FRUCTOSE, GLUCOSE, AND GALACTOSE TOLERANCE IN DOGS.

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(Received for publication, March 14, 1923.)

In a recent study, Folin and Berglund (1) describe certain phenomena associated with the transportation, retention, and excretion of carbohydrates. Data are presented to show that both fructose and galactose are less effective than glucose in raising the level of the blood sugar. The explanation offered is that the tissues, being relatively well stored with glucose and empty of other sugars may be able to absorb these other sugars more readily than glucose. Quite different results have been reported by Foster (2, 3). The latter finds that the ingestion of 40 to 100 gm. of galactose by normal adults produces a very marked hyperglycemia. This accords well with the generally accepted notion that galactose is a poorer glycogen former than glucose. Similarly, the failure of moderate amounts of fructose to alter markedly the blood sugar level is attributed to a very rapid conversion of this sugar into glycogen. Foster is therefore led to conclude that glycogen formation is the chief factor tending to prevent alimentary hyperglycemia.

In connection with certain studies on the utilization of carbohydrates in experimental derangements of the liver, it appeared desirable to determine in a fairly large number of animals the tolerance for fructose, glucose, and galactose. For this purpose twenty healthy dogs, weighing between 6 and 20 kilos, were selected. In each case, the tolerance tests were preceded by a fast of about 20 hours. The blood was obtained by cutting one of the marginal veins of the ear. After collecting an initial blood specimen, the sugar, dissolved in about 200 cc. of water,
was given by mouth (3 gm. per kilo of body weight). Following
the sugar administration, additional blood samples were collected
at definite intervals. In determining blood sugar, we used the
method of Folin and Wu (4). The glucose was Merck’s c.p.
preparation. Both the levulose and galactose were Pfanstiehl’s
c.p. special grade.

In all the animals the tolerance for levulose, as determined by
blood analyses, was better than either that for glucose or galac-
tose. With but a single exception, galactose produced a more
pronounced hyperglycemia than dextrose. These findings are
therefore more comparable to those obtained by Foster in human
subjects than to the results reported by Folin and Berglund.

For the purpose of economizing space, the data of but one
experiment are given in detail (Table I). In addition, the
averages obtained on the twenty dogs are presented in Table II.
Results of other tests on individual animals are included in the
data recorded in Tables III and IV.

In the present investigation, little attempt was made to deter-
mine the nature of the sugars in the circulation following the
administration of the monosaccharides. It is to be recalled that
Folin and Berglund were able to demonstrate levulose in blood
plasma 20 minutes after the ingestion of this carbohydrate.
However, the “sugar” appearing in the urine after fructose
feeding did not give the tests for levulose. Folin and Berglund
therefore suggest that the glycuresis was due not to levulose,
but to reducing decomposition products of levulose. Our results
point to the same conclusion. In not a single instance did we
obtain well defined tests for levulose in the urines of the normal
dogs. Still more interesting are the findings with respect to
the glycuresis following galactose ingestion. In these experi-
ments, as much as one-third of the total sugar administered,
and in a few cases even more, was excreted in the urine during
the 24 hours following the test. Nevertheless, the urines con-
tained relatively little or no galactose. In only two cases were
we able to establish the presence of appreciable amounts of this
sugar (mucic acid and osazone tests).

Folin and Berglund have called attention to the remarkable
effect of dextrose in increasing the retention and utilization of
galactose. In one of their experiments, the administration of
100 gm. of the latter was followed by the excretion of 5,685 mg. of "extra" sugar, whereas the ingestion of 100 gm. of dextrose together with 100 gm. of galactose resulted in the elimination of less than one-tenth this amount; namely, 371 mg. This phenomenon can be demonstrated even more directly. It can be shown that the blood sugar curve produced by galactose is invariably depressed if both galactose and glucose are fed. On examining the data in Table III, it will be seen that when galactose and dextrose are administered together, the hyperglycemia produced is not much more marked than that following ingestion of glucose alone.

### Table I.

**Tolerance for Fructose, Glucose, and Galactose in Dog 15.**

<table>
<thead>
<tr>
<th>Time after ingestion</th>
<th>Blood sugar per 100 cc.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Experiment 1.</td>
</tr>
<tr>
<td></td>
<td>38.7 gm. fructose.</td>
</tr>
<tr>
<td>min.</td>
<td>ma.</td>
</tr>
<tr>
<td>Before.</td>
<td>105</td>
</tr>
<tr>
<td>15</td>
<td>126</td>
</tr>
<tr>
<td>45</td>
<td>125</td>
</tr>
<tr>
<td>75</td>
<td>111</td>
</tr>
<tr>
<td>135</td>
<td>109</td>
</tr>
</tbody>
</table>

### Table II.

**Average Tolerance for Fructose, Glucose, and Galactose in Twenty Dogs.**

3 gm. of the sugar per kilo of body weight.

<table>
<thead>
<tr>
<th>Time after ingestion</th>
<th>Blood sugar per 100 cc.</th>
</tr>
</thead>
<tbody>
<tr>
<td>min.</td>
<td>mg.</td>
</tr>
<tr>
<td>Before.</td>
<td>95</td>
</tr>
<tr>
<td>15</td>
<td>111</td>
</tr>
<tr>
<td>45</td>
<td>114</td>
</tr>
<tr>
<td>75</td>
<td>110</td>
</tr>
<tr>
<td>135</td>
<td>101</td>
</tr>
</tbody>
</table>
The possible effect of an altered rate of absorption of galactose when the two sugars are fed together, must not be omitted from Table III. 

