	30 units insulin subcut. and 6 tablets daily		50		sugar free	
	9	30 units insulin alone		142		sugar free	
	1924					sugar exc. 24 hrs. gm.	
E. M.	Jan. 7-12	6 to 12 tablets daily	Jan. 7	500		61.6	Both blood and urine
		steady drop to	Jan. 12	265		13.7	had been on increase
	15-19	16 tablets daily	Jan. 15	344		42.7	previous to use of tablets.
		steady drop to	Jan. 19	303		19.8	

[1] This case is reported from Highland Hospital by the courtesy of Dr. John R. Williams.

Two of those giving the best reactions are shown in the table together with several additional tests by duodenal administration not previously reported.

In all of the four cases reported the patients were on constant diets. The results show: (1) that insulin contained in 0.1 or 0.2 per cent HCl is absorbed from the human intestine; (2) that addition of alcohol to 5 to 8 per cent increases the absorption somewhat; (3) that alcohol alone, however, produces a drop in blood sugar but only a slight effect on the 24 hour elimination of sugar by the kidney; (4) that insulin combined with a weak organic acid or acid salt, the whole contained in an enteric coating which survives the stomach for at least three hours, can be absorbed in sufficient amount to lower blood sugar and urine sugar very materially. Failure to produce such effects in some cases seems to be due to retention of the tablets in the stomach until they are finally destroyed.

Other means of delaying the action of trypsin temporarily are now being tried.