

Mushroom Extracts Decrease Bone Resorption and Improve Bone Formation

Igor Erjavec,¹ Jelena Brkljacic,¹ Slobodan Vukicevic,¹ Boris Jakopovic,² & Ivan Jakopovich^{2,*}

¹Laboratory for Mineralized Tissues, University of Zagreb School of Medicine, Zagreb, Croatia; ²Dr Myko San, Zagreb, Croatia

*Address all correspondence to: Ivan Jakopovich, Dr Myko San, Miramarska 109, 10000 Zagreb, Croatia; ivan.jakopovic@inet.hr

ABSTRACT: Mushroom extracts have shown promising effects in the treatment of cancer and various chronic diseases. Osteoporosis is considered one of the most widespread chronic diseases, for which currently available therapies show mixed results. In this research we investigated the *in vitro* effects of water extracts of the culinary-medicinal mushrooms *Trametes versicolor*, *Grifola frondosa*, *Lentinus edodes*, and *Pleurotus ostreatus* on a MC3T3-E1 mouse osteoblast-like cell line, primary rat osteoblasts, and primary rat osteoclasts. In an animal osteoporosis model, rats were ovariectomized and then fed 2 mushroom blends of *G. frondosa* and *L. edodes* for 42 days. Bone loss was monitored using densitometry (dual-energy X-ray absorptiometry) and micro computed tomography. In the concentration test, mushroom extracts showed no toxic effect on MC3T3-E1 cells; a dose of 24 µg/mL showed the most proliferative effect. Mushroom extracts of *T. versicolor*, *G. frondosa*, and *L. edodes* inhibited osteoclast activity, whereas the extract of *L. edodes* increased osteoblast mineralization and the production of osteocalcin, a specific osteoblastic marker. In animals, mushroom extracts did not prevent trabecular bone loss in the long bones. However, we show for the first time that the treatment with a combination of extracts from *L. edodes* and *G. frondosa* significantly reduced trabecular bone loss at the lumbar spine. Inhibitory properties of extracts from *L. edodes* on osteoclasts and the promotion of osteoblasts *in vitro*, together with the potential to decrease lumbar spine bone loss in an animal osteoporosis model, indicate that medicinal mushroom extracts can be considered as a preventive treatment and/or a supplement to pharmacotherapy to enhance its effectiveness and ameliorate its harmful side effects.

KEY WORDS: biological drug, bone formation, bone resorption, *Grifola frondosa*, *Lentinus edodes*, mushroom β-glucan dietary supplement, osteogenic, postmenopausal osteoporosis

ABBREVIATIONS: ALP, alkaline phosphatase; BMD, bone mineral density; BV/TV, bone volume-to-tissue volume ratio; CT, computed tomography; diH₂O, deionized water; DXA, dual-energy x-ray absorptiometry; FBS, fetal bovine serum; GF, *Grifola frondosa*; LE, *Lentinus edodes*; OVX, ovariectomy; PBS, phosphate-buffered saline; PO, *Pleurotus ostreatus*; TRAP, tartrate-resistant acid phosphatase; TV, *Trametes versicolor*