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3,3'-Diindolylmethane suppresses high-fat diet-induced obesity through inhibiting adipogenesis of pre-adipocytes by targeting USP2 activity.

Yang H[1], Seo SG[1], Shin SH[1], Min S[1], Kang MJ[1], Yoo R[1], Kwon JY[2], Yue S[3], Kim KH[2], Cheng JX[3,4], Kim JR[5], Park JS[6], Kim JH[7], Park JHY[7], Lee HJ[1], Lee KW[1,7,8].

Author information

1 Department of Agricultural Biotechnology, Seoul National University, Seoul, Republic of Korea.
2 Department of Food Science, Purdue University, West Lafayette, IN, USA.
3 Weldon School of Biomedical Engineering, Purdue University, West Lafayette, IN, USA.
4 Department of Chemistry, Purdue University, West Lafayette, IN, USA.
5 R&D Evaluation Center, Korea Institute of Science and Technology Evaluation and Planning, Seoul, Republic of Korea.
6 Laboratory Animal Center, Daegu-GyeongBuk Medical Innovation Foundation, Daegu, Republic of Korea.
7 Research Institute of Agriculture and Life Sciences, Seoul National University, Seoul, Republic of Korea.
8 Advanced Institutes of Convergence Technology, Seoul National University, Suwon, Republic of Korea.

Abstract

SCOPE: Indole-3-carbinol (I3C), a derivative abundant in cruciferous vegetables such as cabbage, is well known for its various health benefits such as chemo-preventive and anti-obesity effects. I3C is easily metabolized to 3,3'-diindolylmethane (DIM), a more stable form, in acidic conditions of the stomach. However, the anti-obesity effect of DIM has not been investigated clearly. We sought to investigate the effect of DIM on diet-induced obesity and to elucidate its underlying mechanisms.

METHODS AND RESULTS: High-fat diet (HFD)-fed obese mouse and MDI-induced 3T3-L1 adipogenesis models were used to study the effect of DIM. We observed that the administration of DIM (50 mg/kg BW) significantly suppressed HFD-induced obesity, associated with a decrease in adipose tissue. Additionally, we observed that DIM treatment (40 and 60 μM), but not I3C treatment, significantly inhibited MDI-induced adipogenesis by reducing the levels of several adipogenic proteins such as PPAR-γ and C/EBPα. DIM, but not I3C, suppressed cell cycle progression in the G1 phase, which occurred in the early stage of adipogenesis, inducing post-translational degradation of cyclin D1 by inhibiting ubiquitin specific peptidase 2 (USP2) activities.

CONCLUSION: Our findings indicate that cruciferous vegetables, which can produce DIM as a metabolite, have the potential to prevent or treat chronic obesity.

KEYWORDS: 3,3'-Diindolylmethane; Cyclin D1; Indole-3-carbinol; Obesity; USP2 enzyme

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