A review on the prevalent fabrication methods, microstructural, mechanical properties, and corrosion resistance of nanostructured hydroxyapatite containing bilayer and multilayer coatings used in biomedical applications

Mir Saman Safavi, Mohamadreza Etminanfar*

Faculty of Materials Engineering, Research Center for Advanced Materials, Sahand University of Technology, Tabriz, Iran.

Received: 06 March 2019 ; Accepted: 23 April 2019
* Corresponding author email: etminanfar@sut.ac.ir

ABSTRACT
Surface treatments of the biomaterials are of great interest in many biomedical applications. Hydroxyapatite is a favorable candidate for surface modification of the implants. To date, a wide variety of methods have been developed to produce bio-active/biocompatible coatings with desirable features in order to improve the performance of the implants. This paper strives to overview the present prevalent methods for synthesizing the hydroxyapatite based multilayer coatings as well as the various properties of such coatings. The common methods for fabrication of HAp-containing multilayer coatings including electrochemical, sol-gel, and plasma spray routs. It was clearly highlighted that the main drawback in pure HAp coatings is their poor adhesion to the implants. The studies in the field of HAp-ceramic systems showed that the deposited ceramic layers, e.g. TiO$_2$ and ZrO$_2$, are strongly adherent to HAp and substrate which leads to a remarkable improvement in the mechanical properties of pure HAp coatings. Unlike HAp-ceramic systems, there are less studies dealt with the HAp-polymeric systems. The performed studies demonstrated that the corrosion resistance and adhesion strength of the coatings to the substrates can be considerably improved with the deposition of HAp/polymer multilayer coatings. Altogether, HAp based multilayer coatings have bright prospect since they benefit from HAp biocompatibility as well as the enhanced adhesion to the substrate.

Keywords: Hydroxyapatite, Nanostructured Multilayers, Mechanical Properties, Corrosion Resistance, Implants, Biomedical Applications.

1. Introduction
A wide variety of metals and alloys can be successfully fabricated to serve as promising biomaterials in human body [1, 2]. One of the most distinguishing feature of these materials is their mechanical properties including low elastic modulus which is similar to human bone, low plasticity, and fatigue resistance [3-7]. Moreover, favorable wear and corrosion resistance as well as suitable biocompatibility are the other outstanding features of biomaterials [8, 9]. Titanium and its alloys such as Ti$_6$Al$_4$V, Ti$_6$Al$_7$Nb, and Ni-Ti shape memory alloys, stainless steel, and cobalt chromium molybdenum alloys have recently been developed for implant applications. They can be satisfactorily employed to fix or replace the damaged bones [2, 10]. According to the statistics, these materials supply more than 70 % of the bio-implant
requirements [11, 12]. Nevertheless, an undesirable phenomenon namely, releasing toxic ions when exposing to body environment, have restricted their potential benefits in bio applications. On the other hand, poor connection of the implants to the adjacent tissue, especially for Ti-based ones, remains as a critical challenge to overcome. This is why a great demand for adhesive-biocompatible coatings is generated [13-15].

Hydroxyapatite \((\text{Ca}_10(\text{PO}_4)_6(\text{OH})_2)\) is an eligible candidate for improving the bioactivity, mechanical properties, and corrosion resistance of these implants [10, 16, 17]. It has not found vast applications as a conventional ceramic, however, it is well-established as a biomaterial. Hydroxyapatite (HAp) is a kind of calcium phosphate with hexagonal lattice structure which can be formed in plate-like or needle-like morphologies based on its synthesis situation. It is to be noted that HAp is the primary inorganic calcium phosphate mineral part of the bone and teeth which contains more than half of bone's weight. Therefore, it is widely used for fabrication of the dental and bone implants [18-20].

All in all, application of a biocompatible layer on the fabricated bio-implants dramatically promotes their physicochemical and biological properties. In addition, hyaluronic acid, collagen, chitosan, and etc. are the other common bioactive coatings which can contribute to obtain a surface with similar topography and chemical composition to extra cellular matrix (ECM) [21-24].

Despite the aforementioned advantageous of HAp, it has poor adhesion to the surface of the metallic implants. There are several approaches including grit blasting, sand blasting, chemical treatments, and high temperature methods which have been introduced in order to meet this shortage [25-27]. Although high temperature methods such as pulse laser deposition, thermal spray, and etc. improve the adhesion to the substrate, they may adversely affect the final properties of the coatings. For example, the high temperature may decompose the existing HAp to \(\text{Ca}_3\text{PO}_4\) and \(\text{CaO}\). These compounds are not biocompatible and may noticeably degrade the benefits of HAp coatings [28]. A practical way to overcome this challenge is deposition of an interlayer between substrate and HAp, in other words, producing a bilayer coating. A wide variety of functional molecules can be introduced into the growing layered coating, thereby obtaining versatile properties [29, 30]. As a particular feature of the HAp-chitosan multilayer coatings, it is possible to alter the hydrophilicity of system with inclusion of various layers [31]. In addition, the deposited interlayers can satisfactorily give rise to the mechanical, biological, and corrosion performance of the substrates. For instance, Narayan et al. [32] have demonstrated that the deposition of diamond carbon interlayer not only minimize the probability of inducing corrosion of HAp in body fluids, but also improves implant fixation due to the minimal fibrous capsule around the implant. Literature have confirmed that the deposited interlayers, e.g. \(\text{TiO}_2\), play a vital role, in particular when using high temperature methods such as plasma spray, so that these interlayers diminish the mismatch of the coefficients of thermal expansion, slow down the fast cooling rates, decrease the thermal decomposition of HAp, and enhance the crystallinity of the coatings. Furthermore, results showed the superior fatigue resistance of the HAp-based multilayer coatings than the single layer ones [33, 34].

