Daidzein promotes osteoblast proliferation and differentiation in OCT1 cells through stimulating the activation of BMP-2/Smads pathway

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ABSTRACT. Daidzein, the most widely studied soy phytoestrogen, is not only a potential antiosteoporosis agent owing to its possible osteogenic activity, but also shows anticancer activity. However, the mechanisms through which daidzein affects osteoblast function have not been investigated thoroughly. Here, we show that daidzein stimulated cell proliferation and differentiation of osteoblasts, demonstrated by upregulation of XTT activity, enhancement of alkaline phosphatase (ALP) activity, and upregulation of osteoblast-specific marker genes, including Runx-related transcription factor 2 (Runx2) and Smad1, as well as upregulation of Runx2 and Smad1 protein expression. To determine the mechanisms underlying daidzein’s effects on osteoblast differentiation, we first tested the role of daidzein in
bone morphogenetic protein (BMP)-2 gene expression in OCT1 cells, and found that it significantly upregulated the expression of BMP-2. Furthermore, it significantly enhanced the phosphorylated protein level of Smad1/5/8 and the protein level of Osterix and increased the activity of 12xSBE-OC-Luc. Finally, we demonstrated that daidzein stimulated Col I, Runx2, and ALP expression, while these effects were significantly blocked by the BMP signaling inhibitor noggin. Together, our data indicate that daidzein acts through stimulating the activation of BMP-2/Smads pathway to promote osteoblast proliferation and differentiation.

**Key words:** Daidzein; Phytoestrogen; BMP-2; Smad; Osteoblast; Cell signaling