STUDIES IN CARBOHYDRATE METABOLISM.

XI. INVESTIGATIONS INTO THE OCCURRENCE OF NEW-GLUCOSE IN THE COURSE OF THE FERMENTATION OF α-GLUCOSE.

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INTRODUCTION.

Metabolism, Glycolysis, and Fermentation.

In earlier articles (1) we have shown that new-glucose is an essential link in the transformation of glucose which takes place in the animal organism. In all probability new-glucose is the first step in the transformation which glucose has to take whether it is burnt up into carbonic acid and water, converted into glycogen, or deposited as fat. Besides this transformation of glucose which occurs in the animal body, other ways in which glucose is broken up are met with in nature. Of special biological interest are the two processes called glycolysis and fermentation. Of these the first very probably occurs in the human organism but to such a small extent that it can play no rôle in the energy transformation of the organism. Since, moreover, it was proved in the paper referred to that the enzymatic breaking down of glucose in the glycolytic process also occurs in the blood of diabetics although to a rather less degree than in normal blood, new-glucose cannot be an essential step in the process.

Regarding the nature of the process taking place when glucose ferments, it is uncertain whether in its initial stage it passes through the same links as those occurring in the breaking down of glucose which takes placed in the animal organism, or whether it pursues another course. In this connection it may be recalled that

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Collip (2) in 1923 demonstrated that in various respiring plants, as well as in yeast, a hormone resembling insulin can be detected which he calls glucokinin.

Besides the general biological importance of the problem of the nature of the fermentation, a point more particularly of medical interest is associated with it. Since Leo (3) (1898) recommended the administration of yeast in the treatment of diabetes, this therapy has been discussed time and again in medical literature. Practically every author who has subjected this method of treatment to scientific investigation and criticism has arrived at the conclusion that it is useless in all serious cases of diabetes mellitus. On the other hand it is admitted by different observers that the administration of different forms of yeast by the mouth may be followed at any rate by a temporary decrease in the glycosuria. The yeast treatment has never been extensively employed in diabetic therapy, but it is used by a number of patients themselves as a household remedy. No scientific basis for the yeast treatment exists.

From our earlier investigations it appears, as mentioned, that in its decomposition in the organism during metabolism, glucose must pass through the stage which we have called new-glucose. As, moreover, we have worked out a method for demonstrating new-glucose in vitro one is led to investigate by this means whether new-glucose can be detected during glucose fermentation in accordance with what occurs during the transformation of glucose in the organism with the help of insulin and insulin complement. In order to study the question further we have attempted to determine in a series of experiments whether new-glucose can be demonstrated during the fermentation of α-β-glucose.

**EXPERIMENTAL.**

**Technique.**

After a solution of α-β-glucose (the strength of the solution generally varied between 5 and 10 per cent) was started fermenting by one of the methods referred to below, a sample was withdrawn and put in a dialyzing membrane at a temperature of 20°C. When dialysis had proceeded for half an hour the dialysate was removed and its glucose content determined both by reduction
and rotation estimations. The reduction estimations were done by the Hagedorn and Norman Jensen method. The rotation values were the mean of twenty readings.

