Preparation and Deposition of Hydroxyapatite on Biomaterials by Sol-Gel Technique-A Review

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ABSTRACT Hydroxyapatite Ca₁₀(PO₄)₆(OH)₂ (HAP) is an important inorganic biomaterial which has attracted the attention of researchers in recent years. Due to its chemical and structural similarity with the mineral phase of bone and teeth, it is widely used for hard tissues repair. Amongst various methods, sol–gel technique has achieved more popularity recently due to synthesis of ceramics powders. The sol–gel process is easily applicable to surface coating as it allows the preparation of high-quality HA thin films on metal substrates. It has been observed from the studies that the protective atmosphere during sintering process accomplished after sol-gel coating produces good uniformity of coating material which significantly leads to a reduction in the porosity of the coating film. In another study it was revealed that mechanical properties of commercial HAP can be significantly improved by adding P₂O₅ and Na₂CO₃ without altering its biocompatibility. It has been found from the extensive literature review that homogeneous and crack-free coatings were obtained on biocompatible substrate implant at higher sintering temperatures. The particle size of the HAP powder increases with the increase of the sintering time and sintering temperature. In this paper a review of the studies done for the preparation and deposition of HAP powder with the sol-gel technique has been detailed.

Keywords: Hydroxyapatite Biomaterials Sol-gel Composite and Sintering.

INTRODUCTION

Todays, more than 600,000 total hip and knee arthroplasties are being performed annually in Europe and the United States Barden, (1998). It has been found that in India alone, about 7 crore people suffer from joint related problems and this incidence is expected to rise Wadhwa, (2008). Biomaterials are the class of materials which are used for developing body...
implants. The predominant purpose of biomaterials is to produce a part or facilitate a function of the human body in a safe, reliable, economical, and physiologically acceptable manner Lalor et al. (1991). Biomaterials can be metals, ceramics, polymer or glasses. Commonly used biomaterials are Ti, Co or stainless steel. Stainless steel is commonly used for temporary devices in orthopedic surgery due to its relatively low cost and acceptable biocompatibility. However, this alloy tends to localized corrosion and releases significant quantities of iron to the neighbouring tissues, which can lead to fibrosis. More expensive materials are often employed for longer implantation times, such as Co-Cr alloys and Ti alloys. Titanium is the newest metallic material among the three main metallic biomaterials (stainless steels and Co-based alloys).

Surface modification is considered an economical method for improving corrosion resistance and bioactivity of these existing materials. Due to wear and corrosion, metals or their alloys cannot be directly used in human body. Since the metals secrete metallic ions in vicinity of the organs, it may lead to fibrosis, which is harmful for body. So these materials should be coated with such a material which is biocompatible and whose composition is almost similar to that of bones, which may further help in growth and development of bones Bonfield and Tanner (1997). Further the coating should be bioactive and bioresorable.

Hydroxyapatite (HAP) or calcium phosphate coatings are commonly used. HAP is widely used as the coating material because it shows biocompatibility, bioactivity, bioresorbility and also the ossoinduction (it stimulates bone formation) Hench (1982). Hydroxyapatite coatings are used on these alloys to enhance the bone bonding ability, improve the biocompatibility and reduce the toxic effect of bio implants on living organism. Sometimes ceramic materials like Ti, Zr are also used as bond coats, these are bioinert and also enhance the adhesion strength of the biomaterials. It reduces the direct contact between base metal and HAP and the damage of biomaterials by cyclic movements Pereira et al. (1995).

2. METHODS OF PREPARATION OF HYDROXYAPATITE (HAP)

There are different methods of preparation of HAP like precipitation technique, sol-gel approach, hydrothermal technique, biomimetic deposition technique, electro deposition technique etc. Some commonly used techniques are discussed below:

2.1 Precipitation technique/Wet/chemical/aqueous precipitation technique

Precipitation technique also known as wet, chemical or aqueous precipitation technique. It is commonly used for precipitation of HAP powder. In this method HAP is prepared by adding orthophosphoric acid to lime. The size, shape and
surface area of HAP particles depends upon the reaction temperature and rate of addition of orthophosphoric acid Santos et al. (2004).

\[ 10\text{Ca(OH)}_2 + 6 \text{H}_3\text{PO}_4 \rightarrow \text{Ca}_{10}\!(\text{PO}_4)_6\!(\text{OH})_2 + 18\text{H}_2\text{O} \quad (1) \]

Even \[ (\text{NH}_4)_2\cdot\text{HPO}_4 \] can be used as starting material. The following reaction takes place:

\[ 10\text{Ca(OH)}_2 + 6 (\text{NH}_4)_2\cdot\text{HPO}_4 \rightarrow \text{Ca}_{10}\!(\text{PO}_4)_6\!(\text{OH})_2 + 6\text{H}_2\text{O} + 12 \text{NH}_4\text{OH} \quad (2) \]

2.2 Hydrothermal technique

The hydrothermal technology has been found to be successful with reference to the processing of advanced materials for nanotechnology. This is another method for synthesis of HAP. It works at elevated temperature greater than 25°C and pressure greater than 100Pa. However, with increase in hydrothermal temperature and pressure, the Ca/P ratio of the precipitates gets improved Suchanek and Riman (2006), Sadat-Shojai (2009).

