

Osthole: a natural approach to speed up bone fracture healing

Bone fractures are among the most common orthopedic problems happen to many of us. Although our body will naturally repair broken bone, the healing process takes weeks, months, or even years depending on severity of injury and complications. Even worse cases, elderly, smoker patients and patients with metabolic diseases such as osteoporosis or diabetes have much longer healing time and higher risk of developing nonunion (non-healing of the bone). Fortunately, we can make a significant augmentation during the recovery process simply by working with nature. There are many different herbal remedies for speeding bone healing including arnica, wild comfrey, boneset; and numerous effective ingredients was isolated from those herbs. Herbal therapy not only helps fracture repair but also strengthen bones and lessen the chances of bone fragility. Here we introduce another promising herb ingredient that can help to heal broken bones.

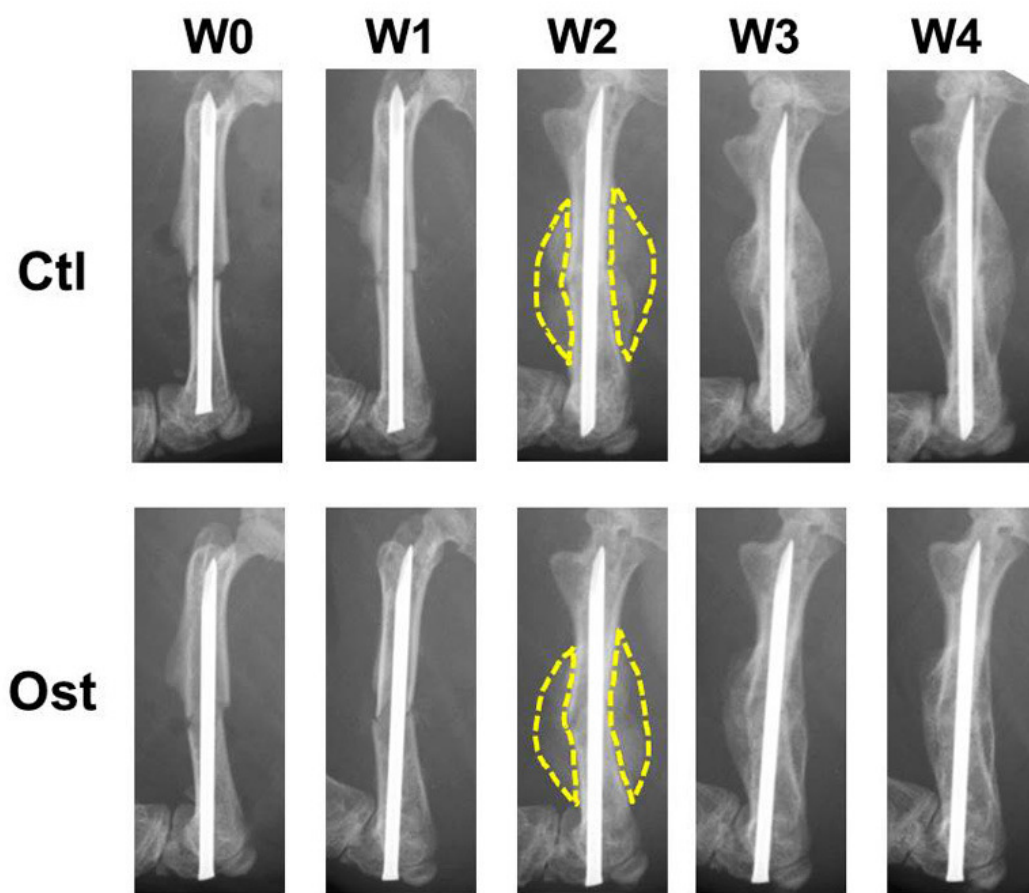


Fig. 1. Oral administration of osthole accelerated fracture healing process in mice. Mice received femur osteotomy were orally administrated with vehicle solvent or 20 mg/kg of osthole daily from postoperative week 1 to 4. Representative serial radiographs of fracture healing process in control and osthole-treated group was shown. Dotted line: Region of Interest (ROI) of callus for quantitative analysis.

Osthole is a naturally derived coumarin, which is the main bioactive compound isolated from medicinal plant *Cnidium monnieri* (L.) Cusson. This herb is commonly used as one component in herbal formulas for bone strengthening by traditional Chinese medicine practitioners. In this study, we investigated the effect of osthole on bone fracture repair using femoral open fracture model in mice. A transverse fracture was created at the middle of femur with saw. Operated mice were given with 20 mg/kg osthole solution or solvent alone by oral gavage every day since postoperative week 1. Bone healing process of both groups was assessed by commonly used techniques like plain radiography, micro-computed tomography, histology analysis as well as molecular imaging showing bone regeneration.

Fracture healing can be divided into three stages including inflammation phase, reparative phase and remodeling. During reparative phase, fracture ends are firstly joined together by soft (fibrocartilage) callus, and then the soft tissues are calcified into woven bone from periphery of callus into central fracture site and form a more mechanically resistant hard (bony) callus. Finally, low mineral density woven bone is gradually remodeled into highly dense cortical bone during remodeling phase. Through in vivo (in living animals) radiographic and molecular imaging results and ex vivo (outside living animals) micro-computed tomography, histological results, we found that the bony callus formation was significantly faster and the whole reparative phase was much shorter in osthole fed mice. Plain radiography allowed monitoring callus morphology in living mouse during fracture repair. As shown in the figure, clear callus contour could be defined from week 2, quantitative analysis of region of interest (ROI) of callus estimated the size and mineral content in callus. In osthole-treated group, and the bone content in callus at week 2 was significantly higher than that in control group. Moreover the callus size at week 3 was apparently reduced compared to size at week 2, which was much smaller than control, suggesting transition from reparative phase to remodeling phase.

In summary, oral intake of osthole promotes bone formation during reparative phase and hence accelerates the whole bone fracture healing process. Osthole may be another promising natural supplement that facilitates bone healing and benefits bone health.

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