Preparation of Copper-Doped Hydroxyapatite with Varying \( x \) in the Composition \( \text{Ca}_{10}(\text{PO}_4)_6\text{Cu}_x\text{O}_y\text{H}_z \)

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Preparation of materials

Calcium hydrogen phosphate (CaHPO₄, Acros, 97%), calcium carbonate (CaCO₃, Sigma-Aldrich, ACS reagent) and copper (II) oxide (CuO, Aldrich, 99.99% trace metals basis) were thoroughly homogenised with a pestle and mortar. Powders were pressed into discs and heated in a furnace at 1100°C. Copper-containing mixtures were heated for 24 h, quenched in air, ground up and re-pelletized, and heated again for 2 h before quenching in air to give the final product. The copper-free composition was heated for two periods of 24 h to give a pure phase product, slow-cooling to room temperature at 2.5°C/min and then the mixture was heated again for 2 h before quenching in air to give the final product. Copper-containing mixtures were heated for 24 h, quenched in air, ground up and re-pelletized, and heated again for 2 h before quenching in air to give the final product.

Characterisation of materials

Powder X-ray diffraction patterns were collected from 5-100° 2\( ^\circ \) with a step size of 0.02° and time per step of 10 s, using Cu K\( ^{\alpha} \) radiation in a Siemens D5000 X-ray diffractometer operating at 40 kV and 25 mA. Rietveld analysis of the collected data was performed using TOPAS-Academic software. Fourier-transform infrared spectra of the product powders as KBr discs (0.002 g of sample diluted with 0.198 g spectroscopic grade KBr) were recorded using a Nicolet Nexus FT-IR spectrometer equipped with a DTGS detector, resolution 4.0 cm\(^{-1}\), over the range 4000-400 cm\(^{-1}\), with 256 scans. Diffuse reflectance UV-visible spectra of the powders were recorded with respect to BaSO₄ as a reference in a Varian Cary 50 UV-visible spectrometer.

Results and Discussion

Powder X-ray diffraction (PXRD)

The synthesised materials were pure-phase apatite by PXRD.
The nominal formula \( \text{Ca}_{10}(\text{PO}_4)_6\text{Cu}_x\text{O}_y\text{H}_z \). Table 1:

| \( x \) | \( a=b \) (Å) | \( c \) (Å) | \( V \) (Å³) |
|---|---|---|---|
| 0  | 9.423(2) | 6.685(2) | 529.4(3) |
| 0.5 | 9.427(3) | 6.907(3) | 531.6(4) |
| 0.75 | 9.439(3) | 6.924(3) | 534.2(4) |
| 1  | 9.448(6) | 6.938(5) | 536.4(8) |

Figure 1. As the doped amount of Cu was increased, both \( a \) and \( c \) lattice parameters (Table 1) increased. This confirmed the substitution of Cu for a (much smaller) proton on the OH lattice site. The structural expansion was in agreement with results in the literature for similarly doped calcium, barium and strontium apatite materials [4-8].

**Fourier-transform infrared (FT-IR) spectroscopy**

FT-IR spectra (Figure 2) showed phosphate bands typical of hydroxyapatite. The presence of Cu-O species was confirmed by a band at 771-778 cm\(^{-1}\), most obvious in the spectrum of the hydroxyapatite. The presence of Cu-O species was confirmed by a band at 771-778 cm\(^{-1}\) assigned to a Cu-O stretch characteristic of Cu\(^{+}\) and with decreasing intensity of the OH stretch (3572 cm\(^{-1}\)) and the OH libration (631 cm\(^{-1}\)) bands upon Cu doping. Bands related to OH stretches disturbed by nearby Cu [5] were observed between 3100 and 3500 cm\(^{-1}\).

**UV-visible diffuse reflectance spectroscopy**

The presence of Cu\(^{2+}\) in the Cu-doped samples was confirmed by UV-visible spectra (Figure 3), which showed three bands at 419, 515 and 774 nm. The bands at 515 and 774 nm are in good agreement with those attributed by Kazin [6] to d-d transitions in linearly coordinated Cu\(^{2+}\). The band at 419 nm could be a charge transition due to Cu\(^{2+}\) in another site, as proposed by Kazin with regard to a band observed at 450 nm [6].

**Conclusions**

Cu-doped hydroxyapatites with \( x = 0, 0.5, 0.75 \) and 1 in the nominal formula \( \text{Ca}_x(\text{PO}_4)_6\text{Cu}_y\text{O}_z\text{H}_t \) were successfully prepared by a solid state method. PXRD confirmed the phase purity of the materials. Rietveld analysis showed an increase in unit cell volume with increasing Cu content, which confirmed the substitution of Cu onto the OH sites in the hexagonal channels of the apatite structure. FT-IR spectra confirmed the presence of Cu-O species on the OH sites, with a band at 771-778 cm\(^{-1}\) assigned to a Cu-O stretch characteristic of Cu\(^{+}\) and with decreasing intensity of the OH stretch (3572 cm\(^{-1}\)) and the OH libration (631 cm\(^{-1}\)) bands as \( x \) was increased. Bands related to OH stretches disturbed by nearby Cu were observed between 3140 and 3500 cm\(^{-1}\). UV-Vis spectra showed bands assignable to d-d transitions of Cu\(^{2+}\). Therefore we propose that Cu is present in these materials as both Cu\(^{+}\) and Cu\(^{2+}\), which could have implications for the bioactivity of the materials due to the general insolubility of Cu\(^{2+}\) salts. The obvious presence of Cu ions in two valence states, but lack of quantitative information as to the proportions of these, meant that the proportions of O and H ions (and possibly vacancies) necessary for charge balance were not determined. Thus the non-specific formula of \( \text{Ca}_x(\text{PO}_4)_6\text{Cu}_y\text{O}_z\text{H}_t \) as proposed by Baikie et al. for these materials [8], was used throughout this work.

**Acknowledgement**

This work was supported by a studentship from the BBSRC.

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