The present review addresses the prevalent fabrication methods of HAp based multilayer coatings include electrophoretic deposition (EPD), electrodeposition (ED), sol gel, and plasma spray. Also, the microstructural, mechanical, and corrosion properties of HAp-ceramic and HAp-polymer systems will be reviewed in some detail.

2. Prevalent fabrication methods
2.1. Electrochemical methods
2.1.1. Electrophoretic deposition

EPD is one of the colloidal methods for fabricating ceramic containing products, which has gained great attention owing to its unique features [35]. Albeit this method was first introduced at 1808, it’s first empirical use dates back to 1933. In EPD, existing charged particles in a liquid medium, usually called electrolyte or plating bath, move toward the conductive substrate which located in opposite charge under the application of electric field. Depending on the charge of the used electrode, EPD can be divided into two groups, as: (i) cathodic EPD for positively charged particles; and (ii) anodic EPD for negatively charged particles [36]. Fig. 1 a-b shows the schematic representation of both types of EPD process.

Generally speaking, the quality of the deposited bio-active coatings deeply affected by the type of the employed deposition technique. A broad variety of materials such as ceramics, polymers,
and glasses can be satisfactorily deposited by means of EPD. This method is known as an appropriate choice when the goal is deposition of the polymeric coatings, e.g. chitosan [37-40]. Furthermore, there are numerous studies reporting the successful use of EPD for deposition of HAp on the metallic surfaces, however, the poor adhesion of this kind of coatings is a challenge [15, 41-43]. In these cases, post sintering treatments can be a practical solution. Empirical results confirm the faster procedure of deposition in EPD than other electrolyte deposition methods. It is ascribed to the presence of particles rather than ions in this method [44, 45]. There are two major factors controlling the final properties of the produced films by EPD, as: (i) processing parameters such as applied voltage and temperature and (ii) embedded particles characteristic such as shape and size [46].

2.1.2. Electrodeposition

A simple electrodeposition system composed of electrolyte and at least two electrodes, i.e. anode and cathode. The mechanism involved in the generation of the films on the substrates through ED process is movement of metallic ions from the anode toward the cathode surface. These ions can be reduced at the electrolyte/cathode interface. To exploit the full benefits of electrodeposited films, it is essential to deeply understand the exact role of the each component in the process. The current density, stirring rate, electrolyte temperature, electrolyte pH, distance between anode and cathode, and deposition time are the factors which can markedly alter the final properties of electrodeposited films [47-58].

The electrodeposition technique is well established for protection of metallic implants by deposition of HAp-based coatings. Platinum and/ or graphite is suggested as an impressive anode material [59, 60].

There are two approaches to deposit the multilayer coatings by electrochemical methods, i.e. (i) using a single bath with altering voltage value; and (ii) using two or more different electrolytes for deposition of the each layer. Nevertheless, for HAp-containing multilayer coatings, there is a great tendency to employ the second way [61]. For instance, Pang et al. [62] have alternatively put the substrate (cathode) into the various suspensions. During this process, care should be taken to avoid washing the individual layers after bringing out the cathode from each electrolyte. A schematic of synthesis procedure of HAp containing multilayer coatings through two step electrochemical methods is represented in fig. 2. On the other hand, several investigations have employed dissimilar methods for production each layer of the multilayer coatings [63, 64].

2.2. Sol gel

Sol-gel is a well-established technique to synthesis the various types of coatings in which an inorganic colloidal suspension (sol) firstly forms followed by gelation of this sol within a continuous liquid phase (gel). Recently, sol gel method has been extensively employed for deposition of HAp
containing bio-active coatings. Two common processes of sol gel method are dip coating and spin coating. The HAp sol can be prepared using Ca-P precursors and incorporation of different solvents, e.g. ethanol and water [65-68]. Table 1 summarizes the used precursors in sol gel method accompanied by their required solvents. A schematic diagram exhibiting the various steps of the sol gel process for fabrication of HAp containing biocompatible coatings is represented in fig. 3.

Sol gel process provides appropriate condition for achieving multilayer coatings, wherein it is possible to control the thickness of each layer as well as chemical structure of the layers through tailoring the properties of the solution [69].

The multilayer deposits fabricated by sol gel process can be formed through two diverse ways, as: (i) single sol and (ii) two or more sols depending on the number of different components which should be deposited as separate layers [70-73]. For instance, Un et al. [71] used a single sol to synthesis HAp-TiO$_2$ multilayer film. They produced hybrid sol through incorporation of HAp powders into the as-prepared TiO$_2$ sol during gelling stage. The multilayer coatings synthesized through dip coating method, wherein the substrates were immersed into the prepared sol and bring out with a constant velocity. On the other hand, Xu et al.

![Fig. 2](image2.png)

Fig. 2- A schematic of synthesis procedure of HAp containing multilayer coatings through two step electrochemical methods.

![Fig. 3](image3.png)

Fig. 3- Schematic representation of the sol gel process for fabrication of HAp containing biocompatible coatings. The HAp containing multilayer coatings are deposited during second stage, i.e. sol gel process.

