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A Comparison of the Ketolytic Effect of Succinic Acid with Glucose.

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Korányi and Szent-Györgyi[1] have reported recently that succinic acid given as the calcium salt in daily amounts of 5 to 10 gm. or less is able to decrease the ketosis in diabetics. In the present investigations we have compared the ketolytic action of succinic acid with that of glucose when administered twice daily to fasting male rats weighing approximately 200 gm., in which the endogenous ketonuria was induced by the previous administration of a high butter-fat diet low in protein, as reported earlier.[2] The studies on ketonuria were made on the second to fifth fast days inclusive during which sodium chloride solution (fasting controls), sodium succinate in doses from 9.95 to 149.2 mg. per 100 gm. rat daily, or glucose in equivalent amounts (7.55 to 113.2 mg. per 100 gm. rat) was fed. Urine collections were made daily. The ketonuria of the fasting controls usually rises to a maximum on the third fast day, after which it diminishes rapidly. In Table I a summary of the data is

TABLE I.
Ketolytic Action of Glucose and Succinic Acid.

Fasting Controls		Glucose			Sodium Succinate		
(1)	(3)	(1)	(2)	(3)	(1)	(2)	(3)
16	49.2	16	7.55	45.8	14	9.95	52.1
40	33.7	36	37.8	19.4	29	49.7	38.1
16	29.1	14	75.5	10.0	11	99.5	28.2
11	21.5	14	113.2	5.2	11	149.2	21.5

(1) Number of experiments.
(2) Dose in mg. per 100 gm. rat.
(3) Acetone bodies as acetone in mg. per 100 gm. rat.

given. No ketolytic effect obtained when as much as 149.2 mg. of succinic acid per 100 gm. rat was given although glucose at a comparable level gave a marked decrease in the acetonuria. This amount of succinic acid on a surface area basis is 50% greater than

[1] Korányi, A., and Szent-Györgyi, A., *Orvosi Hetilap*, 1937, **81**, 615. Cited from *Chemical Abstracts*, 1937, **31**, 6335.

[2] Deuel, H. J., Jr., Hallman, L., and Murray, S. *J. Biol. Chem.*, 1937, **119**, 257.

the largest dose employed by Korányi and Szent-Györgyi. A slight decrease in ketonuria appears when only 7.55 mg. of glucose is given while a dose of 37.8 mg. caused an average decrease of acetone-bodies in the urine from 33.7 mg. per 100 gm. rat in the control tests to 19.4 mg. There was no evidence of diarrhea in any experiments nor of other toxic effects ascribable to the succinic acid. It is concluded that succinic acid is ineffective in preventing the ketonuria in fasting rats previously fed a high fat diet when this acid is administered in amounts far in excess of the quantity of glucose required to bring about a marked lowering in the excretion of the ketone bodies.

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Effect of Feeding and Fasting on Sugar Utilization of Eviscerated Rabbits.

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In an earlier paper by one of us[1] it was shown that the eviscerated rabbit utilizes glucose at a rate that is quite definite and fairly constant for a given animal. The rate varies, however, between different rabbits. The suggestion was made in that paper that this variation was due to the differences in the degree of fasting to which the different animals had been subjected prior to operation and that the effect of fasting is to reduce the utilization rate of the eviscerated animal. The work here reported was planned to investigate this relationship. The same technique was used as in the previous work. Essentially this consisted of measuring the rate at which glucose had to be administered to the eviscerated rabbit to maintain the blood sugar at a constant normal level.

Frequent blood sugar determinations served as a guide to the injection rate; if the blood sugar level rose the rate would be diminished, and *vice versa.* The determination was started 3 hours after completion of the operation and continued for 4 hours thereafter. Only those animals that sat up in normal posture and had normal righting reflexes after operation were used. The animals were also tested for kidney function by injecting phenol red after the opera-

[1] Drury, D. R., *Am. J. Physiol.*, 1935, **111**, 289.