**In vivo** effects of high-dose methotrexate on bone remodeling in rats

Urszula Cegiela, Leszek Śliwiński, Ilona Kaczmarczyk-Sedlak, Joanna Folwarczna

Department of Pharmacology, Silesian Medical University, Jagiellonska 4, PL 41-200 Sosnowiec, Poland

**Correspondence:** Urszula Cegiela

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**Abstract:**
Methotrexate (MTX) is a folic antagonist. MTX osteopathy is well recognized to accompany a high-dose therapy with this drug for the treatment of childhood malignancy. Clinical tests also show that low-dose MTX used in the treatment of rheumatoid arthritis may impair bone formation in a population already predisposed to osteoporosis. However, results of clinical tests are hard to interpret, as it is necessary to take into account malignancy-induced changes in the osseous tissue, long-term immobility and concurrent administration of glucocorticosteroids.

We conducted *in vivo* tests to evaluate the effects of oral and intramuscular administration of high dose of MTX on bone remodeling processes in rats. Effects of MTX on the processes of bone remodeling were evaluated by assessing macrometric and histomorphometric parameters as well as mechanical properties of the femur.

The tests were carried out on male Wistar rats. Animals were divided into four groups, composed of 7 animals each: Control group (0.9% NaCl solution), MTX-1po group (MTX at the dose of 1 mg/kg *po* daily for 10 days; every day for the first five days, and after an 18-day interval, every day for five days), MTX-1im group (MTX at the dose of 1 mg/kg *im* daily for 10 days; every day for the first five days, and after an 18-day interval, every day for five days), MTX-5im group (MTX at the dose 5 mg/kg *im* daily for 2 days a week for the period of four weeks). Changes in bone remodeling were examined 4 weeks after the first MTX administration.

These results show that MTX administered intramuscularly at high doses inhibited the formation and mineralization of new osseous matrix and impaired mechanical properties of the femoral bone, whereas its oral administration had no effect on bone remodeling in rats.

**Key words:** methotrexate, macrometric parameters, histomorphometric parameters, mechanical properties of the femur, bones, rats