

Title:

Differential Cellular Uptake and Metabolism of Curcuminoids in Monocytes/Macrophages: A Possible Mechanism of Differential Effects of Curcuminoids on Lipid Uptake and Bacterial Phagocytosis

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Abstract:

Objective: Curcumin (CUR) is obtained from the rhizome of turmeric (*Curcuma Longa* L.) and is present in dried turmeric powder. CUR has been shown to have several activities such as anti-bacterial and anti-inflammatory properties or the enhancement of phagocytosis of bacteria and parasites such as *Plasmodium falciparum*. Just like the phagocytotic effect, we previously showed that curcumin (CUR) can increase lipid accumulation in cultured THP-1 monocytes/macrophages (J.M. Zingg, et al., *J. Cell. Biochem.*, 113, 833-840, 2012). CUR-induced accumulation of lipids in macrophages may be part of a mechanism aimed at the removal of lipids from the blood stream, which help to prevent diseases such as atherosclerosis. Since tetrahydrocurcumin (THC, an *in vivo* metabolite of CUR) had no such effect, in the present study, we have hypothesized that different cellular binding, uptake and/or metabolism of CUR and THC may be responsible for differential accumulation of lipids in macrophages.

Methods & Results: Chromatography with tandem mass spectrometry revealed that CUR was readily taken up by THP-1 monocytes/macrophages and slowly metabolized to hexahydrocurcumin sulfate. In contrast, uptake of THC was low. In parallel with CUR uptake, lipid uptake was observed in THP-1 macrophages but not with THC nor with another CUR metabolite and structurally related compounds.

Discussion: From these results, it is possible to conclude that CUR and THC are taken up and metabolized differently in THP-1 cells. The efficient cellular uptake of CUR, relative to the low uptake of the other curcuminoids (e.g., THC), may imply that CUR uptake in cells may occur via a transporter capable of distinguishing their structures. CUR-induced lipid uptake in THP-1 cells is an event that appears to be correlated to CUR transport inside the cells. These results would be useful for not only understanding

physiological function of curcuminoids for nutritional and medicinal purposes but also mechanism of phagocytosis of bacteria by macrophages.

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