# T50 NEWSLETTER

OCTOBER 2022

# Growing evidence that phosphate toxicity is caused by calciprotein particles (CPP)

Chronic kidney disease (CKD) is associated with high rates of cardiovascular (CV) events. Elevated plasma concentrations of phosphate have long been considered causal for phosphate toxicity.

In recent years however, accumulating evidence indicates, that not soluble phosphate, but rather crystalline (calcium) phosphate in the form of circulating calciprotein particles (CPP), causes phosphate toxicity. CPP are part of the physiological calcium phosphate transportation and clearance system of the body.

**Intake of 2000 mg/day sucroferric oxyhydroxide led to:**

Lowering of serum phosphate by 0.65 mmol/l (2.28→1.63 mmol/l)[1]

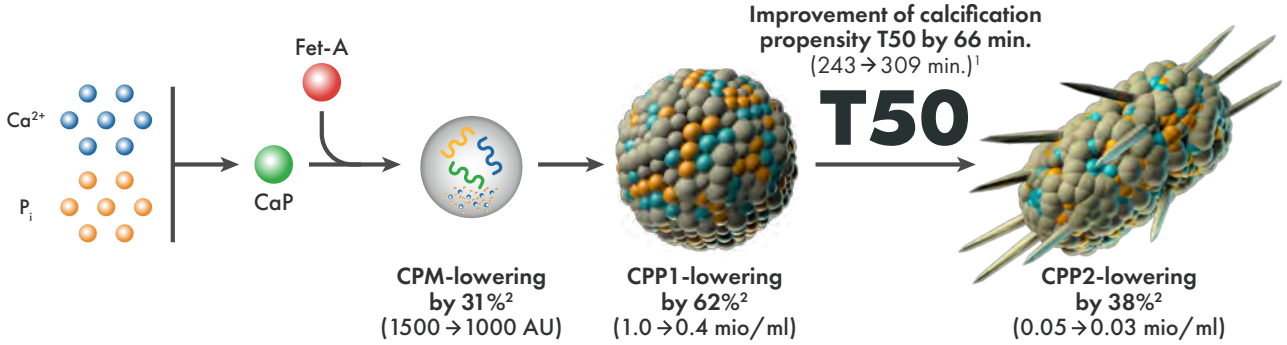


**Figure 1:** Schematic illustration of the results from two studies[1,2] performed with the same patient samples.

Professor E. Smith from Melbourne, Australia, together with colleagues from Linz, Austria, studied the impact of sucroferric oxyhydroxide (SO, Velphoro®), a strong phosphate binder, on CPP formation in 28 dialysis patients[2].

They found that the use of SO reduced calciprotein monomers (CPM) by 31% ($p<0.01$), CPP1 by 62% ($p<0.0001$) and CPP2 by 38% ($p<0.001$), when compared to washout. Interleukin-6 (IL-6) and IL-8 were consistently reduced in serum from SO-treated patients. Furthermore, serum from SO-treated patients induced reduced calcification and IL-6 and IL-8 in vitro. The removal of the CPP-containing fraction from serum led to the amelioration of calcification and inflammatory markers in vitro.

According to the authors, «this is the first clinical trial in hemodialysis patients showing that phosphate binder therapy [...] lowered serum levels of CPM, CPP1, and CPP2 and was associated with immunomodulatory effects.»

[1] The effect of phosphate binder therapy with sucroferric oxyhydroxide on calcification propensity in chronic haemodialysis patients: a randomized, controlled, crossover trial. Thiem, U, Soellradl, I, Robl, B, Watorek, E, Blum, S, Dumfarth, A, Marculescu, R, Pasch, A, Haller, MC, Cejka, D. Clin Kidney J. 2021

[2] Effect of the phosphate binder sucroferric oxyhydroxide in dialysis patients on endogenous calciprotein particles, inflammation, and vascular cells. Thiem, U, Hewitson, TD, Toussaint, ND, Holt, SG, Haller, MC, Pasch, A, Cejka, D, Smith, ER. Nephrol Dial Transplant. 2022 Sep 15

**Commentary by Prof. Andreas Pasch:**

**This study[2] adds to the growing evidence about the physiological CPP system and it's high relevance in (renal) medicine. A standard clinical intervention led to CPP-lowering and the amelioration of inflammation. The in vitro data add exciting evidence, that CPP are indeed the carriers of phosphate toxicity. Of note, the therapeutic intervention, also had a profound impact on *T50 calcification propensity*[1], which measures the formation of CPP2 in a patient blood sample in vitro.**

The T50 Newsletter presents News concerning T50, CPP and Calciscon to the interested medical, scientific and business community.

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