Bioavailability of oral curcumin

In our research article, we conclude that the regimen of curcumin we tested exerted no beneficial pharmacodynamic effect on the outcomes we assessed in the setting of elective abdominal aortic aneurysm repair.[1] These findings advance knowledge.

Dr. Lora Aller seems to suggest that the lack of observed effect is entirely owing to poor pharmacokinetic properties of the regimen we selected.[2] It is true that a concern with curcumin is that it is poorly absorbed from the gastrointestinal tract and is rapidly metabolized, resulting in low free blood and tissue concentrations. We acknowledge this in our article, and in the "Limitations" section write, "Curcumin is notorious for being poorly absorbed from the gastrointestinal tract."[1] However, animal studies of the plasma and tissue distribution of curcumin do prove there are detectable levels of radiolabelled curcumin in the blood and kidney after its oral administration.[3] We also share with Dr. Aller and others the following details.

Everything Dr. Aller mentions was fully discussed in planning this trial and was addressed in our successful grant application funded by the nutrition, food and health peer-review panel at the Canadian Institutes of Health Research (CIHR).

We tested a regimen of oral curcumin that we hypothesized would have beneficial effects. Seven factors to justify the curcumin regimen we tested are fully described in section 4 of Appendix 1 of the article.[1] Patients were instructed to take the capsules with food to improve curcumin absorption (which occurred for all doses in more than 85% of patients based on their self-report).

The fact that free curcumin is difficult to measure in the blood does not equate to an assertion that the agent is not biologically active. In our article, we cite a smaller randomized controlled trial involving 121 consecutive patients undergoing coronary artery bypass graft surgery at a single centre in Thailand, in which oral curcumin relative to placebo reduced the risk of postoperative myocardial infarction and lowered concentrations of plasma biomarkers for inflammation, oxidation and injury.[4] This justified further testing of oral curcumin in the perioperative setting as done in our study. Our curcumin regimen of 4000 mg a day is a common dose used in many published small single-centre trials that reported biological effects.[5]

Unlike free curcumin, major curcumin metabolites (glucuronide and sulfate conjugates) are readily detected after an oral dose, and these metabolites exert biological activity. In the "Results" section of our paper, we state, "In the curcumin group, curcumin metabolites were detected in the urine using high-performance liquid chromatography and mass spectrometry, as described in section 9 of Appendix 1, at a concentration significantly higher than detected in the placebo group."[1]

We considered co-administering oral curcumin with another agent such as piperine (from black pepper), turmeric oil or quercetin to increase its bioavailability. However, the addition of these adjuvants had regulatory implications for trial conduct and could have resulted in a highly selected participant population. For example, possible pleiotropic effects of piperine, the most well-studied adjuvant, raised concerns about safety. Piperine is a nonspecific inhibitor of drug metabolism and enhances the bioavailability of several standard drugs, including β-lactam antibiotics, phenytoin and several β-blockers.

We remain open-minded about the possible health benefits of novel formulations of curcumin, including nanoparticle-based delivery systems, liposomal curcumin, and micelle and phospholipids complexes. Funded by CIHR, we are now conducting a multicentre controlled trial of a microparticle curcumin in patients at risk of progressive chronic kidney disease.[6] We encourage others to do the same with preparations of turmeric or curcumin and in settings where they believe there may be health benefits.

Our position is that it is responsible to rigorously test what we think might be beneficial according to best standards in medicine before espousing health benefits, as often occurs in the popular media when it comes to curcumin and other natural health products.

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