<table>
<thead>
<tr>
<th>Chemical composition of precursors</th>
<th>Used solvents</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phosphorous precursor such as triethyl phosphate and phosphorous pentoxide</td>
<td>Ethanol. Moreover, a little amount of water can be added to hydrolyze the sol.</td>
</tr>
<tr>
<td>Calcium precursor such as calcium nitrate</td>
<td>Ethanol</td>
</tr>
</tbody>
</table>

Table 1- Used precursors in sol gel method accompanied by their required solvents [65, 66, 69]
applied two various sols including TiO$_2$ and HAp sols to develop HAp-TiO$_2$ multilayer coating. The chemical composition of used sols by Xu et al. [70] is presented in Table 2.

2.3. Plasma spray

Generally, plasma spray is a well-developed method for protection of various substrates, wherein a molten or heat softened material is sprayed all over the given surface. The input materials should be in a powder form, then inject into a plasma flame which was previously heated, and finally accelerated toward the substrate. The powders hit the surface of the substrate, followed by a rapid cooling and sticking to the substrate [74]. Plasma spray approach was firstly used for deposition of HAp during the mid-1990s. The produced layers rapidly fix to the implant and give rise to the bone growth at the interface of implant-bone [75]. Nevertheless, the method was progressively improved so far. That is why plasma spray has become a hot topic in the deposition of HAp bio-active films [76].

To synthesis multilayer films via plasma spray method, the layers should be deposited on the substrate from different materials. In addition, each material is composed of dispersant and favored particles. The processing parameters may vary from a layer to another layer or be the same for all of the deposited layers. For example, Palanivelu et al. [77] demonstrated that the processing parameters such as plasma current, plasma voltage, powder feed rate, and spray distance for HAp single layer coating is different from the parameters employed for HAp/Al$_2$O$_3$-TiO$_2$ multilayer one. The reason is to meet the enhanced crystallinity of the multilayer coatings. Table 3 summarizes the foremost advantages of the introduced methods for the deposition of the multilayer HAp containing bio-coatings.

2.4. Other fabrication techniques

Beside the mentioned techniques developed for deposition of HAp-based multilayer coatings, there are other methods including micro arc oxidation (MAO), electron beam deposition, magnetron sputtering, and etc. [78-81]. In this section, the principles of these methods will be shortly reviewed.

Micro arc oxidation is an electrochemical surface treatment which can be satisfactorily employed for deposition of the oxide coatings. Within this method, a high potential applies to produce plasma which can modify the structure of oxide layer. The employed equipment for MAO process are similar to those used in electrochemical methods, namely electrolyte, usually a dilute alkaline solution, and at least two electrodes. To deposit HAp-based coatings through this technique, HAp is dispersed in an aqueous media. HAp powders can be adsorbed on the anode under the applied electrical field during MAO if they negatively charged in the electrolyte [79, 80].

<table>
<thead>
<tr>
<th>Fabrication method</th>
<th>Prominent advantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Electrochemical methods</td>
<td><strong>EPD</strong>&lt;br&gt;Cost efficiency, versatility, short operation time, ease of use for complex geometries, and simple procedure.</td>
</tr>
<tr>
<td></td>
<td><strong>ED</strong>&lt;br&gt;Enhanced homogeneity (rise from atomic level mixing), low crystallization temperature about 350 °C, nice ability to tune the chemical composition, fine structure, low cost, and potency for deposit on the complex shapes of the implants.</td>
</tr>
<tr>
<td>Sol gel method</td>
<td><strong>Plasma spray</strong>&lt;br&gt;Great control on the microstructure of the coatings, flexibility of the process, desirable rate of deposition, and enhanced adhesion of the films.</td>
</tr>
</tbody>
</table>

Table 2- The chemical composition of used sols by Xu et al. [71]

<table>
<thead>
<tr>
<th>HAp Sol</th>
<th>TiO$_2$ Sol</th>
</tr>
</thead>
<tbody>
<tr>
<td>C$_3$H$_6$O$_3$PO diluted with anhydrous ethanol+ distilled water+ Ca(NO$_3$)$_2$-4H$_2$O dissolved in anhydrous ethanol. Coating technique: spin coating at 1500 rpm for 15 s.</td>
<td>C$_{10}$H$_8$TiO$_2$ diluted in ethanol + NH(CH$_2$CH$_2$OH)$_2$ mixed with distilled water+ aging for 24 h. Coating technique: spin coating at 1500 rpm for 15 s.</td>
</tr>
</tbody>
</table>

Table 3- The foremost advantages of the introduced methods for deposition of the multilayer HAp containing bio-coatings
Electron beam deposition and magnetron sputtering are two main groups of physical vapor deposition (PVD) technique. Within electron beam deposition technique, a target material is bombarded via an electron beam to supply the chemical composition of the coating. The commonly used target material for HAp-containing coatings is heat treated HAp-CaO composite which provides the closest composition to the pure phase and stoichiometric HAp. The electron beam often generates from a charged tungsten filament. This electron beam is able to evaporate the target material. The formed gaseous can move through the high vacuum chamber and deposit on the defined substrate [78, 82].

The magnetron sputtering technique possess two successive steps, as: (i) acceleration of gas ions toward target material which have been supposed to deposit on the substrate; (ii) detachment (sputtering) of the atoms of target material followed by condensing of these sputtered atoms on the defined substrate. The size of target material, distance between the substrate and target material, and pressure of the sputtering chamber may deeply affect the quality of deposited coating by this technique [81, 83].

