Mechanism of erroneous Dextrostix readings

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SUMMARY The mechanism of hyper-reactivity of the Dextrostix system when contaminated with alcoholic skin cleaning agents was investigated. When sodium fluoride was supplied to block glucose oxidase activity and hydrogen peroxide was exogenously provided benzidine peroxidation could be preferentially studied. Benzidine hydrochloride was the most likely site of the hyper-reaction. Repeated measurement of blood sugar is especially important in newborn infants who are susceptible to hypoglycaemia. Dextrostix (Ames Co, United States) is a blood sugar measuring system that uses dry chemistry and is often used in intensive care medicine because of its accuracy and convenience. The system consists of two enzymatic steps:

\[
\text{glucose oxidase} \\
\text{Glucose} + 2\text{H}_2\text{O} \rightarrow \text{2H}_2\text{O}_2 + \text{glucuronic acid}
\]

\[
\text{peroxidase} \\
\text{2H}_2\text{O}_2 + \text{Benzidine} \rightarrow \text{4H}_2\text{O} + \text{ox-benzidine}
\]

where ox-benzidine is the oxidised form of benzidine. These reactions are highly dependent on the quantity of glucose. The system does not respond to reduced sugars, and substances such as lactose, fructose, galactose, glutathione, ascorbic acid, uric acid, creatinine, amino acid, and glycolytic intermediate in its routine clinical use. Haemolysis, bilirubin, and the addition of glycolysis blocking agents, such as ascorbic acid, are known to interfere with the system. Isopropyl alcohol, often used during the preparation of the blood sampling site, causes an erroneously high glucose reading as measured by Dextrostix. In the present study we investigated the mechanism of serum glucose measurement when the Dextrostix system was contaminated with various alcoholic agents and reiterate the potential problems of interpreting such factitious results.

Methods

To determine the site of hyper-reaction caused by alcohol in the Dextrostix system, 0.5 ml of isotonic saline sodium fluoride solution was used to block glucose oxidase activity, the first step of the system, and 0.5 ml of 1% hydrogen peroxide (first grade) then added to the tip of Dextrostix. Blood sugar measurements were performed by routine technique except for pretreatment with these agents. The effect of alcohol on dye was analysed using two other systems that also measure pure glucose using the same enzymes but different dyes. The tip of a Reffomat system (Yamanouchi Co, Japan), which contains propylcarbazol and toluidine as dye, and the Seralyzer system (Ames Co), which contains tri-methylbenzidine, were directly soaked and contaminated to 45% isopropyl alcohol. Fifty percent isopropyl alcohol, 50% N-propanol, and 50% ethylalcohol, used in the analysis of other alcoholic agents to the Dextrostix system, were all of analytical reagent grade. 0.5ml Of artificially developed serum, packaged with Dextrostix Dextrometer system, was used as control serum.
nated with 45% isopropyl alcohol, one of the skin cleaning agents routinely used with capillary blood sampling. Alcohol probably reacts on the second step of the Dextrostix system.

From the facts that toluidine is one of the components of both the Dextrostix and Reflomat systems and that a significant decrease in blood glucose reading was found when tri-methylbenzidine was used as a dye, benzidine hydrochloride would be the most likely site of the hyper-reaction. Other alcoholic agents also gave erroneously high readings, indicating that alcohol is the main cause of the reaction. The enhanced colour development is probably due to increased solubility of the reduced indicator dyes. A 32% decrease after contamination of the Seralyzer system with isopropyl alcohol should be elucidated, however, by further studies.

It is also important to note that the colour of the tip does not change at all by contamination of alcohol before application of blood samples. This is especially important as the contamination cannot be judged from the colour change or even from the glucose reading by the system.

The results indicate that the Dextrostix tip must be kept away from the alcohol pad, and repeated measurement is recommended when unexpectedly high or low readings are observed.

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References

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Results
As shown in Table 1, pretreatment with sodium fluoride significantly blocked the reaction of the first step and decreased the blood sugar readings from 8.19 mmol/l to the base concentration of 1.65 mmol/l. No change in blood sugar reading was found after the addition of 45% isopropyl alcohol, indicating that alcohol has no effect on the recovery of glucose oxidase activity.

Hydrogen peroxide significantly increased the blood sugar concentration to the initial value, where the first step was equally blocked by sodium fluoride. Subsequently, a profound increase of blood sugar was observed by the addition of 45% isopropyl alcohol.

Table 2 summarises blood sugar readings when control serum samples were applied to three different systems. An increase of 111% in blood sugar measurements using the Dextrostix system was found by the addition of 45% isopropyl alcohol, while a 9% increase and a 32% decrease were observed when measured by the Reflomat and the Seralyzer systems, respectively.

Fifty per cent isopropyl alcohol, 50% N-propanol, and 50% ethylalcohol also gave significantly high readings (mean (SD)) of 21.13 (1.09) mmol/l, 19.01 (0.36) mmol/l, and 18.58 (1.49) mmol/l, respectively, while the control serum showed only 6.99 (0.55) mmol/l (n=5 in all four cases).

Discussion
The Dextrostix system was confirmed as giving erroneously high glucose readings when contaminated with 45% isopropyl alcohol, one of the skin cleaning agents routinely used with capillary blood sampling. Alcohol probably reacts on the second step of the Dextrostix system.

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<table>
<thead>
<tr>
<th>System</th>
<th>Dye</th>
<th>Mean (SD) blood sugar (mmol/l)</th>
<th>% Increase</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Control (n=5)</td>
<td>Contaminated with isopropyl alcohol (n=5)</td>
<td></td>
</tr>
<tr>
<td>Dextrostix</td>
<td>3.91 (0.11)</td>
<td>8.21 (0.22)</td>
<td>111</td>
</tr>
<tr>
<td>Reflomat</td>
<td>7.76 (0.17)</td>
<td>8.45 (0.10)</td>
<td>9</td>
</tr>
<tr>
<td>Seralyzer</td>
<td>5.38 (0.12)</td>
<td>3.66 (0.13)</td>
<td>-32</td>
</tr>
</tbody>
</table>
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