LXXVIII. ON THE TYPE OF SUGAR EXCRETED IN THE URINE OF NORMAL PERSONS.

By KENNETH TALLERMAN.

From the Medical Unit Laboratories, St Thomas's Hospital.

(Received April 11th, 1924.)

FOR some considerable time, investigators have regarded the possibility of glucose passing through some intermediate form prior to utilisation in the body as very probable.

Hewitt and Pryde [1920] carried out experiments from which it appeared that glucose was to some extent converted into the γ -form by the intestinal mucous membrane.

Winter and Smith [1923] claimed to have shown that the form in which glucose circulates in the blood is that of γ -glucose, and they suggest that the transition into glucose is essential for utilisation in the organism. In diabetic patients, who are more or less unable to utilise glucose, these authors found that the sugar present in the blood was the ordinary α - β -glucose.

The fact that administration of glucose by mouth increases the blood sugar concentration in the normal individual, while laevulose does not do so, but appears to be immediately removed from the blood, might be explained on the supposition that laevulose is more adapted for assimilation than glucose, and that, prior to utilisation, glucose and certain other sugars must pass into some form more nearly allied to laevulose. According to Bornstein and Holm [1922] laevulose produces a rise in the respiratory quotient immediately after ingestion, while glucose does not do so for 40 minutes or more. From this observation it would seem that laevulose is both more easily stored, and more easily oxidised, than glucose.

If the sugar normally circulating in the blood be γ -glucose, its absence in diabetes may be due to the lack of an enzyme for the conversion of the ordinary α - β -variety into this form as Winter and Smith have postulated. To come to a definite decision on this point is a matter of both scientific and clinical interest, but the problem is a very complex one, and many other explanations of Winter and Smith's experimental results have been advanced. The extremely reactive nature of γ -glucose must render its isolation from animal tissues in the unchanged form a matter of almost insuperable difficulty, and, as pointed out by Hewitt [1923], it is not easy to see how the optical activities of the protein-free filtrates obtained from the blood by Winter and Smith throw any light on the nature of the original blood sugar. On the other hand, it is now well known that the blood contains unstable reducing

complexes other than glucose, such as phosphoric acid esters, which tend to complicate the experimental results.

It would, therefore, seem that examination of the sugar present in the urine might yield more conclusive evidence than could be obtained from the blood, and on this assumption the experiments quoted below were carried out. If γ -glucose is the sugar of normal blood, then γ -glucose should be the sugar of normal urine, unless the kidney changes it during secretion. The amount of sugar present in normal urine, however, is too small for satisfactory investigation, and the problem presenting itself was how best to increase the urinary sugar in a normal subject. Since the healthy kidney does not allow sugar to escape into the urine except in very minute quantities, it was obvious that some means by which the kidneys of the normal individual would cause the blood sugar to appear in concentration in the urine would have to be employed in order to throw light on the nature of the blood sugar. As is well known, phloridzin produces a marked glycosuria in normal subjects, and it was resolved to take advantage of this fact and ascertain the nature of the sugar produced after the administration of this drug. Phloridzin should not cause any change in the nature of the blood sugar, since its mode of action in increasing the output of blood sugar in the urine apparently depends on the fact that it lowers the threshold value of the kidney.

Some hours previous to the experiment a good carbohydrate meal was taken. An injection of 0.005 g. of phloridzin dissolved in sterile water was then given subcutaneously. To eliminate any tendency for the normally acid urine to act on the sugar present, small doses of sodium bicarbonate, just sufficient to produce neutral or very faintly alkaline urines, were given in some cases. Shortly after the phloridzin injection, the bladder was emptied, and as soon as possible afterwards a specimen was obtained for analysis. Care was taken to prevent the urine remaining in the bladder longer than was necessary. These experiments were carried out on students and convalescent patients. The specimens of urine examined contained from 1.5 to 4 % sugar.

These urines were tested for the presence of γ -glucose which, along with other properties, has the power to decolorise potassium permanganate, and to reduce Fehling's solution in the cold.

In no instance did a specimen of urine obtained after phloridzin injection reduce Fehling's solution in the cold, nor did it ever show a greater reducing action on potassium permanganate than was exerted by any average normal urine. The sugar present possessed none of the labile properties usually assigned to γ -glucose.

Further investigations were carried out by comparing the copper reducing power with the polarimetric reading. Polarimetric examination was always conducted as soon as possible after the urine was passed, so as to avoid or minimise any possible change. The volumetric estimation of sugar was done by Bertrand's method.

Generally speaking, the percentage of sugar, as estimated from polarimetric

observations, was somewhat less than that obtained by Bertrand's method, but since the urine contains several reducing bodies besides sugar, this is only what might be expected. The difference, on the whole, was very slight. Examination of the urine at varying intervals later did not show any appreciable change in the polarimetric readings. The urine obtained from two diabetic patients who had marked glycosuria, but were practically free from ketosis, gave exactly similar results to those obtained with urines passed after phloridzin.

From these observations it is certain that the sugar present in the urine of normal individuals after phloridzin is not γ -glucose; indeed, it appears to be ordinary α - β -glucose. No difference could be ascertained between the sugar of diabetic urine and that passed as the result of phloridzin injection in the healthy subject.

Protocols of some of the experiments are annexed.

Results of experiments on sugar passed in normal and diabetic individuals.

(Numbers 1 to 8 inclusive in urine from normal subjects after phloridzin; numbers 9 and 10 in diabetic urines.)

No.	Result of Fehling's test in cold	cc. of N/10 potassium permanganate reduced		% sugar by Bertrand's method	% sugar as calculated polarimetrically immediately after urine passed, and at 24 hourly intervals			
		by 5 cc. phloridzin urine	by 5 cc. normal urine					
1	No change	0.5	0.4	1.75	1.6			
2	"	0.55	0.75	3.62	3.35	3.37		
3	"	0.6	0.5	1.33	1.18			
4	"	0.5	0.6	1.45	1.06	1.08	1.08	1.06
5	"	0.65	0.6	0.7	—			
6	"	0.5	0.6	1.72	1.60	1.63	1.81	
7	"	0.5	0.6	4.5	4.14	4.11	4.19	
8	"	0.5	0.5	2.84	2.44	2.47	2.47	
9	"	0.7	0.6	3.1	2.9	2.83	2.92	
10	"	0.6	0.6	2.2	1.8	1.71	1.9	

CONCLUSIONS.

(1) The sugar excreted in the urine of the normal subject, as the result of an injection of phloridzin, is not γ -glucose but appears to be the ordinary α - β -variety.

(2) Since no evidence of the presence of γ -glucose was obtained in the urine of healthy individuals, it is unlikely that this form of sugar is the variety present in normal blood.

(3) The sugar passed by the diabetic subject, and that passed by the normal individual as the result of the use of phloridzin, appear to be of the same nature.

REFERENCES.

- Bornstein and Holm (1922). *Biochem. Z.* **130**, 432.
Hewitt (1923). *Brit. Med. J.* i, 590.
Hewitt and Pryde (1920). *Biochem. J.* **14**, 395.
Winter and Smith (1923). *J. Physiol.* **57**, 100.