3. HAp-ceramic systems
3.1. HAp-TiO$_2$

A review on literature indicates that HAp-TiO$_2$ multilayer coatings can be successfully synthesized via a wide variety of methods including electrochemical methods [84], sol gel [71], plasma spray [85], micro arc oxidation (MAO) [79], electron beam deposition [78], airbrush [86], and magnetron sputtering [81]. Furthermore, there are some studies which have used two different methods to deposit each of HAp and TiO$_2$ layers. For instance, Yan et al. [87] have employed anodizing and electrodeposition methods to deposit TiO$_2$ and HAp layers, respectively.

In general, deposition of TiO$_2$ layer between substrate and HAp coating has several advantageous over single HAp layer, as follows: (i) increase in adhesion of HAp to substrate [61, 63, 78, 84, 88]; (ii) decrease in HAp decomposition [84]; (iii) improving corrosion resistance [63, 88]; (iv) enhancing the biocompatibility of substrate [80]; (v) Reducing the probability of crack formation in the deposited coating [78]; and (vi) preventing from releasing the metal ions from the substrates [79]. In next sections, a detail review will be done on the various properties of HAp-TiO$_2$ multilayer coatings.

3.1.1. Morphological features

Numerous studies have evaluated the morphological features of HAp-TiO$_2$ coating. It was found that the processing parameters such as arc power and the type of working gases in plasma spray method, voltage level in EPD and MAO procedures, and type of formulation in sol gel process, as well as heat treatment temperature are the factors which may deeply alter the microstructure-related features of these coatings [43, 71, 80, 88, 89].

Generally speaking, the as-deposited multilayer coatings exhibit two types of morphologies, namely (i) uniform and dense morphology [80, 88] and (ii) irregular and heterogeneous morphology [90]. However, several changes can be occurred in the morphology of the synthesized coating with change in both processing parameters and application of post heat treatments [80, 88].

Hereon, several studies will review to elucidate the exact influences of aforementioned factors on the morphological features of the coatings. Kim et al. [88] proved that the uniform and dense surface of as-deposited HAp-TiO$_2$ coating can change to rough and nanoporous one after heat treatment at 500 °C. The generated pores during the heat treatment process may originated form the decomposition of the organic materials. Nevertheless, TiO$_2$ interlayer was found to be poreless [70]. As a general rule, application of post heat treatment can also lead to formation of cracks throughout the microstructure of coatings if desirable temperature is not chosen. Un et al. [71] reported the formation of both macro and micro cracks when heat treated at above 400 °C, while the coatings heat treated at 400 °C have smooth and crack-free structure.

An overwhelming majority of investigations proved that there is no delamination or cracks in either interfaces of HAp and TiO$_2$ layers as well as TiO$_2$ layer and substrate. This can ensure the favorable bonding of layers which will be discussed in next section [70, 80, 88, 91, 92].

Additionally, Lee et al. [80] showed that it is possible to obtain a fully porous HAp layer with increasing the voltage of MAO process from 210 to 230 V. Similar to MAO, in order to guarantee the formation of crack-free and homogeneous microstructure, one should carefully control the voltage amount in EPD process. It was shown that
application of low voltage amounts may lead to generation of more uniform and adherent coatings with less crack numbers. In other words, the more the applied voltage, the more the agglomerated particles are. Actually, when a high voltage applies during EPD, there is no time for particles to deposit in suitable sites and also, they cannot move for rearrangement. Hence, there is a great tendency to form porous structure as well as crack containing coatings with increase in voltage level within EPD process [84, 93].

Fig. 4 exhibits the surface morphology of HAp-TiO₂ bilayer coatings fabricated by pulsed current electrodeposition. As seen in the picture, the coating is free from cracks, but the top layer HAp film has porous structure.

A network of cracks can be formed also by employing sol-gel process, however, a small change in formulation may result in the formation of a crack-free microstructure. The only factor which is responsible for crack formation is difference in physical integrity of TiO₂ layer. Fig. 5 indicates SEM morphology of HAp-TiO₂ multilayer coatings produced via two different types of formulations [71].

As obviously seen, change in sol gel formulation resulted in the elimination of formed cracks. Interestingly, it is possible to tailor the grain size of HAp layer with controlling the grain size of the TiO₂ layer. For example, Lee et al. [78] demonstrated that

![Fig. 4- Surface morphology of HAp-TiO₂ bilayer coatings fabricated by pulsed current electrodeposition [94].](image)

![Fig. 5- SEM morphology of HAp-TiO₂ multilayer coatings produced via two different formulations: (a) Ti-isopropoxide: nitric acid: ethanol: H₂O Ti(OC(CH₃)₃)₄:HNO₃:C₃H₇OH:H₂O 1:0.026:12:1 and (b) Ti-isopropoxide: nitric acid: n-propanol: acetyl acetone: H₂O Ti(OC(CH₃)₃)₄:HNO₃:C₅H₂(OH)₂CH₃:CH₃(C₆H₁₂O₂)₃:H₂O 1:0.016:22:0.5:0.2 [72](image)
the grain size of HAp layer is very similar to the underlying TiO$_2$ layer and it is over the range 250-350 nm.

3.1.2. Phase structure

The structure and present phases of HAp-TiO$_2$ multilayer coatings are widely studied using X-ray diffraction (XRD), fourier transform infrared spectroscopy (FTIR), and Raman spectroscopy [43, 63, 92].

Overall, the investigations are highly focused on detection of present phases and growth planes as well as grain size measurement. Also, the influence of processing parameters and heat treatment, as well as the role of TiO$_2$ layer is widely evaluated [71, 79, 80, 84, 90, 91].

