Ion exchanges in apatites. Effects on composition and properties

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ABSTRACT

The modification of the composition of apatites materials can be made by several processes corresponding to ion exchange reactions which can conveniently be adapted to current coatings and ceramics and are an alternative to the set up of new synthesis methods. In addition to high temperature thermal treatments, which allow to virtually replace partly or totally monovalent OH^- anion of stoichiometric hydroxyapatite by any halogen ion or carbonate, aqueous processes corresponding to dissolution-reprecipitation reactions have also been proposed and used. The most interesting possibilities are however provided by aqueous ion exchange reactions involving nanocrystalline apatites. These apatites are characterised by the existence on the crystal surface of a hydrated layer of loosely bound mineral ions which can be easily exchanged in solution. This layer offers a possibility to trap mineral ions and possibly active molecules which can modify the apatite properties. Such processes are involved in mineralised tissues and could be used in biomaterials for the release of active mineral species.

Keywords : apatite, nanocrystals, ion exchange, bone, strontium, magnesium, fluoride

INTRODUCTION

One of the most interesting property of apatites is their ability to accept ionic substituents and vacancies. Although living creatures have fully used these abilities to adapt mineralised tissues to their physiology and functional needs [1,2], substituted apatites are only at the beginning of their development in elaborated tailored biomaterials and some of them have been shown to exhibit improved biological properties compared to stoichiometric hydroxyapatite (s-HA) [3-7]. Most substituted apatites are obtained by synthesis and in addition to bulk composition alterations, modifications of crystal size, morphology, surface composition, physical-chemical properties (zeta potential, surface energy, solubility) and materials properties (microstructure, texture, porosity) may also occur which do not allow a clear identification of the factors involved in the biological behaviour of these materials [6]. Ion exchange processes have been the subject of different studies and are an interesting alternative to synthesis to modify fully or partly the composition of apatite and their properties in a controlled way. Considering the composition of apatites :

$$Me_{10}(XO_4)_6(Y)_2,$$

where Me are bivalent cations, XO_4 trivalent anions and Y monovalent anions. High temperature reactions allow exchange of Y ions and in a few cases removal of cations. However most exchange reactions involved in living beings concern nanocrystalline apatites and are related to the exchange of surface ions. These ionic exchanges play a considerable role in homeostasis and in intoxication (and sometimes detoxification) by mineral ions, but at a very different time scale they seem also to participate in slower phenomenon resulting in diagenetic alterations of geologic sediments and fossils. Such exchanges are made possible because of the very high specific surface area of the nanocrystals but also, essentially, because of the existence of metastable hydrated layer on the crystals surface containing loosely bound

ions [8]. The aim of this report is to review and describe some of the ions exchange processes in apatites and their related effect on materials properties and biological behaviour.

TYPES OF ION EXCHANGES

High temperature exchanges reactions.

High temperature exchange reactions were the first to be utilised to change apatite composition. Elliott and Young [9] could thus prepare the first synthetic HA monocrystals from Chlorapatite monocrystals obtained by a flux method, and solve the crystal structure of HA [10]:

$$Ca_{10}(PO_4)_6 Cl_2 + H2O \leftrightarrow Ca_{10}(PO_4)_6 (OH)_2 + 2HCl \quad (I)$$

The exchange reaction involved only ion diffusion at temperature close to 1300 °C and kept the monocrystals unchanged. Several other reactions were then done using this principle and it is now possible to replace virtually any Y ion from the apatite structure using an adequate gaseous atmosphere. Thus the reverse reaction of reaction (I) can also be used to prepare Chlorapatite from s-HA crystals and similar reactions may be carried on to prepare Fluorapatite, Bromapatite or carbonate apatite (type A, where OH ions are replaced by CO_3^{2-} ions)[11]:

$$Ca_{10}(PO_4)_6 (OH)_2 + HX \leftrightarrow Ca_{10}(PO_4)_6 X_2 + H_2O \quad (X=Cl, F, Br) \quad (II)$$

$$Ca_{10}(PO_4)_6 (OH)_2 + CO_2 \leftrightarrow Ca_{10}(PO_4)_6 CO_3 + H_2O \quad (III)$$

