

Contribution of Degradation Products to the Anticancer Activity of Curcumin

To the Editors: The recent interesting article by Dhillon et al. (1) evaluated the clinical biological effects of curcumin against advanced pancreatic cancer. One important puzzle arising from this study involves how the biological activities are done with the precondition of the low nanogram levels of circulating curcumin (only 22-41 ng/mL were detectable in plasma even at oral dose of 8 g/d; ref. 1). More efforts are needed to shed new light on the pharmacology of curcumin.

Curcumin possesses low stability under various conditions; for example, about 90% decomposed within 30 minutes when curcumin was incubated in 0.1 mol/L phosphate buffer and serum-free medium (pH 7.2) at 37°C (2). Curcumin is degraded to the bioactive compounds such as ferulic acid and vanillin (2), which may contribute to the observed biological activities of curcumin based on the following two aspects. Firstly, the degradation products overcome the limitation of the extremely poor aqueous solubility for parent curcumin as reflected by their respective logP (1.42 for ferulic acid and 1.09 for vanillin, much lower than those of the keto and enol isomers of curcumin, 2.56 and 2.17). Secondly, the degradation products have been proved to exhibit anticancer potentials through inhibiting the important targets involved in the development of cancer (3-5). For instance, it was reported that ferulic acid can inhibit effectively both the cyclooxygenase-1 and cyclooxygenase-2 enzymes (3) and significantly suppress NF- κ B activation (4). Vanillin can also inhibit NF- κ B activation and cyclooxygenase-2 gene expression (5).

Therefore, it is reasonable to postulate that the bioactive degradation products should play important roles in the anticancer effects of curcumin, which may account, at least in part, for the observed biological activity with the almost detectable concen-

tration of parent curcumin. In addition, in view of the extremely limited bioavailability of curcumin in various clinical trials, the contributions of the degradation products should be given full attention when elucidating the pharmacology of the versatile natural product in various diseases.

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Disclosure of Potential Conflicts of Interest

The authors have declared no conflicts of interest.

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Published OnlineFirst 11/10/09.

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doi: 10.1158/1078-0432.CCR-09-1749