For as-deposited coatings, it can be expected to observe the typical peaks related to HAp and TiO$_2$ phases, accompanied by peaks assigned to the used substrates, especially in the case of the coatings with low thickness. In general, change in processing parameters such as voltage of MAO and formulation in sol gel can remarkably alter the relative intensity of HAp and TiO$_2$ peaks [71]. For instance, Lee et al. [80] proved that the intensity of HAp peaks decreases with increase in voltage amount from 190 to 210 V, however, TiO$_2$ peaks show opposite trend. Interestingly, they demonstrated that HAp peaks fully disappeared with further increase in voltage to 230 V.

It should be noted that TiO$_2$ phase can be emerged in both Rutile and Anatase forms. The reported results about the effects of heat treatment on the phase transition as well as emerging new peaks in the microstructure of the coatings are inconsistent, wherein some studies showed the negligible influence of heat treatment [63, 84], while the others demonstrated the formation of new peaks as well as phase transformations [81, 91]. Hence, choosing optimum temperature for heat treatment is a critical point that must be taken into account.

Fig. 6 indicates the XRD patterns of HAp-TiO$_2$ multilayer coatings deposited by sol gel route after heat treatment at three different temperature. At the calcination temperature of 400˚C there is no sign for presence of TiO$_2$ since this phase is not crystalline and has a limited thickness. Amorphous TiO$_2$ coating produced by sol gel process first crystallizes to Anatase in the temperature range of 400–500˚C. Rutile diffraction peaks can be well distinguished after calcination at 600˚C [72]. In addition, Ozeki et al. [81] indicated the emergence of TiO$_2$ peaks after heat treatment at 500 ˚C due to the enhanced crystallinity. On the other hand, Wen et al. [91] confirmed that there is no noticeable change in XRD patterns of the coatings heat treated at 400 ˚C, while HAp phase can be formed with temperature rise up to 600 ˚C. In addition, the crystallinity of this phase was found to enhance with increase in temperature over the range 700-800 ˚C. Moreover, the studies
on the possibility of reaction between TiO$_2$ and HAp layers during heat treatment have resulted in contradictory conclusions, wherein Ozeki et al. [81] showed that these layer did not react within heat treatment at 500 °C owing to insufficient heat energy for initiation of chemical reactions, while Wen et al. [91] demonstrated that CaTiO$_3$ can be formed throughout the microstructure of the heat treated coatings at 600-800 °C, in accordance with the following equation:

$$\text{Ca}_{10}((\text{PO}_4)_6((\text{OH})_2 + \text{TiO}_2 \rightarrow 3\text{Ca}_3(\text{PO}_4)_2 + \text{CaTiO}_3 + \text{H}_2\text{O}$$

(eq. 1)

Based on reported XRD and Raman spectroscopy results, it can be inferred that the application of TiO$_2$ interlayer has two main effects on the microstructure of the multilayer coatings, as: (i) improvement in crystallization [90]; and (ii) decrement in HAp decomposition because this interlayer acts as barrier which restricts the amount of released metallic ions from the substrate [84]. Nevertheless, Lee et al. [78] confirmed the insignificant effects of this layer on the phase structure and crystallization temperature of the multilayer coatings.

Generally, HAp-TiO$_2$ multilayer coatings are mostly composed of ultrafine or nano sized crystallites [77, 78, 85, 89, 94]. For instance, Palanivelu et al. [77] have indicated that the mean crystallite size of HAp-Al$_2$O$_3$-TiO$_2$ multilayer coatings is 35-65 nm. Furthermore, Lee et al. [78] have measured the mean grain size of both HAp and TiO$_2$ single layers, as well as HAp-TiO$_2$ multilayer coating after heat treatment at 500-600 °C. The reported results are as follows: the grain size of TiO$_2$ single layer 40-100 nm, HAp single layer 250-350 nm, and HAp-TiO$_2$ multilayer coating has similar or slightly larger particles than TiO$_2$ single layer. Tomaszek et al. [85] have demonstrated the deposition of HAp-TiO$_2$ multilayer coating with mean crystallite size of 37-42 nm by plasma spray route. Fig. 7 indicates the HRTEM image of a HAp particle taken from HAp/TiO$_2$ bilayer coating and shows nanosized structure (about 20 nm) of the coating.

3.1.3. Mechanical properties

The studies concerned the mechanical properties of HAp-TiO$_2$ bio-coatings have mainly focused on the evaluation of the adhesion strength and hardness of these coatings. Results indicate that there are four factors including (i) features of TiO$_2$ interlayer such as thickness, (ii) post heat treatments, (iii) processing parameters such as voltage in EPD, and (iv) doping HAp with other elements may outstandingly alter the mechanical properties of the coatings [43, 61, 63, 78, 79, 84, 87, 88, 92].

Practical results demonstrated that the bonding strength of the synthesized HAp-TiO$_2$ coating may
deeply affected by the features of the TiO$_2$ layer including crystallinity, thickness, and uniformity. For instance, it is revealed that the less the thickness, the superior the bonding strength is. This is attributed to the lower thermal mismatch arise from the thinner TiO$_2$ layer [79, 88].

In general, the adhesion strength of HAp coatings can significantly improve (up to 60%) with application of a dense TiO$_2$ interlayer. In order to clarify the issue, Albayrak et al. [84] have deposited the coatings by EPD method using three different voltages, e.g. 10, 20, and 50 V, and they proved that the coatings deposited at 50 and 20 V exhibit lower adhesion strength than the single layer HAp ones. It is to be noted that they incorporated nanosized HAp and TiO$_2$ particles. Nevertheless, the adhesion strength of the bilayer coatings enhance and become more than the single layer ones with decrease in voltage amount to 10 V. This means that the adhesion strength of the HAp coatings can not only increase by incorporation of an interlayer and controlling the processing parameters is also of outstanding significance.

