COMMENTS AND RESPONSES

Comment on: Ramos-Zavala et al. Effect of Diacerein on Insulin Secretion and Metabolic Control in Drug-Naïve Patients With Type 2 Diabetes: A Randomized Clinical Trial. Diabetes Care 2011;34:1591–1594

Ramos-Zavala et al. (1) described in their report the effects of diacerein, an anti-inflammatory drug used in the treatment of rheumatic diseases, on insulin secretion in patients with type 2 diabetes. They showed that diacerein induced a significant decrease in fasting glucose levels, A1C levels, tumor necrosis factor-α levels, and interleukin (IL)-1β serum levels. By using the hyperinsulinemic-euglycemic clamp, they also showed that diacerein is able to improve insulin secretion but does not modify insulin sensitivity.

Our laboratory recently investigated the antihyperglycemic effect of diacerein and the mechanisms responsible for it in an animal model of obesity and type 2 diabetes (2). Swiss mice were assigned to one of three groups as follows: those fed conventional chow, those fed a high-fat diet, and those fed a high-fat diet along with a 10-day dose of diacerein. The groups were submitted to glucose tolerance test, pyruvate tolerance test, and hyperinsulinemic-euglycemic glucose clamp, all of them associated with the evaluation of the insulin signaling and inflammatory markers that downmodulate insulin action, such as serine kinase proteins Jun NH_2-terminal kinase and IκB kinase-β (3–5). According to our experiments, an important effect of diacerein is on adipose tissue lowering macrophage infiltration, reducing cytokine production and their serum levels, and improving inflammatory pathways in the muscle and liver (endoplasmic reticulum stress, Jun NH_2-terminal kinase and IκB kinase-β, and expression of tumor necrosis factor-α, IL-1β, and IL-6). In accordance with the study by Ramos-Zavala et al. (1), a mild improvement in peripheral glucose uptake was found; however, our results also showed that the improved insulin signaling in the liver is accompanied by a reduction in hepatic glucose output and, in turn, lowers fasting plasma glucose in diabetic animals treated with diacerein. Although Ramos-Zavala et al. (1) did not measure hepatic glucose output in their study, it is possible that the reduction in fasting plasma glucose is also secondary to the reduced hepatic glucose production.

In conclusion, our data demonstrated that diacerein treatment of an animal model of type 2 diabetes is able to reduce the chronic subclinical inflammation at the cellular level in liver, muscle, and adipose tissue, and in relation to glucose metabolism, this drug induced a reduction in hepatic glucose output. These data suggest that the potential usefulness of diacerein for the treatment of type 2 diabetes is related not only to the inhibition of inflammatory cytokines but also to the improvement of hepatic glucose metabolism.

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DOI: 10.2337/dc11-1856

Acknowledgments—No potential conflicts of interest relevant to this article were reported.

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