

Effect of curcumin supplementation on blood glucose, plasma insulin, and glucose homeostasis related enzyme activities in diabetic db/db mice.

[Seo KI](#), [Choi MS](#), [Jung UJ](#), [Kim HJ](#), [Yeo J](#), [Jeon SM](#), [Lee MK](#).

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We investigated the effect of curcumin on insulin resistance and glucose homeostasis in male C57BL/KsJ-db/db mice and their age-matched lean non-diabetic db/+ mice. Both db/+ and db/db mice were fed with or without curcumin (0.02%, wt/wt) for 6 wks. Curcumin significantly lowered blood glucose and HbA 1c levels, and it suppressed body weight loss in db/db mice. Curcumin improved homeostasis model assessment of insulin resistance and glucose tolerance, and elevated the plasma insulin level in db/db mice. Hepatic glucokinase activity was significantly higher in the curcumin-supplemented db/db group than in the db/db group, whereas glucose-6-phosphatase and phosphoenolpyruvate carboxykinase activities were significantly lower. In db/db mice, curcumin significantly lowered the hepatic activities of fatty acid synthase, beta-oxidation, 3-hydroxy-3-methylglutaryl coenzyme reductase, and acyl-CoA: cholesterol acyltransferase. Curcumin significantly lowered plasma free fatty acid, cholesterol, and triglyceride concentrations and increased the hepatic glycogen and skeletal muscle lipoprotein lipase in db/db mice. Curcumin normalized erythrocyte and hepatic antioxidant enzyme activities (superoxide dismutase, catalase, glutathione peroxidase) in db/db mice that resulted in a significant reduction in lipid peroxidation. However, curcumin showed no effect on the blood glucose, plasma insulin, and glucose regulating enzyme activities in db/+ mice. These results suggest that curcumin seemed to be a potential glucose-lowering agent and antioxidant in type 2 diabetic db/db mice, but had no affect in non-diabetic db/+ mice.

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Clinical Trials

Phase I Clinical Trial of Oral Curcumin

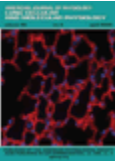

Biomarkers of Systemic Activity and Compliance

Ricky A. Sharma¹, Stephanie A. Euden¹, Sharon L. Platton¹, Darren N. Cooke¹, Aisha Shafayat¹, Heather R. Hewitt¹, Timothy H. Marczylo¹, Bruno Morgan², David Hemingway³, Simon M. Plummer¹, Munir Pirmohamed⁴, Andreas J. Gescher¹ and William P. Steward¹

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Curcumin, a polyphenolic antioxidant derived from a dietary spice, exhibits anticancer activity in rodents and in humans. Its efficacy appears to be related to induction of glutathione *S*-transferase enzymes, inhibition of prostaglandin E₂ (PGE₂) production, or suppression of oxidative DNA adduct (M₁G) formation. We designed a dose-escalation study to explore the pharmacology of curcumin in humans. Fifteen patients with advanced colorectal cancer refractory to standard chemotherapies consumed capsules compatible with curcumin doses between 0.45 and 3.6 g daily for up to 4 months. Levels of curcumin and its metabolites in plasma, urine, and feces were analyzed by high-pressure liquid chromatography and mass spectrometry. Three biomarkers of the potential activity of curcumin were translated from preclinical models and measured in patient blood leukocytes: glutathione *S*-transferase activity, levels of M₁G, and PGE₂ production induced *ex vivo*. Dose-limiting toxicity was not observed. Curcumin and its glucuronide and sulfate metabolites were detected in plasma in the 10 nmol/L range and in urine. A daily dose of 3.6 g curcumin engendered 62% and 57% decreases in inducible PGE₂ production in blood samples taken 1 hour after dose on days 1 and 29, respectively, of treatment compared with levels observed immediately predose (*P* < 0.05). A daily oral dose of 3.6 g of curcumin is advocated for Phase II evaluation in the prevention or treatment of cancers outside the gastrointestinal tract. PGE₂ production in blood and target tissue may indicate biological activity. Levels of curcumin and its metabolites in the urine can be used to assess general compliance.

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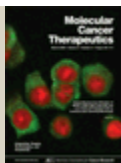
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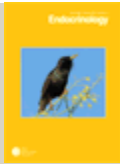
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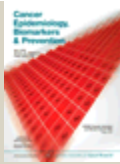
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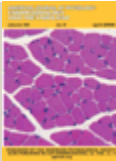
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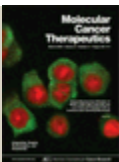
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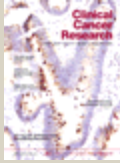
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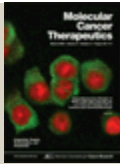
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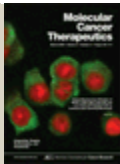
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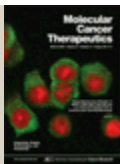
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