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Letter to the Editor

Response to ‘‘Inhibition of p300 and nuclear factor-κB by curcumin and its role in diabetic nephropathy’’

To the Editor:

Several studies have shown the beneficial effects of curcumin in cultured cells and animal models of human diseases. However, a full appreciation of the antioxidant [1], anti-inflammatory [2], antifibrotic [3–5], and antiangiogenic [6] activities of curcumin is hindered by inadequate means of delivery and reduced bioavailability [7]. For in vitro and in vivo studies, curcumin has been solubilized in an organic solvent (such as dimethylsulfoxide [DMSO] [8–10]), emulsified by using carboxymethyl cellulose [11,12], or solubilized in an alkaline solution [13,14]. In addition, curcumin has been added to animal diets [15,16]. An important issue certainly seems to be that different modes of administration (intraperitoneal, intravenous, oral gavage, or modified diet) result in different circulating levels (i.e., bioavailability). This issue is nicely highlighted by a recent review by Anand et al. [7]. For example, an intraperitoneal injection of 100 mg/kg of curcumin dissolved in DMSO in mice resulted in 10-fold higher plasma levels compared with 1 g/kg given by oral gavage (emulsified in carboxymethyl cellulose) [11].

We appreciate the comments of Kurien and Scofield [17] on our recent study of the effects of curcumin in reversing the oxidative stress induced by chronic diabetes [18]. The authors suggested the use of curcumin solubilized in an aqueous solution by heating [19] for our study. The same suggestion has been put forth for other recent curcumin studies [20,21]. This may turn out to be an attractive option to study the effects of curcumin by providing a better delivery system. Currently, however, there are no published studies using heat-solubilized curcumin in cultured cells or in animal models. Therefore, it is not clear that this mode (heat-induced three-fold higher solubility) will be better than what is commonly being used (i.e., DMSO, emulsification, NaOH, etc.) to study the effect of curcumin. It definitely will be interesting to see the effect of heat-solubilized curcumin as suggested by Kurien and Scofield. This, however, needs to be tested in animal and cell culture studies.

Kurien and Scofield have also suggested the inclusion of DMSO/ethanol-treated non-diabetic rats essentially to exclude the possibility of adverse effects of DMSO. Although we recognize the importance of such a group, other investigators have used DMSO as a diluent for curcumin [8,9] and no known toxicities were observed. Even when 250 mg to 1 g of DMSO is given to rats (dose corresponding to 250 μL to 1 mL of 100% DMSO daily), the liver and kidney functional tests appear to be normal [22,23]. To reduce the chances of DMSO-mediated toxic effects, we dissolved curcumin in a mixture of DMSO/ethanol. Each animal in the group received a maximum of 100 μL of combined DMSO/ethanol solution. We have also used this formulation in our previous study [24] in which we did not observe any toxic effects. It should also be noted that we do not assert that DMSO is the most ideal vehicle to deliver curcumin. Although DMSO is a powerful solvent for a number of water-insoluble drugs and is widely used in the laboratory/clinical setting, we appreciate that there may be unwanted effects. Further studies are needed to test these notions and to investigate the optimal dose and the best means of administering curcumin for therapeutic use. This is especially important when designing clinical trials of curcumin.

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