

REVIEW



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Surface functionalized bioceramics coated on metallic implants for biomedical and anticorrosion performance – a review

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In modern days, the usage of trauma fixation devices has significantly increased due to sports injury, age-related issues, accidents, and revision surgery purposes. Numerous materials such as stainless steel, titanium, Co–Cr alloy, polymers, and ceramics have been used to replace the missing or defective parts of the human body. After implantation, body fluids (Na^+ , K^+ , and Cl^-), protein, and blood cells interact with the surface of metallic implants, which favours the release of ions from the metallic surface to surrounding body tissues, leading to a hypersensitive reaction. Body pH, temperature, and interaction of immune cells also cause metal ion leaching and lose host cell interaction and effective mineralization for better durability. Moreover, microbial invasion is another important crisis, which produces extracellular compounds onto the biomaterial surface through which it escapes from the antimicrobial agents. To enhance the performance of materials by improving mechanical, corrosion resistance, antimicrobial, and biocompatibility properties, surface modification is a prerequisite method in which chemical vapour deposition (CVD), physical vapour deposition (PVD), sol–gel method, and electrochemical deposition are generally involved. The properties of bioceramics such as chemical inertness, bioactivity, biocompatibility, and corrosion protection make them most suitable for the surface functionalization of metallic implants. To the best of our knowledge, very limited literature is available to discuss the interaction of body proteins, pH, and temperature onto bioceramic coatings. Hence, the present review focuses on the corrosion behaviour of different ceramic composite coating materials with different conditions. This review initially briefs the properties and surface chemistry of metal implants and the need for surface modifications by different deposition techniques. Further, mechanical, cytotoxicity, antimicrobial property, and electrochemical behaviour of ceramics and metal nitride coatings are discussed. Finally, future perspectives of coatings are outlined for biomedical applications.

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1. Introduction

For the past few decades, metallic implantable materials such as Ni–Cr alloy, Co–Cr alloy, stainless steel, and Ti and Ti alloy have been used in the implant industries for surgical and implant fixation purposes.^{1–4} Titanium (Ti) and its alloys are majorly used in dentistry for prosthodontics implants as teeth or crown (bridge or denture), and commercially pure titanium (cp-Ti) shows higher ductility than triphasic Ti–6Al–4V alloy.⁵ Similarly, medical grade 316L stainless steel (316L SS) is one of the materials predominantly used as cardiovascular stents,⁶ femoral implant, ankle fracture,⁷ etc., due to its low cost, ease of fabrication, good corrosion resistance, and mechanical properties. Even though 316L SS and Ti-based alloys are used for biomedical applications, they exhibit poor surface hardness, low abrasive and wear resistance, and high coefficient of friction, and susceptible nature for localized corrosion in the human body causes a detrimental effect to implant durability.⁸ 316L SS constitutes nickel, chromium, and iron as major elements in which, nickel shows higher toxicity when released into the bloodstream or implant surrounding tissues. Sachiko *et al.*⁹ studied the release of nickel ions in biological environments along with its carcinogenic and allergic reactions in rats. The significance of biomedical materials has dramatically increased due to frequent surgeries, age-related implantations, accidents, and medical complications.

This article presents a comprehensive review of recent research focusing on corrosion protection behaviour of various bioceramic coatings in *in vitro* biological environment conditions for biomedical applications. Also, past works on bioceramic coatings by PVD technique are reviewed, and their impact on the corrosion resistance performance, biomechanical integrity, and biocompatibility are discussed. Microbiologically influenced corrosion on bioceramics surfaces is also discussed. Further, the

importance of surface modification by ceramics for effective bone repair is also discussed in detail. Overall the survey of surface modification conveys the importance of various ceramic coatings and their properties in the biological environment.