Although Fluorapatite are among the most stables apatites it is also possible to replace F^- ions at high temperatures by Cl^- ions using several Chlorinated compounds (SO_2Cl_2, $POCl_3$, or even Cl_2) :

$$Ca_{10}(PO_4)_6 F_2 + Cl_2 \leftrightarrow Ca_{10}(PO_4)_6 Cl_2 + 2ClF$$

The advantage of these processes is that they can be easily performed from existing HA (or FA) synthesis and they do not disturb, generally, the ceramic microstructure (crystal size, porosity) provided the exchange temperature is lower than 1000°C. All these reactions involve ion diffusion in apatites and in some cases restructuration. The reaction rates depend of course on the temperature, on the size of ions and crystals, and on the porosity of the ceramics. Thus fluoridation and chlorination of HA are relatively fast reactions and crystals of a few hundred of microns can be totally exchanged in a few hours at 900°C. Carbonation on the contrary appears much slower.

Such processes have been applied to study the effect of carbonation in type A position on biological properties [12-13]. The surface of a HA dense ceramic could be totally transformed into type A carbonate apatites. The carbonation was related to a decrease of the dipolar component of the surface energy and to a lower initial adhesion and spreading of osteoblast compared to HA associated with a lower production of collagen [12]. The same samples showed a poor adhesion of osteoclasts and a low resorption ability [13].

High temperature solid-gas reactions, using chlorinated gas, may also be used to remove volatile chlorine compounds. These reactions have been involved in the recuperation of Uranium and rare earth from apatites as well as elements such as V and Mn. They could be used for the purification of HA ceramics and the removal of trace elements [14].

Low temperature aqueous ion exchange reactions involving well crystallized apatites.

Although low temperature exchange reactions have also been described [15] they generally occur in aqueous media and they involve in most instances a dissolution-reprecipitation mechanism. Such reaction may be used to modify partly or totally the surface composition of ceramics or coatings. In order to observe such reactions the resulting apatites shall be less soluble than the starting compounds in the solution conditions. This is the case, for example,

of fluoride uptake by HA. Due to the existence of solid solution and epitaxial growth however surface equilibration may often occur limiting the extent of the pseudo-exchange phenomenon especially at physiological temperatures. Such reactions may however be useful and they have been proposed for the transformation of coatings and ceramics surfaces. They essentially lead to more stable, less absorbable coatings with increased surface area, nucleation ability and adsorption properties.

As an example aqueous fluoridation of plasma-sprayed HA coatings can be obtained by treatment of the raw coating in a fluoride-containing solution (KF : 0.05 M at 100 °C). The addition of phosphate (F/P = 1/3) in the solution and the neutral pH, prevent the formation of calcium fluoride and favour the formation of fluoridated apatites [16]. The treatment is completed after 10 hours and results in the formation of fluoridated apatite crystals on the surface of the coating (figure 1) essentially at the expense of the amorphous fraction of the plasma sprayed coating. The modified surfaces have been tested in cell culture with human osteoblasts, although cell adhesion was found about equivalent on treated and raw surfaces, cell proliferation greatly improve, after 10 days, on the fluorinated surface (figure 2 and 3). In addition the fluoridation treatment considerably reduced the degradation of the coating.

The two processes which have been described lead to well crystallised apatites very different from nanocrystalline bone apatites. These offer in addition to simple ionic substitution in the lattice enhanced possibilities of reactivity and ion substitution due to their remarkable surface properties.

Ion exchange reactions involving nanocrystalline apatites.

