

Inhibitory effects of calcium binding to glycosaminoglycans: An isothermal titration calorimetry and chemical speciation study

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Introduction: Glycosaminoglycans such as chondroitin sulfate A (CSA) have been shown to be inhibitors of calcium oxalate (CaOx) crystallization by forming complexes with calcium (Ca)¹. Application of speciation modelling using computer programs such as EQUIL and JESS in stone formation studies is essential for understanding crystallization. The aim of the study was to experimentally determine the formation constants of CSA-Ca complexes and to use them in computer simulations to model chemical speciation of salts with a view to investigating whether CSA forms complexes with Ca, thereby affecting the saturation index (SI) of Ca-containing salts.

Method: The interactions of the CSA disaccharide unit binding with Ca were measured using isothermal titration calorimetry (MiCroCal iTC 200, GE Healthcare) at 37 °C in solutions prepared with 0.137 M ionic strength. A mean log *K* value of 1.42 was obtained and it was added to the JESS database and a CSA concentration of 0.086 mM was used for the modelling². Urinary parameters from healthy subjects were used to calculate the saturation index (SI values) of salts and for investigating the chemical speciation at different CSA concentrations using JESS.

Results: The free Ca concentration decreased by a small amount (1.22×10^{-3} to 1.13×10^{-3} mol/L) when the concentration of CSA was increased by a factor of 100. There was a concomitant small decrease in SI values for the CaOx and Ca phosphate species (Table 1).

Table 1. SI values of salts at different CSA concentrations

Salt	1x CSA	2x CSA	10x CSA	100x CSA
Bru	1.53	1.53	1.52	1.43
COT	2.33	2.32	2.31	2.17
CaOx	5.36	5.36	5.32	4.99
COM	4.54	4.54	4.51	4.23
COD	1.71	1.70	1.69	1.59
OCP	41.4	41.2	40.3	31.1
HAP	1.60×10^6	1.50×10^6	1.55×10^6	1.12×10^6
triCaP	1.85	1.85	1.81	1.49

Conclusion: The present modelling exercise demonstrates that urinary Ca forms a complex with CSA which influences SI values of Ca salts. However, this effect is strongly dependent on concentration. It is noted that the concentration of CSA has been reported in only one paper². This concentration was increased by a factor of 100 for the present project. We speculate that if this concentration has been underestimated, possibly because it is derived from the value of uronic acid, bigger decreases in SI values might occur.

References:

1. Cao LC, et al, 1997. Urology 50(2): 173–83.
2. Shum DKY and Gohel MDI, 1993. Clinical Science 85: 33–39.