Electrochemical Interferences with the YSI Glucose Analyzer

To the Editor:

Recently, Farrance and Aldons showed that 1 mmol of paracetamol (acetaminophen) per liter causes a 1.4 mmol/L increase in the apparent glucose concentration as determined by the Yellow Springs Instruments Model 23 AM glucose analyzer (1). Other reports have shown that 1 mmol of paracetamol per liter increased the apparent glucose concentration by approximately 3.5 to 5 mmol/L (2, 3). A representative for the manufacturer of the glucose analyzer has suggested that this interference is due to "certain subtle variables in enzyme membrane materials" (4).

We have found that 1 mmol of paracetamol per liter, either in blood or distilled water, caused apparent glucose concentration to increase by 2.8 to 4.6 mmol/L, depending on how long the two-layered enzyme membrane has been used. The higher value was observed with a new membrane, and declining concentrations were observed with increasing use of the membrane. Consistent with the observations of Farrance and Aldons, we have found that more "wash cycles" were required to return the reagent response to zero when paracetamol was present in a sample as compared with the number needed in its absence.

We have also found that aqueous solutions containing 1 mmol of isoniazid (isonicotinic acid hydrazide), PAS (p-aminosalicylate), or salicylamine per liter also cause an increase in apparent glucose concentration of 4, 0.4, and 4.3 mmol/L, respectively. No response was obtained with up to 5 mmol of L-dopa (L-3,4-dihydroxyphenylalanine) per liter. Hence, drug interference with a chemical method for glucose based on glucose oxidase and peroxidase in the presence of phenol and 4-aminophenone ("GOD-PAP"; Boehringer Mannheim).

We tested the electrochemical reactivity of the interfering substances, using solutions containing 100 μmol of the component per liter, dissolved in phosphate buffer with the same composition and pH as recommended for use with the YSI glucose analyzer. These solutions were pumped through an LC-4 electrochemical detector (Bioanalytical Systems, West Lafayette, IN) at a constant rate of 1 mL/min. The potential difference between the working and reference electrodes was maintained at +0.7 V (as in the glucose analyzer). We found that all the compounds could be oxidized. Paracetamol was oxidized most easily, followed closely by isoniazid and salicylamine. L-Dopa and PAS were oxidized least readily. Although L-dopa is electrochemically very reactive, it is unstable at pH 7.3 and is therefore not detected at low concentrations.

None of the compounds interfere with the enzymic determination of glucose, so we can conclude that they do not affect the enzymes involved with the glucose analyzer. The detection system of the analyzer is potentiometric with a potential difference of +0.7 V between the electrodes. Hence, it is more likely that these compounds are oxidized and give an electrochemical response. Contrary to the claim made in the manual for the analyzer that the inner cellulose acetate membrane is impermeable to glucose, ascorbic acid, and most potentially interfering substances, our results show that there must be diffusion through the inner membrane.

We obtained an apparent glucose concentration of 40 mmol/L with an aqueous solution containing 100 μmol of paracetamol per liter when we removed the two-layered enzyme membrane to gain direct access to the electrode system, as compared with 0.4 mmol/L in the presence of the membrane. This illustrates that less than 1% of paracetamol or any oxidizable agent needs to diffuse through the inner membrane to give a substantial false signal. We believe that the porosity of the inner membrane decreases with increasing use of the membrane, resulting in a high response that is observed with a new membrane and a decline in response as the membrane gets older. Presumably, the same phenomenon also affects the diffusion of hydrogen peroxide (which the electrode system is supposed to detect), because we find that the calibration of the analyzer has to be altered to compensate for a diminished enzyme membrane function.

The fact that the analyzer requires more "wash cycles" after the analysis of a sample containing an oxidizable drug may depend on two factors. Firstly, the electrode system may be layered with the oxidation products and needs repeated cleaning to restore its function. Secondly, the outward diffusion of the drug may be slower than that for hydrogen peroxide, resulting in a prolonged electrochemical effect.

To conclude, concentrations of the substances in blood vary a lot, depending on factors such as the dose administered, its metabolism, and rate of elimination. Knowledge of these factors may be important in assessing the validity of the glucose concentration of a sample analyzed with the YSI glucose analyzer. However, we feel that it is equally important to realize that the response from the analyzer to a given concentration of the drug can vary, depending on the functional status of the two-layered enzyme membrane.

References

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5'-Nucleotidase Activity Enhanced by Manganese and Magnesium Ions with Inosine Monophosphate Substrate

To the Editor:

The activation and inhibition of 5'-nucleotidase (EC 3.1.3.5) by a variety of metal ions has been known for many years (1). Although most methods of 5'-nucleotidase determination incorporate Mg2+ as the cofactor of choice, 5'-nucleotidase activity in human serum is activated by Mn2+ (2). Manganese ions at 1 mmol/L increase serum activities by 10-20% more than Mg2+ ions at 10 mmol/L (3). Furthermore, not only may 5'-nucleotidase exhibit species-to-species variability (4), but also enzyme from different tissue compartments may show metal ion selectivity, especially in conjunction with buffers of various pH ranges (5).

We have recently described a method for determining 5'-nucleotidase in serum by using inosine 5'-monophosphate (6). Here, we report our examination of the amplification of serum activity in rat or human specimens with either metal ion in this system.

We used the automated kinetic microassay for serum 5'-nucleotidase described previously (6), using 98.5 mmol/L triethanolamine buffer, 5.1 mmol/L inosine 5'-monophosphate, 130.0 mmol/L sodium β-glycerophosphate, 0.86 U/L nucleoside phosphorylase, and 0.26 U/L xanthine oxidase with 0.24 mmol/L manganese acetate or 24.0 mmol/L magnesium sulfate as activator. The within-run coefficient