Red wine, fruit compound could help block fat cell formation

April 4 2012, by Brian Wallheimer

Kee-Hong Kim found that piceatannol, a compound found in red wine and several fruits, blocks immature fat cells from growing. Credit: Purdue Agricultural Communication photo/Tom Campbell

(PhysOrg.com) -- A compound found in red wine, grapes and other fruits, and similar in structure to resveratrol, is able to block cellular processes that allow fat cells to develop, opening a door to a potential method to control obesity, according to a Purdue University study.

Kee-Hong Kim, an assistant professor of food science, and Jung Yeon

Kwon, a graduate student in Kim's laboratory, reported in this week's issue of the Journal of Biological Chemistry that the compound piceatannol blocks an immature fat cell's ability to develop and grow.

While similar in structure to resveratrol -- the compound found in red wine, grapes and peanuts that is thought to combat cancer, heart disease and neurodegenerative diseases -- piceatannol might be an important weapon against obesity. Resveratrol is converted to piceatannol in humans after consumption.

"Piceatannol actually alters the timing of gene expressions, gene functions and insulin action during adipogenesis, the process in which early stage fat cells become mature fat cells," Kim said. "In the presence of piceatannol, you can see delay or complete inhibition of adipogenesis."

Over a period of 10 days or more, immature fat cells, called preadipocytes, go through several stages to become mature fat cells, or adipocytes.

"These precursor cells, even though they have not accumulated lipids, have the potential to become fat cells," Kim said. "We consider that adipogenesis is an important molecular target to delay or prevent fat cell accumulation and, hopefully, body fat mass gain."

Kim found that piceatannol binds to insulin receptors of immature fat cells in the first stage of adipogenesis, blocking insulin's ability to control cell cycles and activate genes that carry out further stages of fat cell formation. Piceatannol essentially blocks the pathways necessary for immature fat cells to mature and grow.

Piceatannol is one of several compounds being studied in Kim's laboratory for its health benefits, and it is also present in different

amounts in red grape seeds and skin, blueberries, passion fruit, and other fruits.

Kim would like to confirm his current finding, which is based on a cell culture system, using an animal model of obesity. His future work would also include determining methods for protecting piceatannol from degrading so that concentrations large enough would be available in the bloodstream to stop adipogenesis or body fat gain.

"We need to work on improving the stability and solubility of piceatannol to create a biological effect," Kim said.

More information: Piceatannol, Natural Polyphenolic Stilbene, Inhibits Adipogenesis via Modulation of Mitotic Clonal Expansion and Insulin Receptor-dependent Insulin Signaling in Early Phase of Differentiation

ABSTRACT
Piceatannol, a natural stilbene, is an analog and a metabolite of resveratrol. Despite a well-documented health benefit of resveratrol in intervention of the development of obesity, the role of piceatannol in the development of adipose tissue and related diseases is unknown. Here, we sought to determine the function of piceatannol in adipogenesis and elucidate the underlying mechanism. We show that piceatannol inhibits adipogenesis of 3T3-L1 preadipocytes in a dose-dependent manner at noncytotoxic concentrations. This anti-adipogenic property of piceatannol was largely limited to the early event of adipogenesis. In the early phase of adipogenesis, piceatannol-treated preadipocytes displayed a delayed cell cycle entry into G2/M phase at 24 h after initiation of adipogenesis. Furthermore, the piceatannol-suppressed mitotic clonal expansion was accompanied by reduced activation of the insulin-signaling pathway. Piceatannol dose-dependently inhibited differentiation mixture-induced phosphorylation of insulin receptor

(IR)/insulin receptor substrate-1 (IRS-1)/Akt pathway in the early phase of adipogenesis. Moreover, we showed that piceatannol is an inhibitor of IR kinase activity and phosphatidylinositol 3-kinase (PI3K). Our kinetics study of IR further identified a Km value for ATP of 57.8 mM and a Ki value for piceatannol of 28.9 mM. We also showed that piceatannol directly binds to IR and inhibits IR kinase activity in a mixed noncompetitive manner to ATP, through which piceatannol appears to inhibit adipogenesis. Taken together, our study reveals an anti-adipogenic function of piceatannol and highlights IR and its downstream insulin signaling as novel targets for piceatannol in the early phase of adipogenesis.

Provided by Purdue University