Xanthohumol attenuates beta-glycerophosphate-induced vascular calcification by inhibiting osteoblastic differentiation

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Background: Vascular calcification is highly correlated with cardiovascular morbidity and mortality. It is characterized by phenotype transition from vascular smooth muscles (VSMCs) to osteoblast-like cells. Xanthohumol is the most abundant prenylated flavonoid in hops. Several studies have identified the protective effects of xanthohumol on the cardiovascular and metabolic systems; however research on the effect and mechanisms of xanthohumol on vascular calcification is still quite rare. Therefore, we used beta-glycerophosphate to induce calcification in rat VSMCs to determine the effects of xanthohumol on osteoblastic differentiation and VSMCs mineralization in vitro. Methods: Incubation of VSMCs with beta-glycerophosphate for 14 days induced an osteoblast-like morphological change. The mineralization was visualized by Von Kossa and Alizarin red staining. Alkaline phosphatase activity (ALP) and calcium content were also detected. The protein expression of osteoblastic differentiation markers and signaling pathways were determined by western blot and immunofluorescence. Results: Our results showed that xanthohumol significantly attenuated the osteoblastic differentiation and mineralization of VSMCs due to decreased ALP activity, calcium content and sodium-phosphate cotransporter Pit-1, Runx2, beta-catenin, and bone morphogenetic protein-2 (BMP-2) protein expressions. Furthermore, xanthohumol inhibited beta-glycerophosphate-induced protein expressions of MMP-9 and p-ERK1/2, which are known contributors to vascular calcification. Conclusion: Xanthohumol attenuated vascular calcification by suppressing osteoblastic differentiation markers and calcification phenotype through the blockade of BMP-2/Smad1/5/8 and Wnt/beta-catenin signaling pathways. The present study will show for the first time that xanthohumol can act as a potential phytochemical in preventing or treating calcification-associated vascular diseases.