Cupric Oxide Should Not Be Used As a Copper Supplement for Either Animals or Humans

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Animal studies have shown conclusively that the copper (Cu) in analytical-grade cupric oxide (CuO) is unavailable for absorption from the gut (Aoyagi and Baker 1993, Baker et al. 1991, Cromwell et al. 1989, Ledoux et al. 1991). In fact, the bioavailability of Cu in CuO relative to that in CuSO₄·5H₂O is not significantly different from zero (Aoyagi and Baker 1993). This finding is important in animal nutrition because before 1990, CuO was the primary source of Cu used in trace-mineral premixes for swine, poultry and companion animals. It was popular because among the Cu sources available in feed-grade form, CuO (80% Cu) was high in Cu and therefore occupied less “space” in trace-mineral premixes.

Cupric oxide continues to be the principal source of Cu used in vitamin-mineral supplements for humans. Because these supplements are provided as tablets, CuO with its high concentration of Cu, occupies less space in the tablet than would CuSO₄·5H₂O (25% Cu), yet it seems gratuitous that this form of Cu is still being used when the animal studies have shown so conclusively that the Cu in CuO is very poorly utilized. In a recent survey of pharmacies, supermarkets and supplement stores, I found only a few (among many) vitamin-mineral products that contained Cu in a form other than CuO. Interestingly, a similar survey of mineral-fortified food products revealed that almost all that contained added Cu used CuSO₄·5H₂O as the source of Cu. Virtually all infant formulas and enteral products contain supplemental Cu, and most of these products use CuSO₄·5H₂O. Among common Cu sources used as supplements, CuSO₄·5H₂O is somewhat unusual in that it is readily soluble in water (cupric chloride and cupric acetate are the other common Cu sources that are water soluble). As shown in Table 1, solubility of Cu salts in either water or acid is not a reliable measure of bioavailability. Cuprous oxide, for example, is very insoluble in both water and acid, but the Cu in this compound is as bioavailable as that in CuSO₄·5H₂O.

Cupric oxide is no longer used as a Cu supplement in animal nutrition, but it continues to be used in vitamin-mineral supplements (tablets) for humans. Teenagers and adults consuming energy-restricted diets often rely on supplements to ensure that vitamin and mineral requirements are being met. It seems possible that such individuals may be Cu deficient, because the CuO in the tablet they are taking is not providing bioavailable Cu. A diet recall survey of 400 rural women in Illinois conducted by Reber et al. (1990) showed that 90% of their sample of women who consumed fewer than 7.53 MJ/d were ingesting <1.5 mg Cu/d, the lower limit of a safe and adequate Cu intake as suggested by the Food and Nutrition Board of the National Academy of Sciences (NRC 1989). Klevay and Medeiros (1996) and Klevay (1998) reported that 61% of the diets in Canada, Belgium, the U.K. and the U.S. provide <1.5 mg Cu/d, and almost one third provide <1 mg Cu/d. Low Cu intakes have been implicated in ischemic heart disease and osteoporosis; control of blood pressure, cholesterol and glucose metabolism also require adequate intakes of Cu (Klevay, 1998).

Unfortunately, reliable noninvasive procedures to assess Cu status in humans are not available. For this reason, there is no RDA for Cu, only a suggested adequate intake level of 1.5–3.0 mg/d for adults (NRC 1989). It is well established that high zinc, ascorbic acid and cysteine intakes reduce Cu absorption (Aoyagi and Baker 1994, Baker and Czarnecki-Maulden 1987, Di Silvestro and Harris 1981, Hill and Starcher 1965, Maggs and Matrone 1962, Milne and Omaye 1980, Murthy et al. 1974, Van Campen and Gross, 1968, Van Campen and Scall, 1967, Van Den Berg and Beynen 1992). A scenario could be suggested in which a segment of the population was restricting energy intake and also consuming megadoses of ascorbic acid and zinc together with a vitamin-mineral supplement containing CuO.

Table 1

<table>
<thead>
<tr>
<th>Source of Cu</th>
<th>Cu level</th>
<th>Color</th>
<th>Water solubility</th>
<th>Relative bioavailability</th>
</tr>
</thead>
<tbody>
<tr>
<td>CuSO₄·5H₂O</td>
<td>25.5</td>
<td>Blue</td>
<td>yes</td>
<td>100</td>
</tr>
<tr>
<td>CuO</td>
<td>79.9</td>
<td>Black</td>
<td>no²</td>
<td>0</td>
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<tr>
<td>Cu₂O</td>
<td>88.8</td>
<td>Red</td>
<td>no²</td>
<td>100</td>
</tr>
<tr>
<td>CuCl</td>
<td>64.2</td>
<td>White</td>
<td>no²</td>
<td>145</td>
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<td>CuCl₂</td>
<td>47.3</td>
<td>Blue</td>
<td>yes</td>
<td>100</td>
</tr>
<tr>
<td>Cu(OAc)₂</td>
<td>35.0</td>
<td>Green</td>
<td>yes</td>
<td>100</td>
</tr>
<tr>
<td>CuOAC</td>
<td>51.8</td>
<td>Green/yellow</td>
<td>yes³</td>
<td>100 ³</td>
</tr>
<tr>
<td>CuCO₃</td>
<td>57.5</td>
<td>Blue/green</td>
<td>no²</td>
<td>100</td>
</tr>
</tbody>
</table>

² CuSO₄·5H₂O was used as a standard, and values not significantly different (P ≤ 0.05) from the standard were given a value of 100%.
³ Rapidly hydrolyzed in water, with partial formation of Cu₂O.
⁴ Best estimate based on very limited bioavailability information.
ing CuO. It seems likely that such individuals would be Cu deficient.

Manufacturers of vitamin-mineral supplements should discontinue use of CuO as a source of Cu. Other Cu compounds are available that provide utilizable forms of Cu. Among these, Cu_2O (88% Cu), CuCl (64.2% Cu), CuCO_3, Cu(OH)_2, known as alkaline Cu carbonate (57% Cu), CuCl_2 (47.3% Cu), cupric acetate (35.0% Cu) and CuSO_4.5H_2O (25.5% Cu) would be good choices. Clearly, chemical, physical and organoleptic properties of Cu salts must be considered. The resulting pill or tablet may be larger, but at least it will furnish Cu in a form that can be utilized.

LITERATURE CITED