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IX. THE FORMATION OF GLUCOSE FROM DIOXYACETONE IN THE DIABETIC ORGANISM.[1]

By A. I. RINGER and E. M. FRANKEL.

(From the Department of Physiological Chemistry of the University of Pennsylvania, Philadelphia, Pa.)

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The formation of glucose from dioxyacetone in the perfused liver was demonstrated recently by Embden, Schmitz and Wittenberg.[2] They found a very marked rise in the glucose concentration of the perfusion fluid after the addition of dioxyacetone.

In these experiments it was our object to study the influence of dioxyacetone on the glucose formation and acidosis in phlorhizinized dogs. We wish to state here that the plans for this work were laid about a year prior to the appearance of Embden's publication.

The dioxyacetone was kindly prepared for us by the Farbwerke-Hoechst vorm. Meister Lucius und Bruning, to whom we take pleasure in expressing our indebtedness.

The methods used were the same as those employed in experiments previously described. Because of the reducing properties of dioxyacetone, the glucose was also determined by means of the polariscopic method and the results given in the tables, so that any reduction of Fehling's solution due to dioxyacetone, which may have been secreted by the kidneys, can be detected.

The G:N ratio calculations are based upon the glucose figures obtained with Allihn's method.

In experiment XXXVIII period VI, 9.0 grams ($\frac{M}{10}$) of dioxyacetone, dissolved in 40 cc. of distilled water, were given subcutaneously. The glucose elimination, which was 7.0 grams in the fore period rose to 13.2 and the G:N ratio, which was 3.02 in the fore period and 3.19 in the after period, rose to 5.64. If we assume that the mean ratio of 3.1 would have obtained nor-

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[2] Embden, Schmitz and Wittenberg: *Zeitschr. f. physiol. Chem.*, lxxxviii, p. 210, 1913.

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mally in period VI, we find that 5.94 grams of "extra" glucose were eliminated in that period. In this period the acetone and acetoacetic acid were reduced from 200 mgms. to 103 mgms., to rise again to 190 in the after period.

In experiment XXXIX period VI, 9.0 grams of dioxyacetone were similarly administered subcutaneously. The glucose elimination, which was 10.9 and 11.66 grams in periods IV and V respectively, rose to 19.2 and 12.96 in periods VI and VII. The G:N ratio in periods V and VIII was 3.15 and 3.04. Assuming the mean ratio of 3.1 for periods VI and VII, we find that 9.88 grams of "extra" glucose were eliminated. In this experiment dioxyacetone exercised a fairly strong antiketogenetic effect by causing a drop in the acetone and acetoacetic acid elimination from 227 to 85 mgms., and in the β-hydroxybutyric acid elimination from 910 to 195 mgms.

In experiments XL and XLI the above results are corroborated. The "extra" glucose eliminated in experiment XL was 6.66 grams and in experiment XLI it was 5.3 grams.

In experiment XLI the total carbon[3] output in the urine was also studied. The object was to find whether any other carbonaceous material, not utilized in the body, was eliminated as a result of the dioxyacetone administration. The carbon of the glucose, acetoacetic acid, β-hydroxybutyric acid was calculated from the figures obtained in their determinations. The sum of these, sub-

TABLE I.

Experiment XLI.

PERIOD	I CARBON IN GLUCOSE 1	II CARBON IN ACETONE AND ACETO-ACETIC ACID 2	III CARBON IN β-HYDROXY-BUTERIC ACID 3	IV CARBON IN 1+2+3 α	V TOTAL CARBON IN URINE β	VI UNDETER-MINED CARBON β−α	REMARKS
XI	4.87	0.077	0.156	5.10	9.81	**4.71**	
XII	4.59	0.078	0.137	4.80	9.56	**4.76**	
XIII	4.98	0.075	0.144	5.20	9.93	**4.73**	
XIV	7.39	0.068	0.144	7.60	12.16	**4.56**	9.0 gms. of dioxyacetone administered containing 3.6 gms. of carbon.

[3] The carbon was determined by the method suggested by Tangl and Kereszty: *Biochem. Zeitschr.*, xxxii, p. 266, 1911.

