

Quantification of Iodine in Porous Hydroxyapatite Matrices for Application as Radioactive Sources in Brachytherapy

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ABSTRACT

In this study, non-radioactive iodine was incorporated in two types of biodegradable hydroxyapatite-based porous matrices (HA and HACL) through impregnation process from sodium iodine aqueous solutions with varying concentrations (0.5 and 1.0 mol/L). The results revealed that both systems presented a high capacity of incorporating iodine into their matrices. The quantity of incorporated iodine was measured through Neutron Activation Analysis (NAA). The porous ceramic matrices based on hydroxyapatite demonstrated a great potential for uses in low dose rate (LDR) brachytherapy.

Key words: Hydroxyapatite, brachytherapy, neutron activation analysis (NAA)

INTRODUCTION

One of the fastest developing areas in biomaterials is the preparation of ceramic matrices based on calcium phosphate aiming at their biocompatibility, physico-chemical, and microstructural and mechanical properties similar to those of hard tissues (Hsu, 2002; Ivanova et al., 2001). Calcium hydroxyapatite (HAp), $\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2$, the main calcium phosphate constituent of bone and tooth tissues, have been investigated targeting their potential application as implant materials (Kinari & Gross, 2004; Milev et al., 2003; Silva et al., 2001), controlled drug delivery (Barralet et al., 2004; Itokazu et al., 1998), brachytherapy radioactive sources (IBT Technology Partners, 1997; Nath et al., 1997; Focal Inc., 1997), and tissue engineering (Chen et al., 2004).

One of the applications of the materials is as brachytherapeutic sources for the treatment of cancer. The code for the practice of medical physics and the clinical procedure of brachytherapy (Nath et al., 1997) deals with the use of small radioactive sources for in situ treatment of cancer in several body sites such as the brain, neck, uterus colon, endometrium, and prostate. The advantages of brachytherapy relative to external beam therapy (teletherapy) are several. The location of the dose in the tumor, the dose gradients around the implant, and the homogeneity of the dose within the tumor are better than those of teletherapy. Contrary to fractionated teletherapy, in low dose brachytherapy (LDR - low-dose rate), radiation is continuously applied for a longer period and the doses are between 0.4 and 0.8 Gy/h. In this work, the nuclear analytical technique of neutron activation analysis was used to quantify

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iodine incorporated in hydroxyapatite biodegradable porous matrices for application as radioactive sources in the treatment of cancer tumors by brachytherapy. The quantification of iodine would afford the characterization of the porous matrices for brachytherapy. The values of iodine determined by NAA were used to compare the activity of porous ceramic sources with those of commercial metal seeds used in brachytherapy. The neutron activation (NA) process consists of exposing a sample to a neutron flux in which the reaction (n,γ) produces a radioactive nuclide (Lieser, 1997). The energy of the radioactive emission allows the identification of the element and the intensity of emission is proportional to the mass of that element. This nuclear method enables to identify and analyze the composition of trace elements in samples of a large variety of materials (Skoog et al., 2002) aiming applications in areas of environmental biotechnology, foods, geology, and material sciences.

MATERIALS AND METHODS

Hydroxyapatite matrices preparation

Porous hydroxyapatite matrices were prepared using synthetic and commercial hydroxyapatite powders. The synthetic powder (HA) was obtained by a co-precipitative route (Lacerda, 2005). The commercial powder (HACL) was purchased from Vetec Química Fina Ltda. Both powders were uniaxially pressed in a hydraulic press with floating cylindrical matrix ($\varnothing = 8.1$ mm) at 100 MPa. The ceramic matrices were sintered in air at 900° C for 1 h. The physico-chemical and microstructural characteristics of the powders and ceramic matrices are presented in Table 1 (Lacerda, 2005).

Sodium iodine solutions preparation

Iodine solutions were prepared in different concentrations, ranging from 0.5 to 1.0 mol.L⁻¹.

Table 1- Experimental data of synthetic powder (HA) and commercial powder (HACL) matrices

Samples	ρ PI(g.m ⁻³)	ρ G(g.m ⁻³)	OP (%)	TP (%)
HA	1.41±0.05 ⁽¹⁾	1.36±0.01 ⁽¹⁾	53.60±0.20 ⁽¹⁾	55.30±1.35 ⁽¹⁾
HACL	1.44±0.01 ⁽¹⁾	1.41±0.01 ⁽¹⁾	52.60±0.51 ⁽¹⁾	54.40±0.50 ⁽¹⁾

ρ PI – Density, penetration and immersion method; ρ G – geometric density; OP – Open porosity; TP – Total porosity ⁽¹⁾
Confidence level = 95%.

