Dear Sir,

We are writing in response to the recent paper by Toegel et al. (2008) Osteoarthritis and Cartilage comparing the chondroprotective effects of glucosamine, curcumin and diacerein in interleukin 1-beta (IL-1β)-stimulated C-28/I2 chondrocytes. It was with great interest that we noted the authors’ findings of increased expression of cartilage-chondrocytes. It was with great interest that we noted the authors’ findings of increased expression of cartilage-chondrocytes. It was with great interest that we noted the authors’ findings of increased expression of cartilage-chondrocytes. It was with great interest that we noted the authors’ findings of increased expression of cartilage-chondrocytes. It was with great interest that we noted the authors’ findings of increased expression of cartilage-chondrocytes.

Initially, these results appeared to be markedly different from observations made in several laboratories where concentrations of curcumin, up to and including 100 μM, had no effect on the viability of freshly isolated chondrocytes from a number of species. However, our recent data suggests that curcumin at 50 μM and above exerts cytotoxic effects on primary chondrocytes.

We have been developing ex vivo cartilage explant models for the purpose of screening various extracts. One model assesses the effects of different compounds on unstimulated, ‘normal’ cartilage cultured in media alone. The other, an inflammatory model, assesses whether these compounds exhibit any anti-catabolic activity by using IL-1β to induce catabolic changes similar to those observed in osteoarthritis (OA). Using these models, we have found that curcumin at concentrations between 0.1 μM and 100 μM does not alter the quantity of glycosaminoglycans (GAGs) released from unstimulated cartilage explants compared to their controls that received no curcumin treatment. In the inflammatory model, we found that the IL-1β-stimulated increase in GAG release was significantly reduced to levels found in unstimulated explants by the addition of curcumin at 100 μM. Further studies from our laboratories suggest that IL-1β-induced GAG release is attenuated by curcumin concentrations as low as 3 μM (unpublished observations). Explants are more appropriate for studies of extracellular matrix turnover than monolayer cultures of primary chondrocytes and transformed chondrocyte-like cell lines, due to the fact the chondrocytes are being maintained in their natural physicochemical environment in situ (the extracellular matrix of articular cartilage). Thus far, we have not observed any detrimental effects of curcumin at high concentrations in the explants we have tested. However, in monolayer cultures of equine articular chondrocytes, we have observed cell death between 50 μM and up to 100 μM which is in agreement with the results of Toegel et al. Consequently, these results are not in agreement with several studies using primary human chondrocytes.

Initially, we surmised that the conflicting findings of published work compared to the results of Toegel et al. could be due to the differences between using primary chondrocytes and transformed chondrocyte cell lines. The cytotoxic effects of curcumin are well documented with regard to its pro-apoptotic effects in cancer cells and transformed cells. Thus, the apparent toxic effects of curcumin on the transformed chondrocyte cell line C-28/I2 used in the Toegel study could have been due to the known apoptosis-inducing effects of curcumin on cancer cells and transformed cells in general. However, our recent observations suggest that high concentrations of curcumin (i.e. 50 to 100 μM) are also toxic to primary articular chondrocytes. In conclusion, we wish to thank the authors for bringing this apparent toxicity of curcumin to our attention. Their observations are in agreement with the literature on transformed cells, and we can now confirm that this is also the case with primary isolated, non-transformed chondrocytes. Clearly further studies are required in this area to establish the optimal physiological concentration at which curcumin may exert beneficial effects on chondrocytes without cytotoxic sequelae. In addition, it would be beneficial to compare the effects of curcumin on chondrocyte function and viability across a number of different species.

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