2. Properties of ideal implants

The properties of ideal implant materials depend on the following three major factors determining the fate of implant materials. Firstly, bacterial adherence followed by surrounding tissue interactions¹⁰ is a crucial factor affecting subsequent tissue and cellular responses.¹¹ *Pseudomonas aeruginosa* (*P. aeruginosa*) is a vital microorganism that causes implant-associated infections, and it is isolated from patients frequently with cystic fibrosis, burns, and clinical environments.¹² Secondly, the whole blood interaction on the implanted material surface will primarily initiate (i) adsorption of proteins, (ii) platelet adhesion and activation, (iii) thrombi stabilization through the formation of fibrin network, and (iv) surface-induced thrombosis as well as subsequent embolism.¹³ The implanted material should not cause platelet adhesion and activation. Third, the biocompatibility of implant–cell interactions plays a significant role in determining the implant's durability. In general, biocompatibility defines the ability of implant materials to interact with surrounding cells, tissues or the body without harmful effects (Fig. 1).¹⁴

Therefore, biocompatibility is a prerequisite parameter for artificial implants to explore the chemical bonding of living tissues to form a bone-like apatite layer on its surface in any physiological environment.^{15,16}

3. Surface chemistry and biofilm formation

The development of initial bacterial invasion and subsequent biofilm formation on biomaterial surfaces may be influenced



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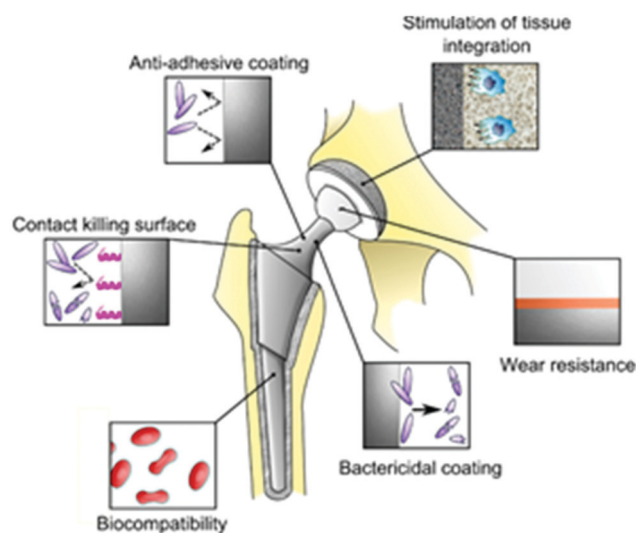


Fig. 1 Properties of an ideal bio-implant. Reproduced with permission from ref. 14. Copyright 2014, MDPI.

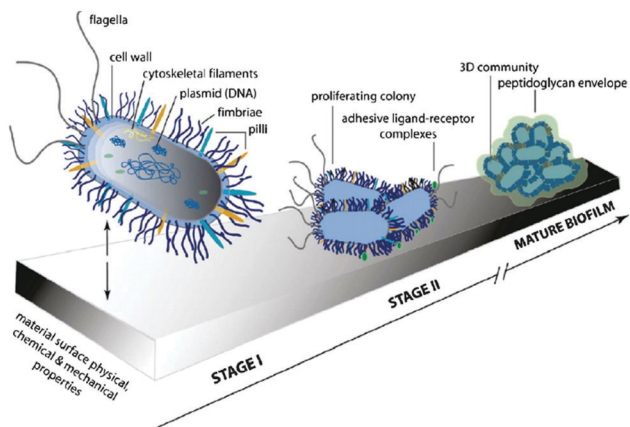


Fig. 2 Different stages of biofilm formation. Reprinted with permission from ref. 21. Copyright 2013, Royal Society of Chemistry.

by their surface energy, surface roughness, chemical structure, and other surface characteristics, such as summit density, skewness, and texture aspect ratio.^{17,18} Also, bacterial cell and biomaterial surface properties, such as hydrophobicity and hydrophilicity, affect bacterial invasion and subsequent biofilm formation.¹⁹ The mechanical properties, microbial invasion, and subsequent biofilm formation of the implant materials could substantially determine long-term survival in the oral environment. Bacterially driven biofilm formation causes inflammation in adjacent mucosa and develops peri-implantitis, leading to implant failure (Fig. 2).^{20,21}

