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Abstract

Demethoxycurcumin and Bisdemethoxycurcumin Are More Bioavailable than Curcumin: A Meta-Analysis of Randomized Cross-Over Trials in Healthy Humans and an In Vitro Mechanistic Exploration †

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Abstract: Background: Curcuminoids are secondary plant metabolites found in turmeric and many dietary supplements. They usually consist of a mixture of curcumin (CUR), demethoxycurcumin (dCUR) and bisdemethoxycurcumin (bdCUR). CUR, the main curcuminoid, has been intensely investigated for its putative effects against, e.g., inflammation, oxidative stress and cancer. However, CUR displays very poor bioavailability. We have previously shown that, when brought by turmeric, dCUR and bdCUR, which can also exert health effects, display greater in vitro bioaccessibility than CUR (PMID: 37073511). However, their bioavailability relative to that of CUR has not been thoroughly investigated. Objective: We aimed to compare the bioavailability of dCUR and bdCUR to that of CUR in a meta-analysis of clinical trials in healthy humans and to compare their in vitro bioaccessibility and enterocyte uptake efficiency. Methods and Results: Studies published until 2022 were searched for using Medline and Scopus. The included studies were randomized trials that measured the bioavailability of CUR, dCUR and bdCUR in healthy participants. Estimates were calculated using a random-effects model. Fifteen trials were included in the study, representing a total of 50 interventions, i.e., each trial investigated several curcuminoid formulations, in 762 participants. The relative bioavailabilities were calculated using the inverse variance method. dCUR was 2.32 (95% CI:1.70, 3.13) times more bioavailable than CUR, while bdCUR was 2.57 (95% CI: 1.58, 4.16) times more bioavailable than CUR, with some heterogeneity across the formulations used. Using an in vitro gastro-intestinal digestion model with pure curcuminoids, we showed that dCUR solubilization efficiency was 4.8 and 5.3 times higher than that of CUR and bdCUR, respectively ($p < 0.001$), while its micellization efficiency was 10.3 and 5.1 times higher than that of CUR and bdCUR, respectively ($p < 0.001$). Conclusions: bdCUR and dCUR display greater bioavailability in humans compared to CUR. A subgroup analysis by formulation is undergoing investigation and will be presented. For dCUR, this difference is partly explained by higher in vitro bioaccessibility. Uptake efficiency measurements of pure curcuminoids and of curcuminoids from in vitro digestion fluids are undergoing investigation and will be presented. bdCUR and dCUR might therefore represent relevant alternatives to CUR for the systematic delivery of curcuminoids.

Keywords: curcuminoid; turmeric; bioaccessibility; enterocyte; cell uptake; stability; solubility; digestion; small intestine; absorption

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