To the Editor:

During our evaluation of commercial radioimmunoassay (RIA) test kits for prostatic acid phosphatase (PAP; EC 3.1.3.2) we used a matrix of pH 7.2 phosphate buffer, containing, per liter, 0.2 mol of monobasic sodium phosphate monohydrate, 1 g of sodium azide (J. T. Baker Chemical Co., Phillipsburg, NJ 08865), and 1 g of bovine serum albumin (Cohn Fraction V; Armour Pharmaceutical Co., Kankakee, IL 60901) in the cross-reactivity studies. As shown in Table 1, we obtained the expected low baseline values with this buffer when we tested the following PAP kits: Tandem-R PAP (Hybritech Inc., San Diego, CA 92121), RIAGEN (New England Nuclear, North Billerica, MA 01862), and PAP-Chek (Nuclear Medical Systems, Inc., Newport Beach, CA 92663). However, the fourth kit, RIAGEN (BioGenex Diagnostics, Dublin, CA 94566), gave baseline values between 4.1 and 6.2 μg/L, as much as 2.5-fold the manufacturer’s upper limit of normal for male subjects (2.5 μg/L). We obtained these results with two lots of the kit and two different preparations of the buffer.

To identify the interfering substance, we tested the individual constituents of our buffer and found that sodium azide interferes strongly with the RIAGEN test but not at all with the other three PAP kit procedures. Baseline values obtained with a typical RIAGEN kit increased linearly with sodium azide added up to a concentration of 4.0 g/L (yielding apparent PAP concentrations of 0 to 12 μg/L), but less rapidly at higher concentrations. J. T. Baker Company’s claim of 95% purity for the sodium azide we used in this study does not, of course, preclude an impurity in the material as a source of the interference we observed. We are therefore carrying out further studies to investigate this possibility and to elucidate the mechanism of interference.

Although sodium azide reportedly interferes with certain procedures for measurement of bilirubin (1–3), blood urea nitrogen (4), cholesterol (5), salicylate (6) and uric acid (7), we have found no previous reports of sodium azide interference in an RIA procedure. Indeed, it is widely used as a preservative in many RIA kits and is included in the standards, tracer, and other components of the three PAP kits we found to be unaffected by sodium azide. The kit that is susceptible to interference from sodium azide contains an unidentified preservative (not sodium azide) in the standards, antibodies, and tracer.

We recommend that quality-control materials, calibrators, and other preparations known or suspected to contain sodium azide should not be used with the RIAGEN kit. Sodium azide may be present in some in vitro diagnostic products even though this is not indicated in the labeling because current U.S. and Canadian regulations for medical devices do not require disclosure of the identity of preservatives used. However, amendments proposed to the Canadian Medical Devices Regulations, in response to concerns that sodium azide may react with lead and copper components of plumbing systems to form shock-sensitive heavy-metal azide salts (8), would change this situation.

References


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Aspartame Not a Source of Formate Toxicity

To the Editor:

There has been controversy in the news media over use of the artificial sweetener aspartame. Several groups have recently attempted to ban the use of aspartame (Nutrasweet, Equal) in food products and diet soft drinks, pending further studies. Among the complaints, none scientifically documented, has been temporary loss or impairment of vision.

Methanol is a product of the metabolism of aspartame (L-aspartyl-L-phenylalanine methyl ester) (1) and, considering the relationship between methanol and optical neuropathy (2), concern about the use of aspartame has been raised by some clinicians and scientists.

Methanol poisoning syndrome in humans and monkeys could be attributed to the formate metabolically produced from it (3). We recently developed an enzymic assay for formate in plasma, and used it to measure this analyte in 29 specimens from apparently healthy subjects (4) before aspartame-containing soft drinks were introduced in the U.S. We found a broad range of formate concentrations: 7–63 mg/L (0.2–1.4 mmol/L) (mean ± 2 SD). Projected aspartame consumption is 94 mg/kg of body weight (1, 5); i.e., only 1% of users

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Table 1. Effect of Phosphate–Azide–Bovine Serum Albumin Buffer* and its Constituents on Results with Four Commercial RIA Tests for PAP

<table>
<thead>
<tr>
<th>Substance tested</th>
<th>Kit</th>
<th>Apparent PAP concn. μg/L</th>
</tr>
</thead>
<tbody>
<tr>
<td>Buffer</td>
<td>RIAGEN</td>
<td>0.1 (&lt;1.0)*</td>
</tr>
<tr>
<td>Buffer</td>
<td>PAP-Chek</td>
<td>0.1 (&lt;2.5)</td>
</tr>
<tr>
<td>Buffer</td>
<td>Tandem-R PAP</td>
<td>0.1</td>
</tr>
<tr>
<td>Buffer</td>
<td>RIAGEN</td>
<td>6.2</td>
</tr>
<tr>
<td>Phosphate, 0.2 mol/L</td>
<td>RIAGEN</td>
<td>0.1 (&lt;1.0)</td>
</tr>
<tr>
<td>BSA, 1 g/L</td>
<td>RIAGEN</td>
<td>0.2 (&lt;1.0)</td>
</tr>
<tr>
<td>Phosphate + BSA</td>
<td>RIAGEN</td>
<td>0.1 (&lt;1.0)</td>
</tr>
<tr>
<td>Sodium azide, 1 g/L</td>
<td>RIAGEN</td>
<td>8.5</td>
</tr>
</tbody>
</table>

*Composition as given in the text. Values in parentheses are the lowest standards actually used in determining the calibration curve; lower values shown are therefore based on extrapolation. BSA, bovine serum albumin.