The occurrence of peri-implantitis has been reported in the range of about 28–56% with dental implants.^{22,23} Oral microbiota consists of 700–1000 different species,²⁴ contributing to

the microbial biofilm formation with diverse microbial colonies in the oral cavity.²⁵ The control of bacterial infection is still a growing concern in hospitals and various medical and health care facilities. Ti-based implant materials are commonly used for orthodontic and orthopedic applications, and it acts as photocatalyst upon exposure to ultraviolet light. During irradiation, hydroxyl radicals and superoxide ions will be generated, which will be highly reactive with organic compounds.²⁶

Moreover, some bacteria present in the oral environment secrete calcium-based components such as calcium carbonate/phosphate as an extracellular secretion deposited onto the tooth surfaces. Once the bacterial biofilm gets matured, there will be a possibility to adhere other pathogenic oral bacteria such as *Porphyromonas gingivalis*, *Streptococcus mutans*, etc., in an unclean mouth environment followed by biofilm formation and infection. In order to inhibit the bacterial adhesion, ZrO_2 was deposited on Ti surface (Fig. 3a). Fig. 3b–e shows the calcium precipitating oral bacterial adhesion and its extracellular secretion onto Ti surfaces.²⁷ In this regard, oral calcium precipitating bacterial adhesion was studied on single and multilayer of TiN and TiO_2 coatings.⁵ The study indicated that TiN and TiO_2 single and multilayer-coated 316L SS samples protect, calcium precipitating oral bacterial invasion than bare 316L SS samples (Fig. 4a–d).⁵

The anatase phase of TiO_2 coatings drastically decreases the leaching of metal ions with improved hydrophilicity. Further, the TiO_2 stimulates the hydroxyapatite formation while soaked in SBF solution, which is influenced by different anatase phases present in the coating. Joo *et al.* prepared the anatase phase of TiO_2 coatings using the anodization method, which could improve the photocatalytic effect.²⁸ TiO_2 nanotube formation also plays a significant role in improving bone cell interaction

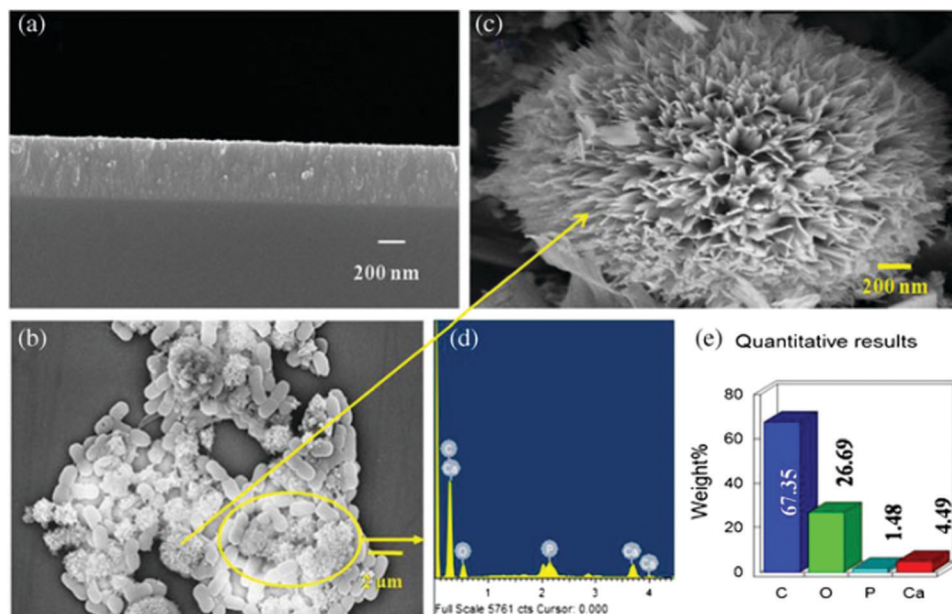


Fig. 3 (a) Cross-sectional images of the ZrO_2 coating, (b and c) calcium precipitation on bacterial cell wall and (d and e) elemental analysis of the precipitated compounds. Reproduced with permission from ref. 27. Copyright 2016, Springer.