The main reason behind the adhesion strength improvement with application of TiO$_2$ interlayer is desirable chemical affinity of TiO$_2$ interlayer to the substrate, especially when using Ti and Ti-based alloys substrates, which may lead to the formation of a defectless, dense, and more uniform interface. On the other hand, it can greatly improve the wettability between HAp and the substrate [43, 63]. Also, incorporation of a TiO$_2$ interlayer was found to alter the failure location, wherein single HAp coatings fail through the interface of HAp and substrate, while HAp-TiO$_2$ failure occurs at only HAp-TiO$_2$ interface [78] or at both interfaces of HAp-TiO$_2$ and TiO$_2$-substrate [88].

Altogether, there are two parameters involved...
in the promotion of the adhesion strength of HAp-
TiO$_2$ coatings after heat treatment, as: (i) Possible
reactions between HAp and TiO$_2$ layers during
the heat treatment process. In the case that both of
HAp and TiO$_2$ layers are in amorphous form before
the heat treatment process, they can interact at
atomic scale. is one of the possible products of such
reactions; and (ii) generation of more powerful
mechanical interlocking originated from the
increased surface roughness at the interface of the
layers during the heat treatment [63, 78]. Although
application of heat treatment is a significant
approach to improve the bonding strength of these
coatings, selecting an optimum temperature for
such treatments are more important, where
Kim et al. [88] have assessed the influence of the
temperature of heat treatment process and
demonstrated that the bonding strength of HAp-
TiO$_2$ coatings markedly increases with temperature
rise from 400 to 500 °C. Fig. 8 shows the bonding
strength of HAp-TiO$_2$ multilayer coatings to the
substrate versus heat treatment temperature.

It is to be noted that doping HAp with Mg can
slightly increases the bonding strength due to
production of the denser of HAp layer [87]. Table 4
presents the effect of application TiO$_2$ interlayer on the
adhesion strength of HAp single layer coatings.

3.1.4. Corrosion behavior

The biomaterials incorporated into the human
body, especially those that are supposed to work
for long period, are exposed to localized attacks
originated from the harsh biological influences.
This can result in relaxation of many cytotoxic
corrosion products which may dramatically alter
the cell life and performance. Therefore, it is
essential to protect the fabricated bio-implants via
anti-corrosive bio-coatings [90, 95].

A vast majority of studies proved the positive
effects of TiO$_2$ interlayer on the corrosion behavior
of HAp-TiO$_2$ bio-coatings. More importantly, the
thickness of this interlayer plays a critical role in
determining the final corrosion performance of
the coatings. Moreover, a dense TiO$_2$ interlayer
satisfactorily prevent the ions and electrons
transportation along the implant and SBF electrolyte
[63, 88]. Generally, the more the thick interlayer
the better the corrosion resistance, however,
according to the effects of interlayer thickness on the
bonding strength of the coatings, care must be
taken to control the thickness in such a way that
it can provide optimum efficiency. Kim et al. [88]
reported that a TiO$_2$ interlayer with approximately
200 nm thickness shows favorable corrosion
properties combined with acceptable adhesion
strength. Furthermore, results demonstrated that
HAp-TiO$_2$ multilayer coatings have the nobler open
circuit potential (OCP) than a single layer HAp
coating. Morphological assessments after corrosion
test confirmed the generation of numerous pores
throughout the microstructure of the HAp- based
coatings. Nevertheless, the size of these pores
noticeably decreases when a dense TiO$_2$ layer
deposits between the implant and HAp coating,
thereby hindering the straight contact between
corrosive medium and implant. The mechanism
concerning the formation of pores during corrosion
test, are as follows: (i) Formation of H$^+$ ions at the
surface of the implant according to the following
reaction:

$$
\text{Ti} + 2\text{H}_2\text{O} \rightarrow \text{TiO}_2 + 4\text{H}^+ + 4\text{e}^-
$$

(eq. 2)

(ii) Acidification of the medium by producing
H$^+$ ions, which consequently dissolves HAp and
forms larger pores, as:

$$
\text{Ca}_{10}((\text{PO}_4)_6(\text{OH})_2 + 2\text{H}^+ \rightarrow 10 \text{Ca}^{2+} + 6\text{PO}_4^{3-} + \text{H}_2\text{O}
$$

(eq. 3)

Yan et al. [87] compared the corrosion
resistance of Ti sheets protected by HAp-TiO$_2$
and magnesium-doped HAp-TiO$_2$ coatings. They
demonstrated that Ti sheets coated by magnesium-
doped HAp-TiO$_2$ coatings exhibit superior
corrosion properties. Nevertheless, the mechanism

<table>
<thead>
<tr>
<th>Reported $E_{corr}$</th>
<th>Reported $I_{corr}$</th>
<th>Fabrication method</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>-75.69 (mV)</td>
<td>0.10 (µA cm$^{-2}$)</td>
<td>EPD</td>
<td>[9]</td>
</tr>
<tr>
<td>-0.315 (V)</td>
<td>---</td>
<td>Electrochemical deposition</td>
<td>[11]</td>
</tr>
<tr>
<td>-339 (mV)</td>
<td>0.28 (µA cm$^{-2}$)</td>
<td>ED</td>
<td>[12]</td>
</tr>
</tbody>
</table>
involved in this enhancement is not reported. On the other hand, the results reported by Etminanfar et al. [94] revealed that the corrosion resistance of NiTi substrate which contains TiO$_2$/HAp bilayer coating is less than a single layer HAp coating. The difference in electrodeposition mechanism of nanostructured HAp coating and localized corrosion of TiO$_2$ layer is proposed to clarify the obtained results. Table 5 provides an overview on the corrosion current density and corrosion potentials of HAp-TiO$_2$ coatings deposited on titanium based alloys by various techniques.

