

Hesperetin: A promising therapeutic for adipose tissue fibrosis in obesity

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Background: The excessive accumulation of extracellular matrix (ECM) in adipose tissue is a defining characteristic of fibrosis, which disrupts tissue homeostasis and contributes to metabolic dysfunction. Hesperetin, a flavonoid known for its anti-inflammatory, anti-obesity, and anti-diabetic effects, may also possess anti-fibrotic properties. This study investigates hesperetin's effects on ECM components and matrix metalloproteinase (MMP) enzymes involved in adipose tissue fibrosis.

Methodology: 3T3-L1 pre-adipocytes were cultured in DMEM supplemented with 10% fetal bovine serum and 1% penicillin/streptomycin. Cells were exposed to different concentrations of hesperetin, and cell viability was measured using the MTT assay. Gene expression levels of collagen VI, osteopontin, MMP2, and MMP9 were assessed using real-time PCR with specific primers. Western blotting was used to evaluate collagen VI and osteopontin protein levels.

Results: Hesperetin demonstrated a dose- and time-dependent effect on 3T3-L1 cell viability, with IC₅₀ values of 447.4 μ M, 339.2 μ M, and 258.8 μ M at 24, 48, and 72 hours, respectively. Treatment with hesperetin significantly reduced the gene and protein expression of collagen VI and osteopontin in a time- and dose-dependent manner. Additionally, hesperetin substantially downregulated the expression of MMP2 and MMP9.