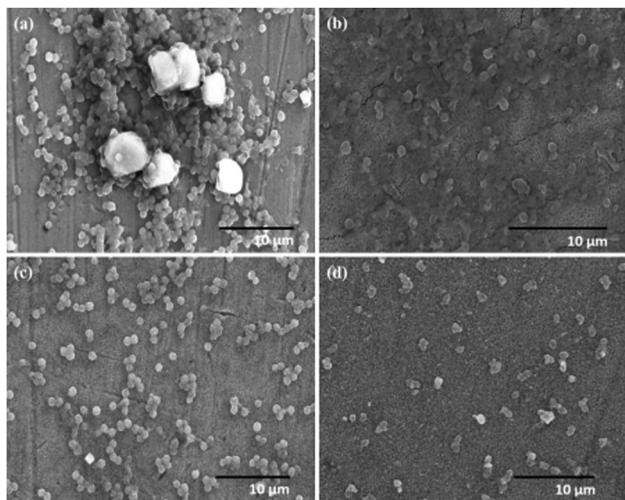


Fig. 4 SEM images of calcium precipitating oral bacterial adhesion onto (a) 316L SS (b) TiN (c) TiO₂ and (d) TiN/TiO₂ multilayer coatings. Replicated with permission from ref. 5. Copyright 2014, Springer.

and integration with coated implants. Also, recent studies suggest that mixed oxide phases (anatase and rutile) exhibit a synergistic effect in photocatalytic response rather than anatase phase alone.²⁹ However, the phase selective coating and patterned coatings are not possible by the anodization process. Huang *et al.* proposed that the anatase phase of TiO₂ underwent improved platelets and adhesion activation; whereas, the rutile phase of TiO₂ significantly reduced platelet adhesions and its activations.³⁰

4. Corrosion behavior of biomaterials

Cp-Ti and Ti-6Al-4V alloys are used as essential biomaterials, owing to their number of advantages such as high corrosion resistance, excellent strength, and good biocompatibility.^{31,32} However, the higher elastic modulus of Cp-Ti (102–105 GPa) than human bone (4–30 GPa) tissues may exhibit some controversy amidst artificial implant and surrounding bone tissues, which is known as the “stress shielding effect”,³³ which impedes broad applications of Ti-alloys. Besides, complex systems such as proteins, blood, and mechanical stress in the human body also promote the leaching of some alloying elements like Ni, Al, and V, which may cause allergic reactions and serious health issues.^{34,35} Also, tribology and hardness properties are essential for metallic implants exhibiting higher shear in the physiological environment causing the metallic ions to release and subsequently affecting the lifespan of the implants.³⁶ Its wear analysis also determines the lifespan of the materials to illustrate the hardness and coefficient of friction of surface-tailored films.³⁷ Moreover, extracellular compounds such as hydrogen peroxide (H₂O₂) and lactic acid (LA) produced by bacteria and the immune system deteriorate the surface of implants.

Since the human blood constitutes proteins, ions, enzymes, and chemical compounds, the implanted materials are exposed

to a complex biological environment, which may lead to corrosion after implantation. Hence, the implanted materials release their metal ions from the metal surface into surrounding cell tissues and bloodstream by biodegradation. For instance, medical-grade stainless steel is highly susceptible to pitting corrosion caused by aggressive metal ions such as Cl[−], K⁺, Na⁺, *etc.*, present in the human physiological solution, creating allergenicity and immunogenicity. Also, once the implant materials are fixed into the human body, the dissolved blood serum proteins present in the blood plasma immediately form a monolayer in implant surroundings, determining its subsequent process. Omanovic and Roscoe³⁸ observed a large amount of metal dissolution from the stainless steel surface in the presence of buffer solution.