3.2. HAp-ZrO$_2$

Compared to HAp-TiO$_2$ system, fewer studies have been done to deal with the various properties of HAp-ZrO$_2$ multilayer coatings. The major aim behind the incorporation of ZrO$_2$ interlayer is to enhance the bonding strength between the implant and HAp coating. Almost all of studies have employed plasma spray method for deposition of these multilayer coatings [96-99]. Besides, pulsed laser deposition method has been used [100].

3.2.1. Morphological features and phase evaluation

A review on the present investigations prove that there is no study dealt with the assessment of surface morphology in the HAp-ZrO$_2$ multilayer coatings. Only one study conducted by Chou et al. [97] in which they compared the morphology of HAp-ZrO$_2$ coating with the single HAp-ZrO$_2$ composite coating. They demonstrated that the inclusion of ZrO$_2$ particles into HAp layer degrades the melting condition of the coating and results in the generation of more unmelted particles throughout the microstructure of this coating than un-reinforced one [97]. The generation of unmelted particles in both coatings may originated from the poor thermal conductivity of HAp layer, which prevents the generated heat during the plasma spray to reach to the some particles. However, these unmelted particles do not always have a negative effect on the properties of the coatings so that they can properly act as binder and preserve the integrity of coating [96].

It is believed that the ZrO$_2$ interlayer can appropriately bond to HAp layer and increase the bonding strength of the coatings which will be discussed in the next section. Here, it should be noted that the surface roughness of the coatings significantly increases with embedding ZrO$_2$ layer. Fig. 9 exhibits the SEM cross-section image of HAp-ZrO$_2$ coatings.

Literature have mainly attempt to assess the probable diffusion between the layers and also finding out the mechanisms involved in such diffusion [98-100]. Studies on the interface of HAp

Fig. 9- SEM cross-section image of HAp-ZrO$_2$ coatings, wherein T, Z, and H letters refer to Ti substrate, ZrO$_2$, and, HAp respectively [99].
and ZrO$_2$ layers clearly reveal the diffusion of Ca ions form HAp to ZrO$_2$ interlayer which can form a diffusion bond, thereby improving the adhesion between the layers. The detailed mechanism for this diffusion is not illustrated in both papers [98, 99]. On the other hand, during synthesizing HAp single layer, it was shown that the present Ti ions in Ti based substrates can diffuse to HAp layer and form TiO$_2$ during next heat treatment process. Application of ZrO$_2$ interlayer can suitably hinder this diffusion [100]. Although, there is no discussion concerning the possible advantageous or disadvantageous of hindering diffusion with application of the interlayer, it was reported in section 3.1.2 that metallic ions can result in HAp decomposition.

Obtained XRD patterns for HAp- ZrO$_2$ multilayer coatings demonstrate the presence of both HAp and ZrO$_2$ phases throughout the microstructure of the coatings and there is no peak indicating the formation of other phases[100].

All in all, the present studies about the morphological features of such coatings cannot fulfill the demands of researchers and deep investigation are needed to fully clarify the relation between the various factors and microstructural properties.

3.2.2. Mechanical properties

Generally speaking, the present investigations mainly address the influences of deposition of ZrO$_2$ interlayer as well as post heat treatment on the mechanical properties of the coatings. Almost all of the results demonstrate the improve in adhesion strength of HAp layer with substrate through application of ZrO$_2$ interlayer [96-98, 100]. The proposed mechanisms for such enhancement are as follows: (i) increase in interfacial reactions at HAp-ZrO$_2$ interface rather than HAp-substrate interface;(ii) decrease in thermal mismatch between substrate and HAp layer; (iii) improvement in mechanical interlocking arise from rough surface of ZrO$_2$ interlayer; and (iv) probable interdiffusion between the existing layers generating diffusion bond [96-98].

In addition, empirical studies demonstrated a further improvement in bonding strength of the multilayer coatings with inclusion of ZrO$_2$ second phase to HAp layer [96]. Note that the adhesion strength of HAp+ZrO$_2$ composite coating is still less than HAp-ZrO$_2$ multilayer one [97]. The fracture surface of the multilayer coatings exhibit less area percentage of adhesive failure than single layer ones, indicating the enhancement in cohesive strength [97].

In order to guarantee the positive effects of post heat treatment on the bonding strength of as-deposited multilayer coatings, it is vital to select optimum temperature. For example, Lee et al. [96] have reported that the coatings heat treated at 650-750 °C exhibit the strongest adhesion to the implant. It is concluded that the higher temperatures may degrade the adhesion due to the generation of more severe dilation mismatch at HAp-ZrO$_2$ interface. Post heat treatment promotes the bonding strength of the plasma sprayed coatings through favorable crystallization of HAp layer which leads to the extensive volume shrinkage of this layer, thereby forming a loose structure accompanied by enhanced fracture toughness. Table 6 represents the bending strength values of HAp single layer and HAp-ZrO$_2$ multilayer coatings.