Nanocrystalline apatites offer faster and improved capabilities for ion exchanges than well crystallized apatites. This phenomenon has been described several decades ago, for the first time by Newman [17], but its interpretation was not clear. Since then several spectroscopic

studies have consistently confirmed the existence in apatite nanocrystals of non-apatitic environments of the mineral ions. Solid state NMR data have indicated that these environements corresponded to a hydrated layer probably located at the crystal surface[18-19]. Very recently it has been shown that the hydrated surface layer was structured in aqueous media, but very fragile and that it was destroyed by drying the samples [20]. However, even in aqueous media, the hydrated layer is metastable, compared to an apatite structure, and it is irreversibly transformed into apatite on ageing in aqueous media [8]. It has been suggested that the hydrated layer could lower the surface energy of the nanocrystals and thus favour their nucleation in aqueous media [21]. With its loosely bounds mineral ions, this layer seems involved in homeostasis and in other interactions of bone mineral crystals with their surrounding media. It might also play a role in mechanical properties of mineralised tissues, strongly related to the hydration level, and also possibly in biological regulation processes involving specific bone proteins and organic constituents [22]. The interactions of the nanocrystal surface with its aqueous environment are summarised in figure 4.

The exchange reactions involving the surface layer are fast and easy. Concerning Ca-Mg exchange, for example, the equilibrium is reached in a few minutes and the reaction can be made at room temperature. The level of exchange seems always related to the maturation stage of the crystals: it decreases considerably in matured crystals (figure 5) due to the reduction of the surface hydrated layer. The exchange level depends also on the nature of the mineral ions. For example for identical solution concentrations the exchange rate of Sr appears always higher than that of Mg at any maturation stage [23]. When the foreign mineral ions remain located in the hydrated surface layer they are available for reverse exchange. Like the direct ion exchange reaction, the reverse reactions are fast and rapid although incomplete: an ion residue remain always in the nanocrystals.

The foreign mineral ions behaviour can however be very different when ageing (maturation) is involved. When the foreign mineral ion can enter the apatitic lattice and substitute for calcium, phosphate or OH^- ions, they do not disturb the maturation process and, as they enter in the growing apatitic domains, their concentration in the hydrated layer progressively decreases and they become unavailable for reverse exchange reactions. On the contrary if the foreign mineral ions cannot enter or enter with difficulties in the apatitic domains they remain exchangeable and they may possibly stabilise the hydrated layer [23]. These different behaviour are illustrated by Sr and Mg ion exchanges. In the case of Sr, which can form continuous solid solutions with calcium phosphate apatites, the exchange rate decreases as the maturation time increase after a primary exchange reaction. This behaviour indicate the incorporation of the ion in the growing apatitic domain during maturation. On the contrary for Mg^{2+} ions, which can only very partly substitute for Ca in the apatitic lattice, it remain exchangeable even in coprecipitated (Ca and Mg) apatites for any maturation time (table 2). The reverse exchange reaction testifies for the availability of the Mg^{2+} ions and their preference for the hydrated layer. Carbonate shows an intermediate behaviour. Part of the ions can be incorporated in apatitic sites but some may remain in the hydrated layer depending on the maturation stage. These ions (Mg^{2+} and carbonate) disturb the growth of the apatite lattice at they may delay the maturation process. Living beings have learned to control and use these specificities to regulate their homeostasis. It can then be understood that fresh mineral crystals with a well developed hydrated layer are a living necessity and it is one of the reasons why energy is spent, in mammals, for bone renewal and remodelling.

An example of use of these possibilities is given by strontium uptake and release from bone mineral. Sr^{2+} ions have been shown to have a direct effect on bone cells and they are proposed for the treatment of osteoporosis [24]. Sr^{2+} has been shown to be taken up, like many other bone seeking elements, preferably by recent mineral deposits, for example the amount of Sr^{2+}

was found to be 2 times higher in cancellous bone than in compact bone [23]. This phenomenon can be due to several causes : better blood supply and contact with the mineral, a faster turn-over rate, but also a higher amount labile non-apatitic environment in cancellous than in compact bone. In fact the non-apatitic environment may appear as a reservoir for the storage and regulation of circulating Sr^{2+}.

