the oral administration of metallic colloids, in particular colloidal silver protein, has been reported to have toxic effects (2). Despite this, dozens of companies sell metal colloids as nutritional supplements.

Many metal colloids have been rebranded as “nano” compounds to further intensify the public’s interest in their utility. Although clinical concern about the use of colloidal metallic compounds is longstanding, their effects on laboratory tests have not been investigated. These particles are of particular concern because their small size allows high oral bioavailability, accumulation within the blood, and excretion through the kidneys (5). We were interested to know whether metal colloids might cause interference in clinical chemistry tests of blood and urine.

We tested 4 nutraceutical products: Mesogold, Mesosilver, Meso-copper, and Mesoplatinum [Purest Colloids, Inc.; daily recommended doses ranged from 50 to 150 µg (4)]. These were colloidal suspensions of nonionic metal with 1- to 10-nm diameter particles. The concentrations of copper, silver, platinum, and gold measured by National Medical Services, Inc. were 0.9, 21, 13, and 18 mg/L of each metal, respectively, whereas the manufacturer’s stated concentrations were 10, 20, 10, and 10 mg/L, respectively.

We tested the mesometals (undiluted and as 1:1 mixtures with saline or pooled serum) for interference in a range of automated assays on a Vitros® Model 950 AT: glucose, blood urea nitrogen, creatinine, ammonia, sodium, potassium, chloride, total CO₂, amylase, lipase, calcium, magnesium, phosphate, cholesterol, triglycerides, uric acid, albumin, aspartate aminotransferase, alanine aminotransferase (ALT), lactate dehydrogenase (LD), creatine kinase, alkaline phosphatase, y-glutamyl transpeptidase, conjugated bilirubin, and unconjugated bilirubin. We also tested various point-of-care methods: Quickvue® One Step hCG Urine (Quidel Corp.); Acceava® hCG Combo (ThermoBiostar); and Chemstrip® 10 S-UA (Roche Diagnostics). The concentrations tested were likely much higher than might be found clinically, and they were chosen to reveal any possible effects.

We found no interferences (1:1 serum:saline vs sera:mesometals) with the exception of LD (10%–20% lower) and ALT (13%–50% higher). Of note, assaying the mesometals directly showed consistently detectable LD (range, 129–182 U/L) and low ALT activities (17–21 U/L) for all metals tested.

We also tested mesometals (undiluted and as 1:1 mixtures in control serum with added drugs [Lyphochek® Immunoassay Positive Control, Ethanol/Ammonia Control; Bio-Rad]) in Emit assays for lidocaine and amikacin, and for ethanol on the Hitachi 911, but we found no interference.

In addition, the Quickvue and Acceava hCG tests demonstrated no interference. The Chemstrip 10 S-UA had 1 aberrant result: mesoplatinum demonstrated a positive hemoglobin of “250 erythrocytes per µL” with a parallel “negative blood”. The Mesogold, Meso-copper, and Mesosilver were negative in the test for hemoglobin. No other analytes were affected by any of the mesometal solutions.

Another nanostructure with potential for drug delivery or as an imaging agent is the carbon nanotube. We tested a suspension of 60- to 100-nm diameter surface-charged carbon nanotubes (NanoTech Port Co.) in pooled sera and found no apparent interference with the panel of Vitros chemistry tests examined.

In summary, nanoparticle nutraceuticals exhibited no major interference with the tests examined. Minor interferences were noted in the LD assay on the Vitros as well as a reagent strip assay for hemoglobin. The mechanism of these aberrations is not clear. Clinical laboratories should remain vigilant for possible nanoparticle interferences, as these structures, with their diverse physical and chemical properties, are being used or advocated for use in a broad range of drug delivery applications and as imaging agents.

References

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Effect of Sample Collection Tubes on Cerebrospinal Fluid Concentrations of Tau Proteins and Amyloid β Peptides

To the Editor:

Tau protein and its phosphorylated forms, and amyloid β peptides ending at amino acid 42 (Aβ42) are used as cerebrospinal fluid (CSF) biomarkers of Alzheimer disease (AD) (1–8). Because preanalytical factors may affect results (4, 9, 10), we measured these biomarkers in CSF samples in collection tubes made of different materials.

After approval by the Ethics Com-
mittee of the University of Erlangen-Nuremberg, patients and/or their closest relatives gave written informed consent. CSF was obtained from patients (n = 20; mean age, 66 years; 9 women and 11 men) with various neuropsychiatric diseases, including dementias (n = 9), mild cognitive impairment (n = 8), recurrent depression (n = 1), bipolar disorder (n = 1), and emotionally unstable personality (n = 1). We included only CSF samples showing no or only minor contamination with erythrocytes (<150/μL), no intrathecal humoral or cellular immune response, and normal or only slightly disturbed blood–CSF barrier as measured by albumin quotient. After collecting 4–5 mL of CSF for routine analyses, we transferred four 0.5-mL fractions directly into 4 test tubes in this order: (a), polycarbonate (PC; Sarstedt; cat. no. 60.9922.936); (b), a copolymer of polystyrene and acrylonitrile [modified polystyrene (PX); Sarstedt; cat. no. 60.9924.952]; (c), polystyrene (PS; Sarstedt; cat. no. 62.553.542PS); and (d), polypropylene (PP; Sarstedt; cat. no. 62.554.502PP). Fractions were centrifuged simultaneously (1600g for 15 min at room temperature) immediately after the spinal puncture and were frozen at −80°C within 30–40 min. The material was never thawed and refrozen.

