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# Molecular Mechanism of Quercitrin on Osteogenic Differentiation and Adipogenic Differentiation of Rat Bone Marrow Stromal Stem Cells (rBMSCs)

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**Abstract: Objective** The study was designed to investigate the molecular mechanism of quercitrin on osteogenic differentiation and adipogenic differentiation of rBMSCs. **Methods** rBMSCs were harvested from SD rats, and determination of alkaline phosphatase (ALP) activity, quantification of mineralization by Alizarin Red S staining, and the mRNA expression of osteogenic differentiation markers (Runx2, BMP-2, and OSX) by RT-PCR after rBMSCs stimulated by osteogenic induction with (0.1-10) μg/mL of quercitrin, quantification of Lipid droplet by Oil Red O staining and the mRNA expression of adipogenic differentiation marker (PPARγ, C/EBPα, and aP2) by RT-PCR after rBMSCs stimulated by adipogenic induction with (0.1-10) μg/mL of quercitrin. **Results** Quercitrin can up-regulate the mRNA expression of osteogenic differentiation markers (Runx2, BMP-2, and OSX) and increase ALP activity and mineralization after osteogenic induction, on the other hand quercitrin can suppress the mRNA expression of adipogenic differentiation markers (PPARγ, C/EBPα, and aP2) and decrease lipid droplet after adipogenic induction. **Conclusion** This study suggested that quercitrin not only stimulated osteogenic differentiation but also inhibited adipogenic differentiation of rBMSCs, which was associated with the up-regulation of Runx2, BMP-2, and OSX mRNA expression and the down-regulation of PPARγ, C/EBPα, and aP2 mRNA expression.
**Keywords:** adipogenic differentiation; quercitrin; osteogenic differentiation; rBMSCs

## 1. Introduction

Osteoporosis (OP) is a systemic metabolic bone disease that is characterized by microarchitectural deterioration, low bone mass and increased risk of fractures, which results from an increase in bone breakdown relative to bone formation (G Karsenty, 2003). Bone remodeling is regulated by several systemic hormones and growth factors (D J Hadjidakis, 2006). Bone homeostasis is maintained through interaction and balance between the bone resorption by osteoclasts and the bone formation by osteoblasts (J Pinkerton, 2014). To date, the most current strategy for treating osteoporosis is to inhibit bone resorption by osteoclasts which would create a new alternative for treating osteoporosis (T Ponnapakkam et al, 2014).

Bone Marrow Stromal Stem Cells (BMSCs) have potential multilineage differention capacity. The applying of BMSCs used to cure bone-related diseases contributes to new bone formation and corrects the imbalance of trabecular microarchitecture characteristic (A V Uihlein, 2012). Previous studies have shown that BMSCs could stimulate cartilage formation when cartilage defects of rabbits were treated by chondrogenesis of BMSCs (Koga H et al, 2008). In the normal bone marrow, BMSCs are able to differentiate into two cell types including osteoblasts and adipocytes. The balance between the two cell lines in favor of bone formation, but the relationship was disrupted in osteoporosis. Therefore, BMSCs may provide a unique model for the better understanding of early differentiation events and a potential clinical treatment that may help to enhance bone formation in osteoporosis.

In recent years, a number of substantial evidences have shown that some Chinese material medica or its components such as icariin, naringin, and poncirin can positively influence the balance between bone formation and skeleton construction (L Song et al, 2013; L Li et al, 2011; H Y Yoon et al, 2011). *Eucommia ulmoides* Oliver has been used in clinical for strengthening the bone and muscle, nourishing the liver and kidney, and treating bone injuries and bone related diseases, such as osteoporosis. Previous studies have shown that *E. ulmoides* extracts have the anti-osteoporotic effects on OVX-induced postmenopausal osteoporosis. Some major components such as rutin, quercitrin, pinoresinol diglucoside, aucubin, caffeic acid, and chlorogenic acid also have been selected from *E. ulmoides* extracts to explore the effecacy and mechanism of the anti-osteoporotic effects. The results showed that quercitrin was effective to stimulate osteoblast proliferation and differentiation. It is thought that quercitrin as the major component of *E. ulmoides* extracts may be a potential candidate for treating osteoporosis (Kim et al, 200). Although it was possible that quercitrin promotes bone formation by increasing osteoblast proliferation and differentiation, the effect of quercitrin on osteogenic differentiation and adipogenic differentiation and the underlying molecular regulation mechanism on bone formation were unknown.

Therefore, based on the potential multilineage differention capacity of BMSCs, the present study was to prove the effect of quercitrin on osteogenic differentiation and adipogenic differentiation of rBMSCs and then to investigate the molecular mechanism on osteogenic differentiation and adipogenic differentiation of quercitrin.

## 2. Materials and Methods

### 2.1 Reagents

Quercitrin (N99% purity) was provided by the Chengdu Must Bio-Technology (Chengdu, China). Fetal bovine serum (FBS) was purchased from Gibco (BRL Life Technologies). Dulbecco's modified Eagle's medium (DMEM) /Low Glucose