

# Effects of silicon on bone

## Clinical observations and experimental cell studies

Akademisk avhandling

Som för avläggande av odontologie doktorsexamen vid Sahlgrenska akademien, Göteborgs universitet kommer att offentligens försvaras i Hörsal Arvid Carlsson, Academicum, Medicinaregatan 3, Göteborg, den 8 september 2023, klockan 9:00

av Catarina Magnusson

Fakultetsopponent:

Professor Göran Andersson, Karolinska Institutet, Sverige

### Avhandlingen baseras på följande delarbeten

- I. **Magnusson C.**, Uribe P., Jugdaohsingh R., Powell J.J., Johansson A., Ransjö M. Inhibitory effects of orthosilicic acid on osteoclastogenesis in RANKL-stimulated RAW264.7 cells *Journal of Biomedical Materials Research Part A*, 2021; 109(10):1967–1978.
- II. **Magnusson C.**, Malmberg P., Jugdaohsingh R., Kinrade S., Powell J.J., Uribe P., Ransjö M. Transmembrane passage of silicon into osteoblast and osteoclast precursors *Manuscript to be submitted*.
- III. **Magnusson C.**, Ransjö M. Orthosilicic acid inhibits human osteoclast differentiation and bone resorption *Manuscript to be submitted*.
- IV. **Magnusson C.**, Jugdaohsingh R., Hulten L., Westerlund A., Powell J.J., Ransjö M. Urinary excretion of silicon in men, non-pregnant women, and pregnant women: a cross-sectional study *Biological Trace Element Research*, 2020; 194(2):321-327
- V. **Magnusson C.**, Augustin H., Jugdaohsingh R., Powell J.J., Hulthen L., Ransjö M. Urinary silicon excretion in relation to lactation and bone mineral density - a longitudinal study post-partum *Manuscript to be submitted*.

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### **Abstract**

Bone health has a major impact on life quality. In Sweden, osteoporosis is a highly prevalent skeletal disease that primarily affects the elderly, causing fragility fractures and pain. Local pathological bone defects due to trauma, infectious (such as periodontitis) or malignant (such as osteosarcoma and bone metastases) diseases, and congenital abnormalities, may need to be corrected for optimal skeletal function.

Silicon (Si), which is a trace element found in beverages and plant-based food, is suggested to promote bone health. Silicon is also a constituent of some bone-substitute materials and the release of Si is suggested to contribute to bone regeneration. In line with this, experimental studies have demonstrated direct stimulatory effects of Si on osteoblast differentiation and function, whereas only a few studies have examined the effects of Si on osteoclasts.

Knowledge regarding the effects of Si on osteoclasts and the regulatory mechanisms of bone cells is currently limited. Thus, the aims of this thesis were to study these aspects further. As reports on Si metabolism among different population groups are scarce, this thesis also aimed to describe Si excretion in relation to gender, pregnancy, and lactation, together with considering the aspects of bone changes in the latter two conditions.

In **Paper I**, the direct effects of Si at different time-points on osteoclast differentiation in a murine macrophage cell line were investigated. In **Paper II**, we examined whether there is transmembrane passage of Si in bone cell precursors, and if the expression of genes for potential Si-transport proteins is regulated. In **Paper III**, the effects of Si were further investigated with regards to human osteoclast differentiation and bone resorption. In **Paper IV**, the 24-hour urinary Si excretion levels were compared between men, non-pregnant women, and pregnant women. In **Paper V**, the levels of Si in spot-urine samples were longitudinally measured from late pregnancy to 18 months post-partum, and compared in relation to lactation length and bone mineral density changes.

The results of the experimental cell studies in this thesis demonstrate a direct inhibitory effect of Si on early osteoclast differentiation and, thereby, inhibition of bone resorption. Here, it is demonstrated that there is transmembrane passage of Si into bone cell precursors, and that Si regulates the expression of the gene encoding aquaporin9, which potentially mediates the passage. Furthermore, the results of the observational studies show that pregnant women excrete higher levels of Si in the urine than men or non-pregnant women. The Si excretion increases post-partum in women who are lactating for 4 months or longer, but are not related to changes in bone mineral density.

This thesis supports that Si has beneficial effects on bone, and describes urinary Si excretion in sub-populations that have never been studied before.

**Keywords:** silicon, osteoclast, pregnancy, lactation, bone metabolism, bone regeneration  
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