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METABOLISM

Narciclasine boosts energy metabolism

A new study in *PLoS Biology* reports that narciclasine — a plant growth modulator found in some species of the Amaryllidaceae family — attenuates diet-induced obesity (DIO) in mice by promoting energy expenditure.

Narciclasine is being investigated as a potential therapeutic for several types of cancer, but some findings indicate that the compound could also affect energy metabolism. These results led Feng Xu and colleagues to investigate the effects of narciclasine on energy metabolism in mice with DIO.

The researchers fed mice a high-fat diet to induce DIO, and then administered either vehicle control or narciclasine (at 1 mg per kg body weight) once a week for 7 weeks. Narciclasine was also given to normal-weight mice fed a diet of normal chow. The body weight, lean mass and fat mass of these mice were not affected, which suggests that narciclasine does not affect mice under energy-balanced conditions, and no adverse effects were noted. By contrast, the mice with DIO that were given narciclasine exhibited reduced body weight gain and fat accumulation. Narciclasine also led to improved metabolic parameters and insulin sensitivity.

Gene expression analyses indicated that narciclasine targets the skeletal muscle, where it enhances mitochondrial respiration and fatty acid consumption. *In vitro* analyses revealed that narciclasine activates the AMP-dependent protein kinase (AMPK) signalling pathway, which has an important role in maintaining energy homeostasis, in skeletal muscle. In cultured muscle cells, narciclasine also increases mitochondrial membrane potential and reduces the production of reactive oxygen species.

"The next step of our work will be determining the direct target (or targets) of narciclasine and characterizing its potential adverse effects," concludes Xu. The researchers hope that their findings will lead to new pharmacological approaches to treat obesity in humans.

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ORIGINAL ARTICLE Julien, S. G. *et al.* Narciclasine attenuates diet-induced obesity by promoting oxidative metabolism in skeletal muscle. *PLoS Biology* **15**, e1002597 (2017)