Several mineral ions have a direct action on cells when they are in solution (Sr^{2+}, Mg^{2+}, Mn^{2+}, Zn^{2+}) and nanocrystalline apatites can be used as ion reservoir for the slow release of these mineral ions. The release would be determined by two processes a spontaneous release by a reverse ion exchange with calcium ions of body fluids, determined only by the local equilibrium conditions and a cell-mediated release resulting from the complete dissolution of the crystals by osteoclast cells. The first process could be interesting for the local stimulation of stem cells or osteoblast on a nanocrystalline Ca-P material. The second would be a long term effect, necessitating a remodelling process to be activated, and involving both osteoblast and osteoclast cells. In addition it shall be emphasized that the hydrated layer offer a wider range of ion substitution and uptake than the apatite lattice.

CONCLUSION

Ion exchange can be used at different levels to modify the properties of apatite ceramics. Nanocrystalline apatites especially offer different levels of ionic susbtitution which are used in certain living creatures but which have not yet been utilised in biomaterials. The main difficulty is the very high reactivity and the unstability of these compounds which raise problems of accurate caracterisation and reproducibility, stability and materials preparation. In order to take advantage of these properties, low temperature processes of ceramic making have to be investigated and developed.

ACKNOWLEDGMENTS

Part of the work reported was caried out within the framework of a European Community funded project: Brite-Euram II.

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Table 1 : Sr^{2+} ions released after primary exchange and increasing ageing time before reversion.

Maturation time	**Sr released (% of initial content)**
no maturation	90
1 day	39
3 days	23
10 days	23
30 days	20

Table 2 : Mg^{2+} ions released from coprecipitated (Ca^{2+} + Mg^{2+}) nanocrystalline apatites after different maturation times.

Maturation time	**Mg released (%)**
1 day	84
3 days	84
10 days	87
30 days	82

Figure Legends :

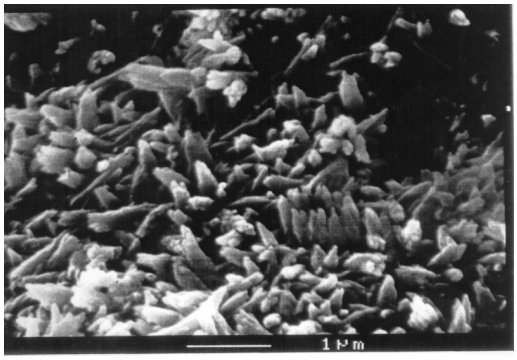
Figure 1: SEM micrograph of the surface after treatment in the fluoridating solution (KF: 0.05 M; KH_2PO_4: 0.15M; pH: 7, temperature: 100 °C). The layer is constituted of thin needle-like crystals (0.5 to 3 micrometer long, 0.1-0.3 width). The fluoridation rate is close to 80%.

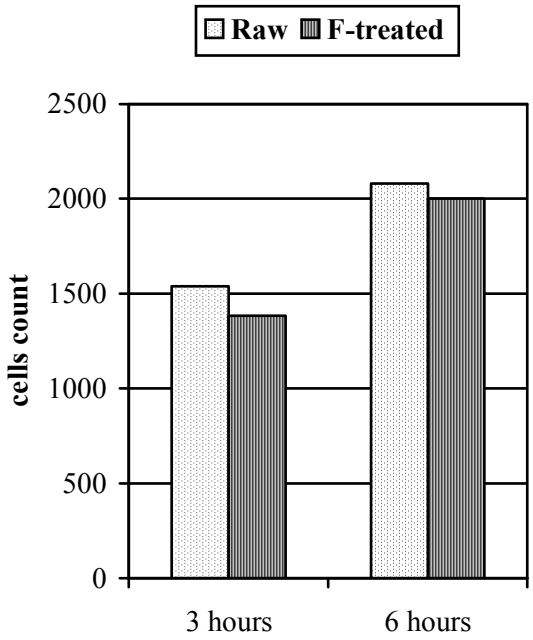
Figure 2: Human osteoblast cells adhesion on the raw (vacuum plasma-sprayed HA) and the Fluoridated surface after 3 and 6 hours.