2.3 Electro deposition technique

A basic feature of electrodeposition technique is that the composition and coating structure can be easily controlled due to its relatively low processing temperature. It is possible to coat irregular surfaces with this method. Previously the \( \text{H}_2 \) gas evolution at the interface lead to a heterogeneous coating. However, by the introduction of electrodeposition technique the use of organic solutions avoids the negative effects of \( \text{H}_2 \) gas and more homogeneous coatings can be obtained Chen et al. (1998). Calcium phosphate coatings have also been obtained by electrophoretic deposition from previously synthesized powders at potentials ranging from 70 to 300 V Ducheyne et al. (1986). The growth induced by constant anodic voltages (2–4 V) in a basic electrolyte has also been tested. This selection is based on reports sustaining that apatitic structure is the most stable calcium phosphate in basic media Narasaraju et al. (1996)

The electrodeposition technique was used to synthesise ultrafine, nanophase HAP coating by using dilute electrolytes \([\text{Ca}^{2+}] = 6.1 \times 10^{-4} \text{ M}, \quad [\text{PO}_4^{3-}] = 3.6 \times 10^{-4} \text{ M}\) at physiological pH Shikhanzadeh (1998), Manso et al. (2002). \( \text{Ca(NO}_3)_2 \) and \( \text{NH}_4\text{H}_2\text{PO}_4 \) were used as precursors. \( \text{NaNO}_3 \) was used to improve the electrolytes ionic strength Manso et al. (2002).
2.4 Biomimetic deposition technique

The biomimetic process is a physicochemical method in which a substrate is soaked in a solution that simulates the physiologic conditions (SBF), for a period of time, long enough to form a desirable layer of calcium phosphate on the substrate surface. In contrast to plasma spraying, biomimetic methods offer the possibility to cover complex shaped implants and elaborate on films of different Ca–P phases Kokubo et al. (1989), Barrere et al. (1999). In recent years, different metal pretreatments, such as alkaline treatment Kim et al. (1997), acid treatment Wen et al. (1998), have been used for accelerating and enhancing the biomimetic coating activity. This process facilitates the spontaneous nucleation and growth of nanosized, carbonated and ‘bone-mimic’ HAP at physiological pH and temperature using SBF with an organic salt composition similar to that of human body fluid (blood plasma). It improves the spontaneous nucleation and growth of nanosized, carbonated and ‘bone-mimic’ HAP at physiological pH and temperature Thamaraiselvi et al. (2006).

2.5 Sol–Gel Technique

Recently, Sol–gel technique has attracted much attention to the researchers Weng et al. (2003, 2002), Cheng et al. (2003, 2001) due to its well-known inherent advantages to generate glass, glass–ceramic and ceramics powders. The sol–gel process is easily applicable to surface coating and it allows the preparation of high quality HAP thin films on metal substrates Choi et al. (2004), Weng et al. (1998). Thus, the sol–gel process can be usefully utilized to synthesize both HAP powders and HAP films under significantly mild conditions. The versatility of the sol-gel method opens a great opportunity to form thin film coatings in a rather simple process, an alternative to thermal spraying which is currently widely used for biomedical applications Haddow et al. (1998), Chai et al. (1995). The sol-gel approach provides significantly easier conditions for the synthesis of HAP. Sol-gel process refers to a low-temperature method using chemical precursors that can produce ceramics and glasses with better purity and homogeneity Weng et al. (1998). This process is becoming a common technique to produce ultra fine and pure ceramic powders, fibers, coatings, thin films and porous membranes. Compared to the conventional methods, the most attractive features and advantages of sol-gel process include:

- Molecular-level homogeneity can be easily achieved through the mixing of two liquids;
- The homogeneous mixture containing all the components in the correct stoichiometry ensures a much higher purity.
More recently, the sol-gel method has been extensively developed and used in biotechnology applications Livage (1994). It has been reported that the HAP materials synthesized by sol-gel process are efficient to improve the contact and stability at the artificial/natural bone interfaces in both in vitro and in vivo environment.