Similarly, Williams *et al.*³⁹ stated that BSA protein in the saline solution accelerates stainless steel corrosion in *in vitro* conditions. Sasikumar and Rajendran⁴⁰ studied the corrosion protection behavior of Ti-15Mo alloy in the presence of acidic and neutral artificial saliva solutions. They conducted the study in the presence of three different concentrations, such as 2500, 5000, and 10 000 ppm of sodium fluoride (NaF) solutions, along with 7.2 and 3.5 pH conditions (Fig. 5a and b). The results revealed that higher concentrations of NaF contents exhibit a detrimental effect on the metallic implant alloys.⁴⁰

The corrosion protection behavior of an implant relies not only on the surface property of the material but also on its interaction efficacy with the surrounding environment.⁴¹ The corrosion behaviour of metal and metal alloys is affected by the pathogens present in the oral environment (contain saliva, gastric acid reflux, dental plaque, and bacteria) as well as at implant fixation sites. In general, the bacteria will be abundant in the oral environment due to warm, humid conditions, temperature levels and moderate pH, and abundance of nutrients, which causes ideal conditions for the bacteria to grow further for bacterial invasion.⁴² Microbiologically induced corrosion (MIC) is the deterioration of metal/implant surface, which is generally observed in the medical industry, owing to the indirect/direct activity of pathogenic living microorganisms. However, the microbial invasion, biofilm formation, maturation, and further metabolite production on implant materials is still unknown.⁴³ Especially, sulphate reducing bacteria (SRB) predominantly invade implant material surface and undergo microbial metabolic activities, which can cause pitting corrosion behaviour on stainless steel.⁴⁴ Biofilm formation onto the surface of implant materials and subsequent implant deterioration is a major challenging factor and hence, it is necessary to protect the implant from bacterial corrosion.

Mystkowska studied the effect of *Desulfotomaculum nigrificans* sulfate-reducing bacterial (SRB) corrosion against Ti6Al4V and Co-Cr-Mo alloy implant materials. After 28 and 56 days of bacterial incubation containing Co-Cr-Mo and Ti-6Al-4V alloy implant materials, Co-Cr-Mo alloy material showed lots of pits on its surface than Ti-6Al-4V alloys. Besides, this pitting nature was highly pronounced after 56 days of incubation.⁴⁵ Similarly, *S. mutans* and *S. sanguinis* species (which created biofilms easily on teeth surfaces) could deteriorate various orthodontic SUS appliances.

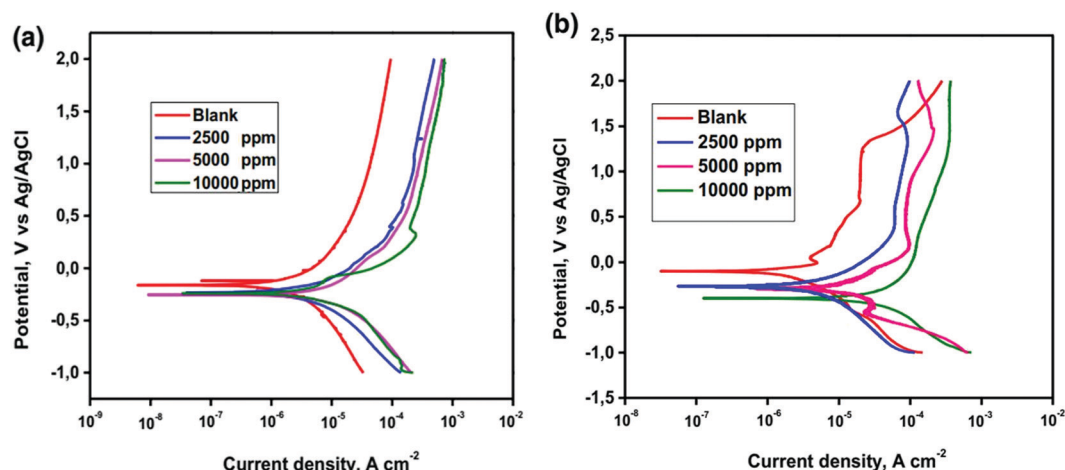


Fig. 5 PDP curves of Ti-15Mo alloy in acidulated artificial saliva solution. Reproduced with permission from ref. 40. Copyright 2017, Elsevier.