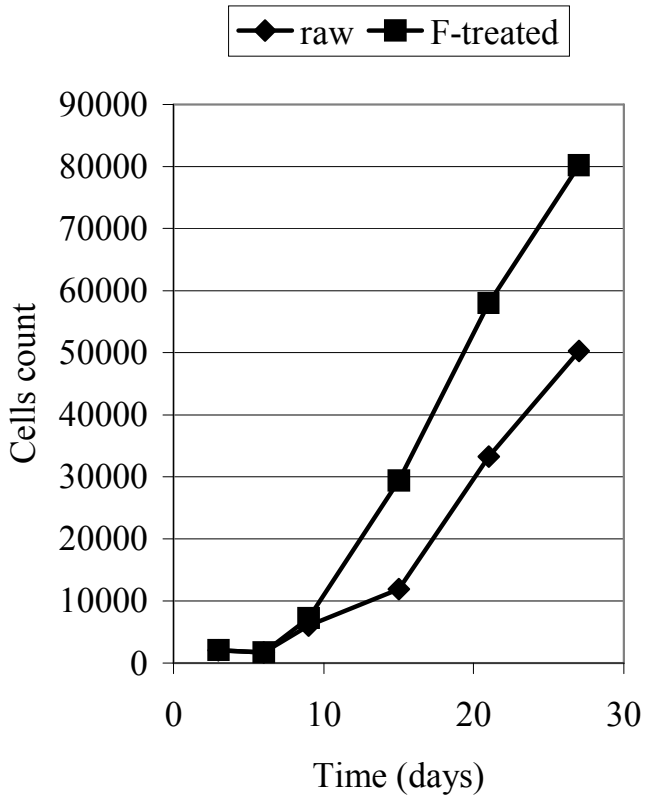
Figure 3: Human osteoblast cells proliferation on the raw (vacuum plasma-sprayed) and fluoridated surface.

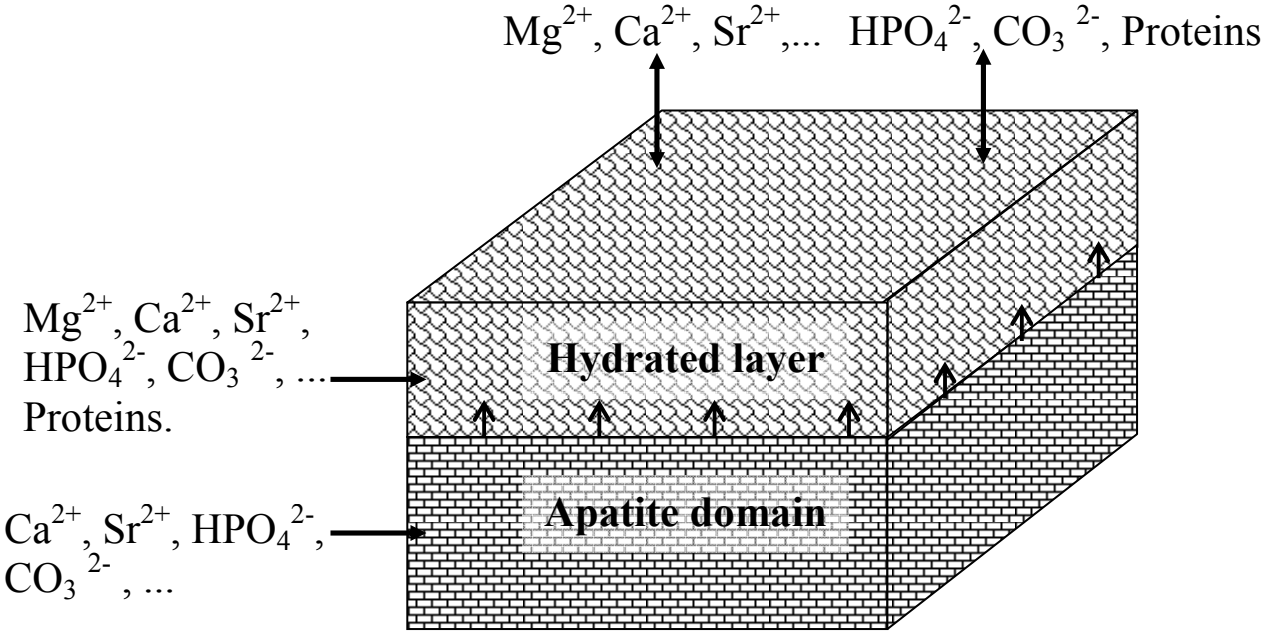
Figure 4: Nanocrystalline apatite model. The hydrated surface layer may trap and release several ions from the solution. Due to ions mobility and disturbances related to substitution, charged proteins moieties may also be attached to the surface layer. Some of the mineral ions may be included in the regular, non-stoichiometric apatite domains during their growth.