We used ABx–40 and ABx–42 methods from The Genetics Co. and Aβ1–42, total Tau, and P-tau_{181P} from Innogenetics. Because different antibodies used in the respective assays show different epitope specificities, they enable detection of either specifically one species, namely Aβ1–42 [the assay of Innogenetics (11)], or the “family” of Aβ peptides ending with a COOH terminus at residue 42 and beginning at different NH2 termini (ABx–42; the assays of The Genetics Co.). All 4 corresponding aliquots from a given patient were applied simultaneously to 1 ELISA plate. All measurements were performed in duplicate. Results are presented in reference to the concentration obtained in PP (set as 100%) and analyzed by ANOVA for repeated measurements, followed by the Scheffé post hoc test.

ABx–40 concentrations were lower in the PS tube than in all other material types (Table 1; n = 13; P <0.001), whereas concentrations in PC, PX, and PP were similar. CSF ABx–42 concentrations were lower in the PS tube than in all other material types (Table 1; n = 19; P <0.001), whereas there were no significant differences among PC, PX, and PP. The ABx–42/ABx–40 concentration ratio was only slightly higher in PC than in PX (n = 13; P = 0.04), with no differences among other tubes. Aβ1–42 was lower on PS (Table 1) than in PC (P <0.01), PX, and PP (P <0.001). Aβ1–42/ABx–42 was higher in PS than in PP and PC (n = 19; P <0.05). Tau was significantly lower (P <0.001) in the PS tube compared with all other tubes. The results also differed between PC and PX (P <0.05; Table 1). Neither Aβ1–42/ABx–40 ratio (n = 13) nor P-tau_{181P} (n = 16) differed significantly among test tubes (Table 1).

<table>
<thead>
<tr>
<th>Biomarker</th>
<th>PC (Mean ± SD)</th>
<th>PX (Mean ± SD)</th>
<th>PS (Mean ± SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABx–40</td>
<td>93.8 (13.9)</td>
<td>101.0 (15.9)</td>
<td>72.1 (11.9)a</td>
</tr>
<tr>
<td>ABx–42</td>
<td>95.5 (12.9)</td>
<td>96.5 (19.0)</td>
<td>71.4 (10.2)a</td>
</tr>
<tr>
<td>ABx–42/x–40</td>
<td>100.6 (9.4)</td>
<td>92.4 (14.6)b</td>
<td>95.8 (9.0)</td>
</tr>
<tr>
<td>Aβ1–42</td>
<td>94.5 (14.3)</td>
<td>99.7 (15.9)</td>
<td>79.9 (12.0)a</td>
</tr>
<tr>
<td>Aβ1–42/x–40</td>
<td>100.0 (14.0)</td>
<td>97.9 (11.5)</td>
<td>106.1 (11.7)</td>
</tr>
<tr>
<td>Aβ1–42/x–42</td>
<td>98.6 (10.6)</td>
<td>105.7 (22.8)</td>
<td>111.4 (6.4)c</td>
</tr>
<tr>
<td>Total tau</td>
<td>100.6 (8.6)</td>
<td>94.8 (8.3)d</td>
<td>84.9 (10.4)a</td>
</tr>
<tr>
<td>P-tau_{181P}</td>
<td>99.5 (3.2)</td>
<td>99.8 (3.2)</td>
<td>101.1 (4.3)</td>
</tr>
</tbody>
</table>

- a P <0.01 compared with all other materials.
- b P <0.05 compared with PC.
- c P <0.05 compared with PP.
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References


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**Microwave-Assisted Derivatization of Glucose and Galactose for Gas Chromatographic Determination in Human Plasma**

To the Editor:

Monosaccharides are usually analyzed by use of automatic monitors or enzymatic immunoassays. However, gas chromatography (GC) is an accurate and precise technique for galactose quantification (1), and it is regarded as a reference method for glucose (2). GC procedures require a long derivatization time in 2 consecutive reactions of 60–90 min to generate the aldonic acid pentacacete derivative. Fast derivatization techniques are often requested today because the bottleneck for sample throughput has moved from analysis to sample preparation. Recently, we dramatically decreased the derivatization time for sugars (mono- and disaccharides) in GC analysis (3) by using trimethylsilyl-oxide derivatives. This derivative, however, gives 2 peaks in the chromatogram, which is acceptable for the glucose–fructose pair but not for the glucose–galactose pair.

In this study, we optimized the aldonic acid pentacacete derivatization step, using microwave-assisted conditions to obtain single-peak derivatives for each sugar. Plasma from healthy adults was used as a model matrix for the recovery experiments.

Glucose and galactose were from Sigma. Plasma samples were prepared as follows: we deproteinized 200 μL of plasma with 500 μL of methanol. After centrifugation at 5000g, the supernatant was withdrawn and evaporated to dryness under a stream of nitrogen. We added 100 μL of hydroxylamine hydrochloride (20 g/L in pyridine) to the vial, vortex-mixed it for 30 s, and then reacted the mixture for 2 min in a microwave oven (200 W, 25% of total exit power). The final step was to add 100 μL of acetic anhydride and allow the reaction to proceed for 6 min. We directly injected 1 μL (split ratio 1:25) into a chromatograph (Varian 3380) equipped with a BP-10 Column (SGE). The column temperature started at 120 °C for 1 min, then was increased to 280 at 10 °C/min rate. The injector and detector (flame ionization detection) were at 280 °C.

Optimal reaction times were 2 min for the oxime reaction and 6 min for the acetylation and aldonic acid formation.

Although galactose and glucose are enantiomers differing in only one optical center, the BP-10 column easily achieved the desired baseline separation (Fig. 1). Calibration curves constructed either with aqueous solutions or by standard additions to plasma showed no differences in slope.

Recovery, calculated with the aqueous calibrators, was 97%–101%.