LETTER

Curcumin and Alzheimer Disease: This Marriage Is Not to Be Performed

The therapeutic use of curcumin in the treatment of Alzheimer disease (AD) proposed by Zhang *et al.* (1) was contradicted by clinical evidence. In a randomized clinical trial, curcumin (1–4 g/day for 6 months) failed to improve cognitive performance in mild-to-moderate AD patients and did not have any beneficial effect on pro-inflammatory biomarkers such as serum amyloid-β peptide and isoprostanes (2). This lack of effect could be attributable to the low bioavailability of oral curcumin. The oral administration of 450–3600 mg of curcumin/day for 1 week to patients affected by colorectal cancer produced a plasma concentration of ~3 nM (3). However, plasma levels up to 160 nM were obtained in healthy volunteers exposed to oral curcumin at supra-therapeutic doses (10–12 g/day) (4). These low plasma concentrations did not depend on the acute regimen of treatment. Indeed, chronic administration of curcumin (1–4 g/day for 6 months *per os*) initiated plasma concentrations in the range 60–270 nM (2). Considering the presence of the blood-brain barrier, it is plausible to conclude that brain curcumin concentration in humans could be even lower than that found in plasma. Therefore, the inhibition of amyloid precursor protein maturation by 1–20 μM curcumin found by Zhang *et al.* (1) in human and rat cells is unlikely to occur in AD subjects. Finally, curcumin is not safe since it initiates several toxic effects including diarrhea, iron-deficient anemia, potential harmful interactions with drug-metabolizing enzymes, and DNA damage, which could be even more severe in elderly individuals such as those suffering from AD (5).

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