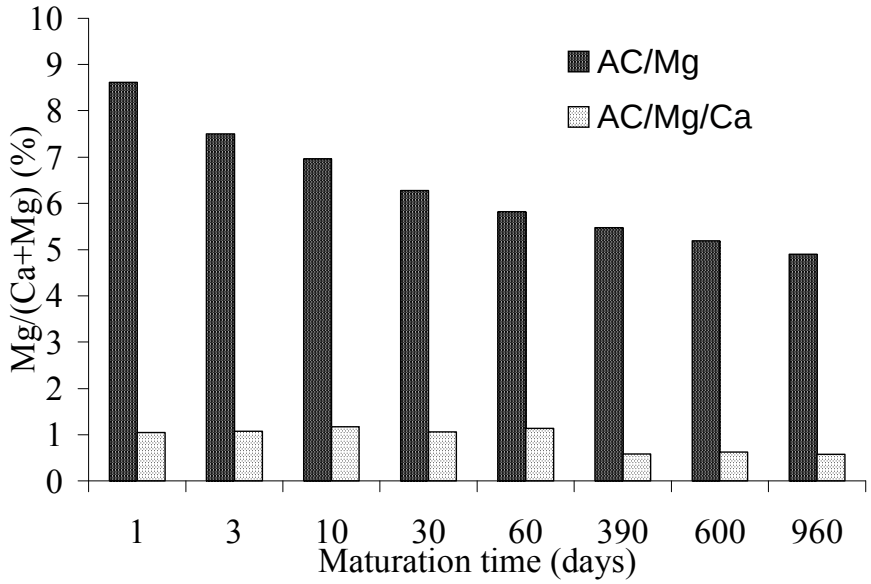
Figure 5: Example of Ca-Mg exchange in apatite at different maturation stages. The exchange rate (Ca/Mg) decreases as the maturation time increase. The exchange is almost totally reversible (Ca/Mg/Ca).


1 µm


Raw
F-treated
2500
2000
1500
1000
500
0
cells count
3 hours
6 hours


raw
F-treated
90000
80000
70000
60000
50000
40000
30000
20000
10000
0
Cells count
0
10
20
30
Time (days)


Mg^{2+}, Ca^{2+}, Sr^{2+},... HPO_4^{2-}, CO_3^{2-}, Proteins
Mg^{2+}, Ca^{2+}, Sr^{2+}, HPO_4^{2-}, CO_3^{2-}, ... Proteins.
Ca^{2+}, Sr^{2+}, HPO_4^{2-}, CO_3^{2-}, ...
Hydrated layer
Apatite domain


10
9
8
7
6
5
4
3
2
1
0
Mg/(Ca+Mg) (%)
AC/Mg
AC/Mg/Ca
1
3
10
30
60
390
600
960
Maturation time (days)