3. SOL GEL SYNTHESIS

It is a new approach for the preparation of glasses and ceramics Livage (1994). It follows two routes:

1) Metal organic route, with metal alkaoxides in organic solvent which leads to oxalation (formation of oxygen bridges) or olation i.e formation of hydroxobridges. Following are the equations:

\[
M\cdot OH + XO\cdot M \rightarrow M\cdot O\cdot M + XOH \quad (3)
\]

\[
M\cdot OH + XO\cdot M \rightarrow M\cdot O\cdot M + XOH \quad \text{(oxalation)} \quad (4)
\]

\[
M\cdot OH + HO\cdot M \rightarrow M\cdot (OH)_2\cdot M \quad (5)
\]

Figure 1: Schematic flow process chart for synthesis of HAP by using \(\text{Ca(NO}_3\text{)}_2\cdot 4\text{H}_2\text{O}\) and \(\text{P}_2\text{O}_5\) Agrawal et al. (2011).
Figure 2: Flow chart of sol synthesis and substrate coating Tkalce et al. 2001.

Where X = H or R (Olation)

2) The inorganic route with metal salts in aqueous solution (chloride, oxychloride and nitrate) is much cheaper and easier to handle than metal alkoxides, but their reactions are more difficult to control.

3.1 Method of preparation of HAP

(A) For the preparation of HAP by sol-gel technique, calcium nitrate tetrahydrate \( \{ \text{Ca(NO}_3\}_2 \cdot 4\text{H}_2\text{O} \} \) is dissolved in ethanol and 0.5 mol/l solution of phosphoric pentaoxide was obtained by dissolving in absolute alcohol. Then both solutions are mixed to obtain the desired \( \text{Ca/P} \) ratio of 1.67. The solutions are slowly stirred for 10-15h, till the formation of gel. Then gel is dried in electric oven at 80°C in air for 20h. It is followed by heat treatment, starting from 400°C to 750°C. Schematic flow process chart for the synthesis of HAP.

(EHP=2-ethyl-hexyl-phosphate (99.2%, Merk) The weight ratio of mono and di-ester equals (0.809:1)
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by the use of Ca(NO₃)₂·4H₂O and P₂O₅ has been shown in Figure 1 Agrawal etal. (2011).

(B) For the preparation of HAP in another method 74g of Ca(OH)₂ (98%) is suspended in 150ml ethanol, which is stirred vigorously. To this 433.5g of ethyl hexanoic acid (EHA) is added dropwise, the molar ratio of Ca/EHA=1:3. The suspension is stirred at 50°C for 3h, cooled to room temperature and diluted by adding 90ml ethanol. Then solution is filtered by pressure filtering to obtain calcium-2-ethylhexanoate. CaEHA solution is diluted with EHA to obtain Ca/EHA=1.8. 2-ethylhexyl-phosphate (99.2wt%) is added in various amounts to obtain solution with Ca/P molar ratios of 1.60, 1.67, 1.70, 1.75, 1.80 by adding ethanol, further solution is stirred at 25°C for 4h. Finally, solutions are dried at 130°C for 4h and gels are treated at various ranges from 400 to 1400°C (Fig. 2) Tkalce etal. 2001. The flow chart of sol synthesis and substrate coating is shown in Figure 2.

3.2 Deposition of HAP Techniques

Protective coatings can be a way to inhibit Fe diffusion and generalized, galvanic and localized corrosion in stainless steel. Furthermore, different coatings have been produced in order to induce bioactivity on metallic prostheses. Plasma sprayed hydroxyapatite (HAP) coatings, for example, are being widely used in orthopedics applications Bloebaum etal., Bawer etal. (1991), Larson (1994), Klein etal. (1994), but this kind of prosthesis shows some shortcomings in its performance, derived from deficient adhesion, difficulties for controlling composition and crystallinity, besides its high cost Kieswetter etal. (1994) For these reasons, great efforts are in progress looking for alternative bioactive coatings Jokinen etal. (1998), Bloyer etal. (1999), Schrooten etal. (1999), G´omez-Vega etal. (2000). The sol-gel method has been proposed as an adequate procedure to produce protective De etal. (1990), de etal. (1995), Galliano etal. (1994) and bioactive Fillaggi and Pillar (1995), Gallardo etal. (1994) coatings. Advantages and technological significance of these coatings have been widely demonstrated, promoting its application over other deposition techniques Guglielmi (1997), Uhlmann etal. (1998).

