More on Interference of N-acetylcysteine in Measurement of Acetaminophen

To the Editor:

In a recent Letter to the Editor, Mayer and Salpeter (1) identified N-acetylcysteine (NAC) interference with GDS AR100 reagent for acetaminophen testing.

GDS Technology, Inc., has performed three separate studies investigating this concern along with a third-party investigator from a major diagnostic supplier and has found no significant NAC interference occurring within the usual treatment concentrations of NAC.

In our studies, stock solutions of NAC (5000 and 180,000 mg/L) in distilled water were prepared. A stock of acetaminophen in pooled normal human serum was also prepared. A matrix of human serum samples containing NAC concentrations in the range of 0–10,000 mg/L and acetaminophen in the range of 0–200 mg/L was created by combining pooled normal human serum, serum containing acetaminophen (200 mg/L), and NAC stock solution in a total volume of 1 mL. The serum samples were then analyzed according to the endpoint method (10-min procedure) described in the package insert for the Enzymatic Acetaminophen Reagent Kit from GDS Technology, Inc. (cat. no. AR100).

Typical results obtained are shown in Table 1. Recoveries were similar with the kinetic method.

The recovery of acetaminophen in the range of 0.4–192 mg/L in the presence of NAC at a therapeutic concentration (100 mg/L) was 93–111%. At a NAC concentration of 1000 mg/L, which exceeds the initial plasma concentration range cited by Mayer and Salpeter (1) the recovery of acetaminophen in the range of concentrations tested was 83.9–92.8%.

Our test results, along with third-party data on file at GDS, show that therapeutic concentrations of NAC do not interfere with GDS AR 100 reagents. We do not question the results of Mayer and Salpeter but would like to know any additional information they may be able to provide that may be helpful in identifying the cause of their observations.

References


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The authors of the letter cited above respond:

To the Editor:

The letter by Tyhach displays results that presumably differ from our finding. However, the data presented by Tyhach show a suppression of acetaminophen recovery amounting to 13% and 21% at an acetaminophen concentration of 200 mg/L in the presence of 1000 and 2000 mg/L N-acetylcysteine (NAC), respectively. Undoubtedly this suppression is milder than the suppression we observed [~30%] when 1000 mg/L NAC was added to 150 mg/L acetaminophen concentration; Fig. 1A of our previous Letter (1), but it still exists. It should be emphasized that in our assays, equal volumes containing various dilutions of a stock solution of 200 g/L acetylcysteine were mixed with equal volumes containing different known concentrations of acetaminophen. Under these conditions, repeated experiments showed mean recoveries of 81%, 71%, and 65% when 100, 1000, and 2000 mg/L NAC, respectively, were added to 150 mg/L acetaminophen. We also would like to indicate that a concentration of 100 mg/L is definitely not a “normal” concentration of NAC, nor is 166 mg/L a “normal therapeutic” concentration. The common intravenous initial loading dose of 140 mg/kg NAC produces a mean plasma concentration of 554 mg/L (range, 304–875 mg/L) (2). Interestingly, we noted that the recoveries in presence of NAC were lower with increasing concentrations of acetaminophen. In the case of the patient described in our letter, the circulating acetaminophen concentration was 139 mg/L. Finally, our interest in the potential interference of NAC in the enzymatic assay was initiated by an earlier report on the interference of NAC with a colorimetric assay of acetaminophen in urine (3).

On the basis of our observation, we still suggest that acetaminophen should either be tested before initiation of NAC treatment or determined by one of the available immunoassays of serum acetaminophen (TDx, Syva Emit, or others) that are not biased by NAC.

References


Michael Mayer*
Lea Salpeter

Table 1. Typical results for the Enzymatic Acetaminophen Reagent Kit.

<table>
<thead>
<tr>
<th>Target acetaminophen conc., mg/L</th>
<th>Actual acetaminophen conc., mg/L</th>
<th>% recovery of acetaminophen at NAC concentration of</th>
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<tbody>
<tr>
<td>0</td>
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</tr>
<tr>
<td>25</td>
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</tr>
<tr>
<td>50</td>
<td>49.8</td>
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<td>100</td>
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</tr>
<tr>
<td>150</td>
<td>149</td>
<td></td>
</tr>
<tr>
<td>200</td>
<td>192</td>
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</tr>
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</table>

* conc., concentration.