4. HAp-polymeric systems

4.1. HAp-Chitosan

Among polymeric materials, chitosan is commonly used for fabrication of HAp-based multilayer coatings. As mentioned previously, pure HAp coatings have inappropriate adhesion to the implants. An incorporation of chitosan layer can properly overcome this challenge [62, 64]. Moreover, it can positively affect the biocompatibility of the coating and provide a precise control on drug release process [101, 102]. Table 6 suggests the adhesion strength values of HAp single layer and HAp-ZrO$_2$ multilayer coatings.
102]. There are multiple studies investigating the fabrication methods as well as the properties of the HAp-chitosan composite coatings, however, the properties of HAp-chitosan multilayer coatings have been less addressed. Unlike HAp-ceramic systems wherein HAp layer is located at the top of the multilayer coating, in HAp-polymeric systems, it can be placed at both bottom and top layer [62]. Electrochemical methods such as ED [102, 103] and EPD [39, 62], dip coating [101], and layer by layer deposition technique [104] have been widely employed in order to produce the HAp-chitosan multilayer coatings.

4.1.1. Morphological features and phase evaluation

Altogether, there are three types of morphologies reported for HAp-chitosan multilayer coatings, as: (i) spindle-like, (ii) regular shape, and (iii) trace needle-like [31, 105]. Also, in some cases, it is observed that the deposited multilayer coatings can preserve the morphology of the incorporated HAp layer. For instance, Liu et al. [101] used HAp nanorods with 20 nm diameter to produce HAp/chitosan/carbon fiber felts multilayer coatings. Also, it is exhibited that the deposited upper layers may satisfactorily fills the present pores in the microstructure of the lower layers, thereby creating an opportunity to achieve a smoother surface [102]. For HAp-chitosan multilayer coatings, almost all of the presented cross section images showed the favorable adhesion of the deposited layers to each other and to the substrate [62, 64, 103].

The phase analysis of HAp-chitosan multilayer coatings exhibits that the main phase of these coatings is HAp with low degree of crystallinity [101, 105]. Nevertheless, the peaks related to chitosan can also be observed. Moreover, the elemental analysis results are slightly different from each other so that the reported value for Ca/P molar ratio of such coatings varies over the range 1.36 [101] to 1.67 [105] which confirms the presence of some other calcium phosphate phases when the Ca/P ratio is not 1.67.

4.1.2. Corrosion behavior

Although the performed studies demonstrated that the corrosion resistance of the substrates can be considerably improved with deposition of HAp-chitosan multilayer coatings, the mechanism involved in such improvement is not discussed so far. Furthermore, the distinct effects of each layer, in other words, the role of each layer e.g. HAp and chitosan, in corrosion behavior enhancement has not been well elucidate [62, 103].

4.2. HAp-other polymers

In addition to chitosan, there are other polymers such as collagen, polycaprolactone and poly-L-Lactide (PLLA) which have been used to produce HAp-polymeric multilayer coatings. Dip coating and layer by layer (LBL) methods have been employed for fabrication of such coatings [30, 106]. Nie et al. [106] have produced HAp-PLLA multilayer coating with 2-5 layers. The deposited coatings was found to be smooth and can suitably reduce the porosity of protected scaffold with increase in the number of layers from 2 to 5. Accordingly, the compressive strength of the coated scaffold is improved with number of layers.

5. Concluding remarks and outlook

The present review has attempted to introduce the common methods for fabrication of HAp-containing multilayer coatings including electrochemical, sol-gel, and plasma spray routs. It also presents a wide overview of the morphological, microstructural, mechanical, and corrosion properties of HAp-ceramic and HAp-polymeric multilayer coatings. It was clearly highlighted that the main drawback in pure HAp coatings is their poor adhesion to the implants.

The studies in the field of HAp-ceramic systems showed that the deposited ceramic layers, e.g. TiO\textsubscript{2} and ZrO\textsubscript{2}, are strongly adherent to HAp and substrate which leads to a remarkable improvement in the mechanical and corrosion behavior of pure HAp coatings. It was found that the (i) processing parameters, (ii) post heat treatments, (iii) doping the HAp layer with other elements, and (iv) features of deposited interlayer, thickness in particular, are of influencing factors which may alter the final properties of theses multilayer coatings. Despite the large number of studies performed so far, drawing a correlation between processing parameters and final properties of the coatings as well as investigating the involved mechanisms in increasing the mechanical and corrosion properties, is still a challenge for HAp-ceramic systems.

Unlike HAp-ceramic systems, there are less studies dealt with the HAp-polymeric systems. It can be easily noted that there is a dramatic need for detailed evaluation of the involved factors in increasing the final properties of HAp coating.
with incorporation of the polymeric layers. Also, practical studies are needed to assess the influence of processing parameters and post heat treatments on the features of such coatings.

Albeit the mechanical and corrosion properties of the implants are of primary significance in biomedical applications, there are no sufficient investigations concerning these properties in the case of HAP containing multilayer coatings, especially in HAP-polymeric ones. Therefore, further studies will be needed to deeply evaluate the mechanisms involved in the mechanical and corrosion behavior accompanied by presenting novel approaches to enhance their properties. Also, application of new and high efficiency techniques such as metal organic chemical vapor deposition (MOCVD) for deposition of either HAp or ceramic/polymeric layers can be a favorable goal for future studies.

Altogether, according to the reviewed features in the previous sections, HAP based multilayer coatings have bright prospect since they benefit from biocompatibility as well as the enhanced adhesion to the substrate.

References
34. Canmillu V, Lusvarghi L, Sola A. Design of Experiments (DOE) for the Optimization of Titania-hydroxyapatite