3.2.1 Sol gel Technique for deposition of HAP

Apart from thermal spraying chemical methods can also be used for obtaining HAP coatings on metals. The sol-gel process is easily applicable to surface coating and it allows the preparation of high-quality HAP thin films on metal substrates Weng and Baptista (1998), Choi etal. (2004). Thus, the sol-gel process can be usefully utilized to synthesize both HAP powders and HAP films
under significantly mild conditions. The versatility of the sol-gel method opens a great opportunity to form thin film coatings in a rather simple process, which is currently widely used for biomedical application Chai et al. (1995), Haddow et al. (1996). The sol-gel process has been widely used in the preparation of various inorganic materials because of the easy formation of crystalline films at relatively low temperature, the possibility to tailor microstructures and its convenience for complex shape coatings Brinker and Scherrer. In this process, the metal alkoxides M(OR)n used as starting materials are converted through hydrolysis and condensation reactions to amorphous gels of metal oxides, which are further transformed to ceramics with relatively low temperatures Tkalce et al. (2001). It is highly cost effective and the mode of application is easier than thermal spray techniques.

4. COATING PROCEDURE

(A) Ti-alloys and single-crystal silicon wafers were coated with prepared sols. Circular titanium-alloy plates (Ti-30Nb-3Al and Ti-5Al-2.5Fe) with 15 mm diameter and 1 mm thickness were polished with 15 µm diamond paste, cleaned in an ultrasonic bath, washed with distilled water and acetone and dried at 80°C before coating. Si wafers (20 × 10 mm) were rinsed in acetone and dried at 80°C. Coating is performed by dipping the substrates into sols at 25°C, and pulling them out with a speed of 1 mm/s, drying them in air at 130°C for 4 h and subsequently calcining them for 10 min. in a preheated furnace at temperatures between 400-900°C Tkalce et al. (2001).

(B) The solution was synthesized by refluxing the ethanol solutions of P2O5 (Riedel-deHaen) and Ca (NO3)2·4H2O (Merck, GR) in a Ca/P ratio of 1.67 for 24 h. Polished Ti6Al-4V sheets were used as substrates. The substrates were dipped into the solution with a withdrawing rate of 4 cm/min. After an as-dipped coating was dried in an oven at 150 for 15 min. the substrate with the dried coating was placed directly into an electric furnace at 500°C in air for 15 min. In order to increase the thickness of the coating, the above procedure was repeated ten times Weng et al. (2000).

5. VARIOUS STUDIES RELATED TO HAP COATINGS BY SOL-GEL ROUTE

Gallard and Galliano (2000) focused at the development of highly corrosion resistant and bioactive sol-gel coatings on AISI 316L SS stainless steel. Hybrid SiO2 sol-gel coatings inhibited corrosion and Fe diffusion, although no signal of bioactivity was detected. The inclusion of Ca- and P-alcoxides in the sol composition did not promote bioactivity. Bioactive coatings were obtained
from suspensions prepared by adding glass (CaO·SiO₂·P₂O₅) particles to a hybrid organic-inorganic SiO₂. So using double-layered coating showed in vitro signals of bioactivity.

Kim et al. (2004) performed the research to deposit hydroxyapatite and fluor-hydroxyapatite (FHAP) films on a titanium substrate using a sol–gel technique. It was found to improve the biocompatibility of Ti biomedical implants. The coating layers were phase-pure, dense, and uniform, and had a thickness of ~5mm. Hydroxyapatite composites with titania (TiO₂) up to 30 mol % were coated on a titanium (Ti) substrate by a sol-gel route in the work done by Kim et al Kim et al. (2005). It was observed that the adhesion strength of the coating layers with respect to Ti substrate increased with increasing the TiO₂ addition. The highest strength obtained was as high as 56 MPa, with an improvement of about 50% when compared to pure HAP (37 MPa). These findings suggested that the sol-gel-derived HAP-TiO₂ composite coatings possess excellent properties for hard tissue applications.

Hydroxyapatite/titania sol–gel coatings on titanium–zirconium alloy for biomedical applications were carried out by Wen et al (2007) they used sol-gel based HAP/TiO₂ coatings over the non toxic Ti/Zr alloy samples. The TiO₂ film was spin-coated at a speed of 3000 rpm for 15 s, followed by a heat treatment at 600°C. The HAP/TiO₂ coated Ti/Zr alloy displayed excellent bioactivity in a simulated body fluid (SBF).

6. CONCLUSION

It can be concluded that HAP can be synthesized by various methods like precipitation technique, hydrothermal technique, biomimetic deposition technique, electrodeposition technique and sol-gel approach. Scientists and researchers are engaged in solving various challenges related with synthesis of HAP with optimum properties for the use in various biomedical applications. Various studies also shows that sol-gel deposition method is a promising technique for obtaining biocoatings and the results obtained are also encouraging for further studies. We expect that, with continuous research efforts there is scope of development of novel and economic synthesis and coating methodologies of HAP in the near future.

REFERENCES


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