A self-hardening biodegradable cement as a drug delivery vehicle

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INTRODUCTION: Injectable, resorbable cements are commonly studied for bone repair, but rarely considered as vehicles for sustained drug release in tissues other than bone. In this study, a self-hardening biodegradable calcium carbonate cement containing the drug hydroxyflutamide was developed. Hydroxyflutamide is used for treatment of pancreas cancer, which is a possible indication for this drug delivery system. Drug release measurements showed a sustained release of the drug for several days.

METHODS: A cement precursor of vaterite phase calcium carbonate was prepared according to a method first descried by Buzágh [1].

First the calcium carbonate powder was prepared as follows. Calcium hydroxide was dispersed in methanol. During stirring, carbon dioxide was bubbled through the dispersion until all of the calcium hydroxide had reacted and formed a gel. When the gel was subsequently dried in air at 70 °C a white powder was obtained. The powder was then stored in a nitrogen atmosphere at 5 ° C. Secondly the cement was prepared by mixing of the calcium carbonate powder with a PBS solution and 10 wt % of the model drug, hydroxyflutamide. The cement was then put into rubber moulds and left to cure at 37 °C and 100 % humidity.

Compression tests were performed on cured cement to evaluate the mechanical strength. The tests were performed on 6 x 12 mm rods after 24 and 48 hours. The chemical compositions of the samples were studied by means of X-ray diffraction analysis. Furthermore, the drug elution properties of the cement were measured with a dissolution tester and UV-absorption analysis. The elution was carried out in deionized water at 37 °C on 3 x 6 mm cylinder shaped samples.

RESULTS: X-ray diffraction analysis of the synthesized calcium carbonate powder indicates that it consisted of vaterite, calcite and amorphous calcium carbonate (ACC). 24H after the same powder was mixed with PBS, cured at 100 % humidity at 37 °C, the vaterite and ACC had transformed into aragonite.

The result from the drug elution measurements is presented in figure 1. 80 % of the drug had been released after four days and 100 % had been released after 11 days.

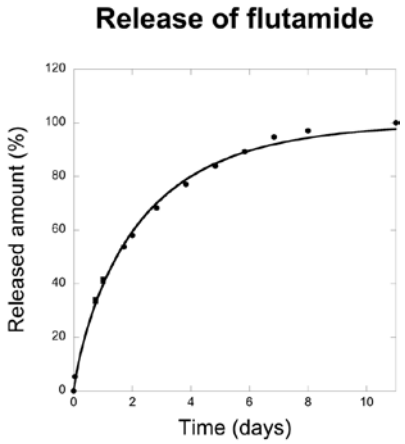

Fig. 1: Release of flutamide in deionized water at 37 °C.

The compression strength of the cement without hydroxyflutamide was 3.1 MPa (std 0.4 MPa) after 24H and 3.3 MPa (std 0.9 MPa) after 48H. With 10 wt % of hydroxyflutamide in the cement the compression strength was measured to be 1.9 MPa (std 0.6 MPa)

DISCUSSION & CONCLUSIONS: The results from this study prove the possibility of using biodegradable calcium carbonate cement as a drug-eluting vehicle. Further studies are needed to determine the setting time of the cement in order to show that the cement can function in an injectable drug delivery system. The drug elution properties are however very promising for such an application.

REFERENCES: [1]A. Buzágh (1926) *Kolloid-Zeitschrift* **38**:222-26.