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Phytanic acid, a natural peroxisome proliferator-activated receptor agonist, regulates glucose metabolism in rat primary hepatocytes

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ABSTRACT

Phytanic acid, a metabolite of the chlorophyll molecule, is part of the human diet and is present in normal human serum at low micromolar concentrations. It was previously shown to be a ligand of the 9-*cis*-retinoic acid receptor and peroxisome proliferator-activated receptor (PPAR) α. PPAR agonists are widely used in the treatment of type 2 diabetes. Here, we report that phytanic acid is not only a transactivator of PPARα, but it also acts via PPARβ and PPARγ in CV-1 cells that have been cotransfected with the respective full-length receptor and an acyl-CoA oxidase-PPAR-responsive element-luciferase construct. We observed that, in contrast to other fatty acids, phytanic acid at physiological concentrations enhances uptake of 2-deoxy-D-glucose in rat primary hepatocytes. This result could be explained by the increase in mRNA expression of glucose transporters-1 and -2 and glucokinase, as determined by quantitative real-time reverse transcriptase-polymerase chain reaction. Compared with the PPARγ-specific agonist ciglitazone, phytanic acid exerts only minor effects on the differentiation of C3H10T1/2 cells into mature adipocytes. These results clearly demonstrate that phytanic acid acts via different PPAR isoforms to modulate expression of genes involved in glucose metabolism, thus suggesting a potential role of phytanic acid in the management of insulin resistance.

Key words: phytol • glucose transporter • glucokinase • insulin resistance • adipocyte