What are systemic sclerosis-related calcinoses made of and can we dissolve them?

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Background

Approximately 25- 40% of patients with systemic sclerosis will develop calcinosis, with the knees, elbows and fingertips being commonly affected (Figure 1). There is limited information in the literature on the composition of calcinotic lumps, and few methods of treatment apart from surgical excision.

Figure 1. X-ray (left) and photo (right) of calcinosis

Aim

The aim of this research was to provide a complete study of the structure and composition of calcinotic lumps associated with systemic sclerosis, using a variety of analytical techniques, and to investigate a variety of compounds able to break them down.

Methods

The calcinotic deposits used in the study had either extruded spontaneously or were surgically removed.

Micro-computed tomography (XCT), thermal (TGA), powder x-ray diffraction (PXRD), elemental, electron microscopy (SEM) and infra-red (IR) analyses were carried out to determine the elemental composition and internal structure of the deposits.

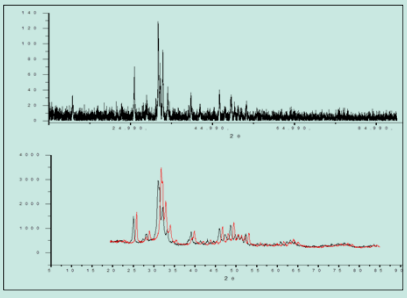

Figure 2. Powder X-ray diffraction patterns of hydroxyapatite (top) and two calcinosis samples (bottom) for comparison, showing almost identical patterns. This indicates the samples are composed of hydroxyapatite

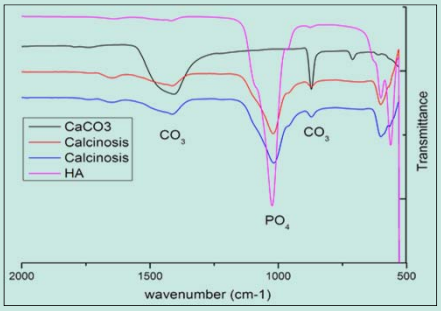

Figure 3. Infra-red spectra of calcinoses, compared to hydroxyapatite and calcium carbonate. The peaks from the calcinosis correspond to hydroxyapatite and $CaCO_3$

For dissolution studies, samples were covered with a solution of the desired reagent and sonicated. The amount of calcium taken up by the solution was measured by elemental analysis.

Results

Hydroxyapatite ($Ca_{10}(PO_4)_6(OH)_2$) was the main component of the four samples examined (as seen by PXRD, Figure 2). The presence of carbonate was confirmed by IR and TGA studies (Figure 3). The internal composition of these deposits was probed by XCT (Figure 4) and SEM (Figure 5), which show that the samples have very different structures, despite having similar elemental compositions. This is especially shown in Figure 4, where the sample on the right is visibly more porous than that on the left.

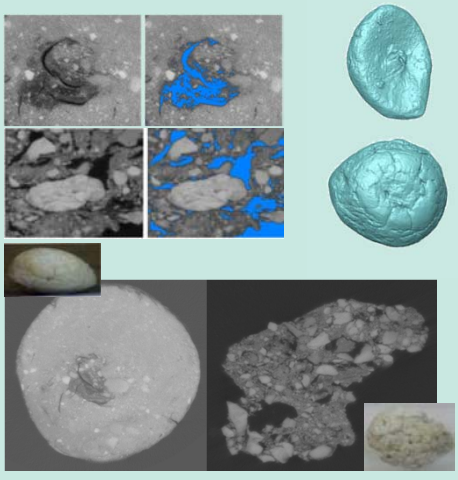

Figure 4. Reconstructed 3D XCT image of a calcinosis sample (top right) and photographs (insets) of two samples of calcinosis and corresponding computed tomography images (bottom). XCT images showing the pores present in the calcinoses and highlighted in blue are also shown (top left)

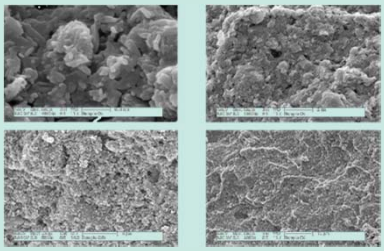

Figure 5. Scanning Electron Microscopy images of calcinoses at 2, 5, 10 and 40 x10^{-3} magnifications (r-l, bottom to top). Crystals can be seen at the highest magnifications.

The images taken were reconstructed into images showing the surface features of the deposit using XCT, as also seen in Figure 4.

The dissolution screening indicated that picolinic and citric acid and selected aminocarboxylate calcium chelators were most effective at breaking down or dissolving the deposits. This is shown in Figure 6.

Figure 6. Calcinosis samples used to investigate dissolution after sonication. Left: control with water and calcinosis intact, right: test compound dissolved in water shows calcinosis sample broken down into fine powder.

Conclusions

Calcinotic deposits were found to consist of hydroxyapatite with a carbonated component. Citric and picolinic acids and aminocarboxylate analogues were identified as potential compounds for treating calcinosis.

Acknowledgements

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