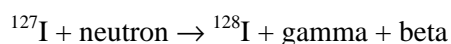
Impregnations solutions were prepared with iodine salt NaI (Riedel De Haen AG Seelze Hanwoven) and deionised water under manual stirring until complete dissolution of the salt. Solution pH was corrected to 12 with NaOH (F. Maia Indústria e Comércio Ltda) (Amersham Biosciences Limited, 2002; Instituto de Pesquisa Energéticas e Nucleares, 2005). The remaining solutions were used to incorporate iodine to the ceramic matrices.

Hydroxyapatite matrices impregnation

The matrices were placed into an oven (FANEM model ORION 515) for 1 h at 120° C, followed by cooling under vacuum ranging from 10⁻¹ to 10⁻² torr for 15 minutes. Next, the dry matrix mass was determined. The matrices were kept under vacuum for 2 h in an appropriate container until impregnation. Impregnation was carried out by immersing the ceramic matrices into the desired iodine solution. After 2 hours rest in the solution, the masses of the impregnated matrices were determined again.

Irradiation procedure of the impregnated hydroxyapatite matrices

The TRIGA MARK I IPR-R1 nuclear research reactor located at the CDTN/CNEN (Nuclear Technology Development Centre), Belo Horizonte, was used to irradiate the impregnated matrices. The samples were conditioned in polyethylene tubes and were irradiated with iodine standards. Both samples and iodine standards were irradiated for 5 minutes in the rotary rack facility, at 100 kW, under thermal neutron flux 6.6 x 10¹¹ neutrons.cm⁻².s⁻¹. During the irradiation, the following reaction took place:



Iodine counting of the irradiated hydroxyapatite matrices

The induced radioactivity was measured by gamma-ray spectrometry after 2-h decay time. Each sample was counted for 200 seconds using a

gamma counter system consisted of a HPGe detector (CANBERRA, model GC5019, nominal efficiency 50% and resolution of 1.9 keV for 1332 keV of ^{60}Co). The acquisition and evaluation of the spectra, were performed using the software Genie 2000, CANBERRA. The counting geometry was kept constant for each measurement. The calculation of the iodine concentration was based on ^{128}I , 25 - minutes half-life and main γ -ray 442.9 keV (90%). Linear regression was applied to calculate the iodine concentration in the samples, after correcting the decay time of ^{128}I .

RESULTS AND DISCUSSION

Iodine determination data of hydroxyapatite matrices by NAA are presented in Table 2. Iodine content is given as percentage of weight of the impregnated matrix. The quantity of iodine impregnated into the matrix was high and it varied with the concentration of the NaI solution, the higher the solution concentration, the larger the iodine mass found in the matrices, in accordance with the high open porosity of the matrices (Table 1). Sample iodine mass measured by NAA was converted to percentage (%w/w) of impregnated matrix mass (Table 2). The calculated iodine mass was determined through stoichiometric calculations (Table 2).

For a better analysis of the data obtained, iodine mass measured by NAA and determined by stoichiometric calculation in the preparation of the NaI solution were compared. The comparison of the measured and calculated values are given in Table 2.

Evidently 1.0 molar solutions, the variations in NAA- measured and calculated iodine masses was smaller than those of 0.5 molar solutions, thus

revealing a larger efficiency of the impregnation processes for more concentrated solutions. Non-radioactive iodine was used in the impregnation process. It was expected that ^{131}I (radioactive) would have the same impregnation behaviour as ^{127}I (stable isotope). Therefore, the same pH and temperature parameters used by the manufacturer to produce the radioactive sodium iodide (Amersham Biosciences Limited, 2002; Instituto de Pesquisa Energéticas e Nucleares, 2005) were also used.

The manufacturers offer a variety of products with different parameters. The most important parameter is the activity of the solution as it has a direct relation with the dose required in the brachytherapy procedure. This variety of activities has a great importance since they are related to the quantity of solution that may be incorporated into the matrix to obtain the doses wanted in the brachytherapy procedure. The volume impregnated in each matrix was used to estimate the activity of each source when the process was carried out with radioactive solutions (Table 3).

According to Table 3, it was possible to obtain brachytherapy sources with a wide range of activity. HAP matrices offer a very important flexibility, as their activity can be adjusted as required. For comparison sake, we can use ^{125}I solutions with high activity as shown in Table 3. The ceramic matrices impregnated with these solutions might reach up to 60 mCi. The commercial sources of ^{125}I present activities in the order of 40 mCi (NATH et al., 1995). Other radionuclides can be tested, mainly those with activities different from that of iodine and with half-life close to that of iodine, such as ^{103}Pd , which is also used in brachytherapy (NATH et al., 1995).