**Table III.**

*Showing the Effect of Glucose and Fructose Ingestion on Galactose Tolerance in Dog 9.*

**Male. Weight 8.2 kilos.**

<table>
<thead>
<tr>
<th>Time after ingestion.</th>
<th>Blood sugar per 100 cc.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>24.6 gm. fructose.</td>
</tr>
<tr>
<td>min.</td>
<td>mg.</td>
</tr>
<tr>
<td>Before.</td>
<td>104</td>
</tr>
<tr>
<td>15</td>
<td>127</td>
</tr>
<tr>
<td>45</td>
<td>138</td>
</tr>
<tr>
<td>75</td>
<td>136</td>
</tr>
<tr>
<td>135</td>
<td>120</td>
</tr>
<tr>
<td>255</td>
<td></td>
</tr>
</tbody>
</table>

**Table IV.**

*Showing the Effect of Glucose and Fructose Ingestion on Galactose Tolerance in Dog 20.*

**Male. Weight 9.8 kilos.**

<table>
<thead>
<tr>
<th>Time after ingestion.</th>
<th>Blood sugar per 100 cc.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>29.4 gm. fructose.</td>
</tr>
<tr>
<td>min.</td>
<td>mg.</td>
</tr>
<tr>
<td>Before.</td>
<td>92</td>
</tr>
<tr>
<td>15</td>
<td>111</td>
</tr>
<tr>
<td>45</td>
<td>130</td>
</tr>
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<td>75</td>
<td>112</td>
</tr>
<tr>
<td>135</td>
<td>110</td>
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<tr>
<td>255</td>
<td></td>
</tr>
</tbody>
</table>

consideration. If for a given period only half as much galactose were to enter the circulation, one might expect a slower increase in the blood sugar than would occur if the absorption rate were
twice as rapid. However, any objection based on this assumption is untenable because if the absorption rate were the important factor, levulose, when fed with galactose should exert an even greater effect in depressing galactose hyperglycemia. This does not occur. In most experiments, the ingestion of levulose together with galactose was followed by as great an increase in the blood sugar as in the feeding experiments with galactose alone. It is to be admitted, however, that in a few cases, levulose depressed to a slight extent the galactose tolerance curve.

MacLean and de Wesselow (5) explain the appearance of the normal sugar tolerance curve by assuming that the carbohydrate storage mechanism comes into action at about a threshold of 0.16 to 0.17 per cent blood sugar. This view finds support in Foster who postulates a stimulation of the glycogenic function. Probable though this may be, there is actually little direct evidence to show that glycogen formation would account for the removal of most of the excess sugar from the circulation. Since the liver is the main site of glycogen synthesis, almost complete destruction of the liver parenchyma should result in a marked carbohydrate intolerance. As will be shown in a forthcoming publication, this does occur to some extent, but the increased hyperglycemia and glycuresis under these conditions account for only a fraction of the absorbed sugar. One might speculate on the possibility that in liver derangements, other tissues assume a greater share of the burden of glycogen formation and storage. There are, however, indications that the maintenance of the blood sugar within certain concentrations is under hormone control and that this mechanism is stimulated to greater activity by excessive amounts of glucose.

We believe that the results of our feeding experiments with galactose plus glucose lend some support to the "stimulation" theory. The accumulation of a certain concentration of glucose in the blood seems to provoke a more rapid rate of sugar removal. When galactose alone is fed, as shown both in the experiments of Foster and in our own experiments, the drop in blood sugar does not begin until after it has reached a relatively high level (240 to 290 mg. in Foster's experiments; 240 to 440 mg. in ours). An explanation that may perhaps be offered is that galactose, as such, does not provide as efficient a stimulus as does dextrose.
The eventual break in the curve is due partly to the excretion of some of the sugar and in part, perhaps, to the accumulation in the blood of some of the transformation products of galactose, including possibly at least one of the isomeric forms of glucose. The mechanism concerned with the removal of sugar from the circulation would thus be provided with the necessary stimulus. That this is not altogether a vague speculation, is supported by our findings that in the presence of sufficient glucose excessive hyperglycemia due to galactose is prevented.

The urinary sugar was determined by Benedict’s method (6). The data in Table V show that the ingestion either of glucose or
of fructose (3 gm. per kilo of body weight) results in a slight
glycuresis. In the case of galactose, on the other hand, the
glycosuria is very marked, more than one-third of the ingested
sugar being excreted. When dextrose is fed together with
galactose, less sugar is excreted than when only galactose is given.
It is to be noted that the diminished glycurisis under these con-
donditions is associated with a lowered blood sugar level.

SUMMARY.

When administered to dogs, fructose is less effective than
glucose in producing alimentary hyperglycemia. On the other
hand, the feeding of galactose results in a very marked increase
in the blood sugar concentration.

Following the ingestion of fructose and galactose, the urine
contains reducing substances other than these monosaccharides.

The presence of sufficient glucose in the circulation prevents
the excessive hyperglycemia due to galactose.

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