EXPERIMENT XXXVIII. *Twelve hour periods.*

DATE 1914	PERIOD	WEIGHT	NITROGEN	GLUCOSE (ALLIHN)	GLUCOSE (POLARISCOPE)	G:N	"EXTRA" GLUCOSE	ACETONE AND ACETOACETIC ACID	β-HYDROXY-BUTYRIC ACID	REMARKS
Feb.										9 gms. of dioxyacetone dissolved in 40 cc. of water given subcut.
24	V		2.32	7.00	6.35	3.02		0.200		
24	VI		**2.34**	**13.20**	**13.30**	**5.64**	**5.94**	**0.103**	**0.364**	
25	VII		2.17	6.94	6.45	3.19		0.190	0.775	
25	VIII		2.39	5.84	5.20	2.44		0.179	0.642	
26	IX		2.44	5.75	5.20	2.35		0.218	0.503	

EXPERIMENT XXXIX. *Twelve hour periods.*

Feb.										
23	IV		3.41	10.90	10.40	3.20		0.234	0.836	
24	V	8.77	3.70	11.66	10.60	3.15		0.227	0.910	9.0 gms. of dioxyacetone as above.
24	VI		**3.46**	**19.20**	**17.10**	**5.55**	**9.88**	**0.085**	**0.195**	
25	VII	8.53	**3.73**	**12.96**	**12.50**	**3.48**		0.165	0.416	
25	VIII		3.42	10.40		3.04		0.150	0.435	

EXPERIMENT XL. *Twelve hour periods.*

Feb.										9.0 gms. of dioxyacetone dissolved in 50 cc. of water given subcut.
3	II		3.54	10.00		2.82		0.075	0.151	
4	III	7.20	**3.15**	**15.70**		**4.99**	**6.66**	**0.046**	**0.081**	
4	IV		3.46	10.10		2.93		0.111	0.238	

EXPERIMENT XLI. *Twelve hour periods.*

May										
8	XI	11.16	4.68	12.19		2.78		0.164	0.339	
8	XII		4.39	11.48		2.62		0.167	0.296	
9	XIII		4.48	12.46	11.23	2.78		0.160	0.312	9.0 gms. of dioxyacetone as above.
9	XIV		**4.72**	**18.46**	**17.65**	**3.92**	**5.3**	**0.145**	**0.312**	
10	XV	10.82				3.20		0.155	0.269	
10	XVI		4.28	12.67	11.86	2.96		0.126	0.273	

tracted from the total carbon, gives the undetermined carbon fraction which would rise if any other product of dioxyacetone metabolism found its way into the urine.

Table I gives the results of this investigation. Column VI gives the values of the undetermined carbon. From the fact that there was no increase in that fraction (period XIV) when dioxyacetone was administered, we feel justified in assuming that all of the dioxyacetone is either converted into glucose or burned. That the conversion of dioxyacetone into glucose may be quantitative is evident from experiment XXXIV.

$$\begin{array}{l} CH_2OH \\ | \\ 2CO \\ | \\ CH_2OH \end{array} \longrightarrow C_6H_{12}O_6$$

$$\begin{array}{rcll} 180 & = & 180 & \\ 9 & = & 9 & \text{(found 9.88)} \end{array}$$

Miller and Taylor[4] recently found that dioxyacetone, in acid solution, acts as a very strong reducing agent of ammonium molybdate. This fact was utilized in detecting its presence in the urine in unchanged form. In experiment XL it was strongly positive; the urine also reduced Fehling's solution in the cold. In none of the other experiments was this observed.

SUMMARY AND CONCLUSIONS.

Four experiments were performed in which dioxyacetone was administered subcutaneously to phlorhizinized dogs. In every case a rise in the glucose elimination followed. The "extra" glucose in one experiment corresponded to an amount of glucose which would arise if all of the carbon of dioxyacetone were converted into glucose.

The effect of dioxyacetone on acidosis is decidedly antiketogenetic in three of the four experiments.

Dioxyacetone was found in the urine in unchanged form in only one of the four experiments. In that case the urine reduced Fehling's solution in the cold and reacted positively with the Miller-Taylor reagent. In none of the other experiments did dioxyacetone appear in the urine.

[4] Miller and Taylor: this *Journal*, xvii, p. 531, 1914.