Table 2 - Iodine quantification data

Sample	Solution NaI (mol.L ⁻¹)	Dry matrix mass (g)	Impregnated matrix mass (g)	I content (%)	Measured I mass (g)	Calculated I mass (g)	Comparison (%)
HA	0.5	0.2807	0.3861	2.1 ± 0.2 ⁽¹⁾	0.00788	0.00819	69.1
HA	1.0	0.2754	0.3748	3.5 ± 0.4 ⁽¹⁾	0.0128	0.0131	99.1
HACL	0.5	0.2810	0.3799	2.1 ± 0.2 ⁽¹⁾	0.00790	0.00798	72.4
HACL	1.0	0.2758	0.3756	3.4 ± 0.3 ⁽¹⁾	0.0125	0.0128	98.9

⁽¹⁾ Confidence level = 95%.

Table 3 - Estimated activity of the brachytherapy sources

Product	Sample	Sample Mass (g)	Solution Activity (mCi.mL ⁻¹)	Total Source Activity (mCi)	Activity / Mass (mCi.g ⁻¹)
¹²⁵ I-IMS30	HA 0.5	0.3861	100	10.0400	26.0036
	HA 1.0	0.3748		9.0690	24.1969
	HACL 0.5	0.3799		9.4240	24.8065
	HACL1.0	0.3756		9.0150	24.0016
¹²⁵ I-IMS300	HA 0.5	0.3861	600	60.2400	156.0218
	HA 1.0	0.3748		54.4140	145.1814
	HACL 0.5	0.3799		56.5440	148.8392
	HACL1.0	0.3756		54.0900	144.0096
¹³¹ I-IBMS3	HA 0.5	0.3861	200	20.0800	52.0073
	HA 1.0	0.3748		18.1380	48.3938
	HACL 0.5	0.3799		18.8480	49.6131
	HACL1.0	0.3756		18.0300	48.0032
¹³¹ I-IBS30	HA 0.5	0.3861	40	4.0160	10.4015
	HA 1.0	0.3748		3.6276	9.6788
	HACL 0.5	0.3799		3.7696	9.9226
	HACL1.0	0.3756		3.6060	9.6006
¹³¹ I-IPEN	HA 0.5	0.3861	200	20.0800	52.0073
	HA 1.0	0.3748		18.1380	48.3938
	HACL 0.5	0.3799		18.8480	49.6131
	HACL1.0	0.3756		18.0300	48.0032

CONCLUSIONS

HA and HACL matrices displayed characteristics of bioabsorbable hydroxyapatite and crosslinked macro and mesopores with average density in the order of 45% of the theoretical density, which showed that it is highly porous with total porosity of about 55% and open porosity around 54%. It was possible to incorporate a sodium iodine aqueous solution to the open pores through an impregnation process, which produced matrices with different quantities of iodine incorporated by varying the concentration of the NaI solution used, and, thus, with varying radioactivities. The use of HAp in the construction of bioabsorbable brachytherapy sources has a great potential due to its flexibility as the matrices present a broad activity range, from low to high (Table 3), which facilitates the use of the material.

ACKNOWLEDGEMENTS

The authors thank the financial support of CNPq and CDTN/CNEN and the collaboration of the Service of Materials and Nuclear Fuel (Nuclear Material and Fuel Laboratory) and the Service for Reactor and Irradiation (Reactor and Neutron Activation Laboratories) both at CDTN.

RESUMO

Materiais cerâmicos porosos à base de compostos de fosfatos de cálcio (CFC) vêm sendo estudados e desenvolvidos para várias aplicações biomédicas tais como implantes, sistemas para liberação de drogas e fontes radioativas para braquiterapia. Dois tipos de matrizes porosas biodegradáveis de hidroxiapatita (HA e HACL) foram avaliadas em termos da capacidade de incorporação de iodo em suas estruturas. Resultados revelaram que as matrizes porosas a base de hidroxiapatita apresentaram alta capacidade de incorporar iodo em sua estrutura. A quantidade de iodo foi mensurada através da técnica de Análise por Ativação Nêutronica (AAN). As matrizes cerâmicas porosas à base de hidroxiapatita demonstraram ter grande potencial para aplicação em braquiterapia de baixa taxa de dose (LDR – Low Dose Rate).

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Received: November 24, 2005;

Revised: May 18, 2006;

Accepted: March 20, 2007.

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