### TABLE I.

<table>
<thead>
<tr>
<th>Experiment No.</th>
<th>Conditions of experiment.</th>
<th>Time at 37°C before dialysis</th>
<th>Glucose,</th>
<th>Rotation value.</th>
<th>Reduction value.</th>
<th>Specific rotation</th>
</tr>
</thead>
<tbody>
<tr>
<td>(1)</td>
<td></td>
<td>min.</td>
<td>per cent</td>
<td>per cent</td>
<td>per cent</td>
<td>per cent</td>
</tr>
<tr>
<td>1</td>
<td>10 gm. fresh bottom yeast + 50 cc. 5 per cent $\alpha\beta$-glucose.</td>
<td>10</td>
<td>0.331</td>
<td>0.337</td>
<td>+51.3°</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>10 gm. fresh top yeast + 50 cc. 10 per cent $\alpha\beta$-glucose.</td>
<td>40</td>
<td>0.236</td>
<td>0.240</td>
<td>+51.6°</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>4 gm. dried bottom yeast + 50 cc. boiled juice of fresh bottom yeast + 10 cc. 50 per cent $\alpha\beta$-glucose.</td>
<td>30</td>
<td>0.644</td>
<td>0.660</td>
<td>+51.2°</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>10 gm. fresh bottom yeast plasmolyzed with 1.5 cc. ether + 35 cc. boiled juice of fresh bottom yeast + 10 cc. 5 per cent $\alpha\beta$-glucose.</td>
<td>30</td>
<td>0.686</td>
<td>0.673</td>
<td>+53.4°</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>30 cc. maceration juice of dried bottom yeast + 10 cc. 20 per cent $\alpha\beta$-glucose.</td>
<td>60</td>
<td>0.575</td>
<td>0.579</td>
<td>+52.2°</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>35 cc. maceration juice of dried bottom yeast, suspended in boiled juice of fresh top yeast + 8 cc. 50 per cent $\alpha\beta$-glucose.</td>
<td>120</td>
<td>0.893</td>
<td>0.890</td>
<td>+52.6°</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>30 cc. expressed juice of fresh bottom yeast + 5 cc. 60 per cent $\alpha\beta$-glucose.</td>
<td>30</td>
<td>1.294</td>
<td>1.282</td>
<td>+52.9°</td>
<td></td>
</tr>
</tbody>
</table>

**Experimental Conditions.**

As appears from Column 2 of Table I, fermentation of $\alpha\beta$-glucose was produced by a variety of methods; namely, with the help of (1) fresh bottom yeast, (2) fresh top yeast, (3) dried bottom yeast to which was added the boiled juice of fresh bottom yeast,
(4) fresh bottom yeast plasmolyzed with ether and then mixed with the boiled juice of fresh bottom yeast, (5) juice obtained by maceration of dried bottom yeast, (6) maceration juice of dried bottom yeast suspended in the boiled juice of fresh top yeast, and (7) the expressed juice of fresh bottom yeast. The special experimental conditions will be seen from the table. In Column 3 is recorded the time the fermentation has lasted at 37°C. before the sample for dialysis at 20°C. was withdrawn.

The bottom yeast used in the experiments was kindly supplied to us from the Fermentation Laboratory at New Carlsberg, while the top yeast was the ordinary commercial baker's yeast. We ourselves prepared the dried bottom yeast by ordinary desiccation of the fresh bottom yeast in the air for 4 days. The juice obtained by maceration of the bottom yeast was prepared according to von Lebedew's (4) directions. Finally the expressed juice of fresh bottom yeast was prepared by Buchner's (5) method. The preparations were made through the kindness of Cand. pharm. Gad-Andresen at the laboratory of the Medicinal Compagni.

Results.

The results are all recorded in Columns 4 to 7 of Table I. In Columns 5 and 6 the values of the glucose concentration in the dialysate, calculated on the basis of the rotation and reduction values, respectively, are entered. It was found in all the experiments without exception that the rotation and reduction values were identical. In accordance with this the specific rotation angle in each experiment showed values which coincided with that of α-β-glucose (+52.5°). It follows from this that in no case was the presence of new-glucose or any other kind of sugar different from α-β-glucose demonstrated during the course of the fermentation process.

Discussion.

The presence of new-glucose could not be detected during the fermentation of α-β-glucose produced by a number of different methods. These results are very much against new-glucose being a connecting link in the process of glucose fermentation, as we found it was in the decomposition of glucose during metabolism in the animal organism. The reason that the experiments cannot
give a decisive answer to this question, however, is because we are unable entirely to rule out the possibility that any new-glucose momentarily formed is further transformed. This possible transformation would then have to take place so rapidly—in statu nascendi—that the new-glucose could not succeed in passing out into the dialysate.

RÉSUMÉ.

1. New-glucose cannot be detected during the fermentation of glucose produced by a variety of different methods.
2. It is, therefore, very improbable—although not finally settled—that the fermentation of glucose proceeds with new-glucose as a connecting link in the process. The fermentation of glucose in its early stage is thus fundamentally different from the breaking down of glucose in the animal organism.

BIBLIOGRAPHY.

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