It is well known that the performance and durability of metallic implants are highly dependent on their wear and corrosion resistance properties. During the manufacturing of patient-specific implant fabrication, the heat treatment process also majorly affects implant materials' properties. Some of the issues like a severe cellular response to wear debris from contact motion and fretting fatigue in artificial joints continue to face many challenges in designing medical implants through surface modifications.

5. Need for surface modification

Surface tailoring is a prerequisite method to mimic foreign material as the host system. In modern implant industries, surface modification of metallic implants by appropriate materials paves the way to elevate corrosion resistance, biocompatibility, mechanical and antimicrobial behaviour. In *in vitro* evaluation, surface-tailored implant materials are the prerequisites to mimic the *in vivo* condition and improve ideal bioimplants.⁴⁶ Numerous methods have been employed to tailor the surface of desired metallic implants, such as chemical vapour deposition (CVD), physical vapour deposition (PVD), electrodeposition, sol-gel coating, dip coating, *etc.* Among the various methods, the PVD technique is a valuable tool to deposit the material by which exact stoichiometry, film density, high adhesion strength, and uniformity can be achieved.

In addition, obtaining nanotextured implant surfaces by chemical etching is another important technique to repel bacterial adhesion and increase osseointegration. Jang *et al.*⁴⁷ prepared nanotextured (NT) surface of medical grade 316L SS with 20–25 nm diameter pores and nano protrusions by electrochemical etching method to repel *E. coli* and *S. aureus* bacterial adhesion (Fig. 6a–c). For *S. aureus*, 86.2% and 81.2% reduction were found after 24 h and 48 h of incubation, respectively, from the NT 316L SS surface, compared to 316L SS. Similarly, 95.9% and 99.6% of gram-negative bacterial reduction were observed on NT 316L SS after 24 and 48 h of exposure, respectively, due to precisely controlled nanopores

that significantly repel bacterial adhesion. In addition, fimbriae formation was clearly seen from un-treated 316L SS; whereas, no morphological changes observed from NT 316L SS surfaces confirmed its less binding nature on the surface.

6. Antimicrobial coatings and their significance

Bacterial invasion and subsequent biofilm formation on implant material surface lead to severe challenges to implant durability and performance. Also, implant failure and revision surgery lead to both an economic crisis and illness.⁴⁸ Microbial adhesion and invasion on medical equipment, implants, and food processing devices can cause severe human health complications. The detachment of microbial colonies on water pipelines and industry instruments is quite easy and expensive. But, the removal of bacterial biofilm by mechanical detachment in biomedical implants or instruments in medical applications is quite a complication, since it involves, extensive debridement and revision surgery. Though antibiotic consumption shows effective prevention, the less sensitivity of bacteria to corresponding antibiotics induced through biofilm mode of growth also leads to an increased probability of multi-resistant strains.⁴⁹

The requirement of ceramic implants increased significantly in the range from 428 000 to 2.16 million per year for various implant surgeries. Hip replacement is one among the implant fixation processes fabricated by ceramic materials. For instance, Chevalier found that more than 600 000 ceramic femoral heads are implanted worldwide.⁵⁰ In this aspect, bacterial invasion and subsequent colonization of ceramic implants are still an important crisis. Jangra *et al.*⁵¹ stated that ZrO₂ coatings exhibit microbicidal activity against *E. coli*, but it does not evolve microbicidal activity against a wide range of bacterial species; thereby, the implanted material is prone to invasion by various microbial species, eventually leading to elevated inflammation and implant destructions. In addition, *E. coli*, *Enterococcus faecalis*, *Corynebacterium* sp., and *Staphylococcus* sp., bacteria

Biocompatible, Nano-Porous & Protrusive Stainless Steel 316L Surfaces Created by Electrochemical Etching for Inhibition of Bacterial Adhesion

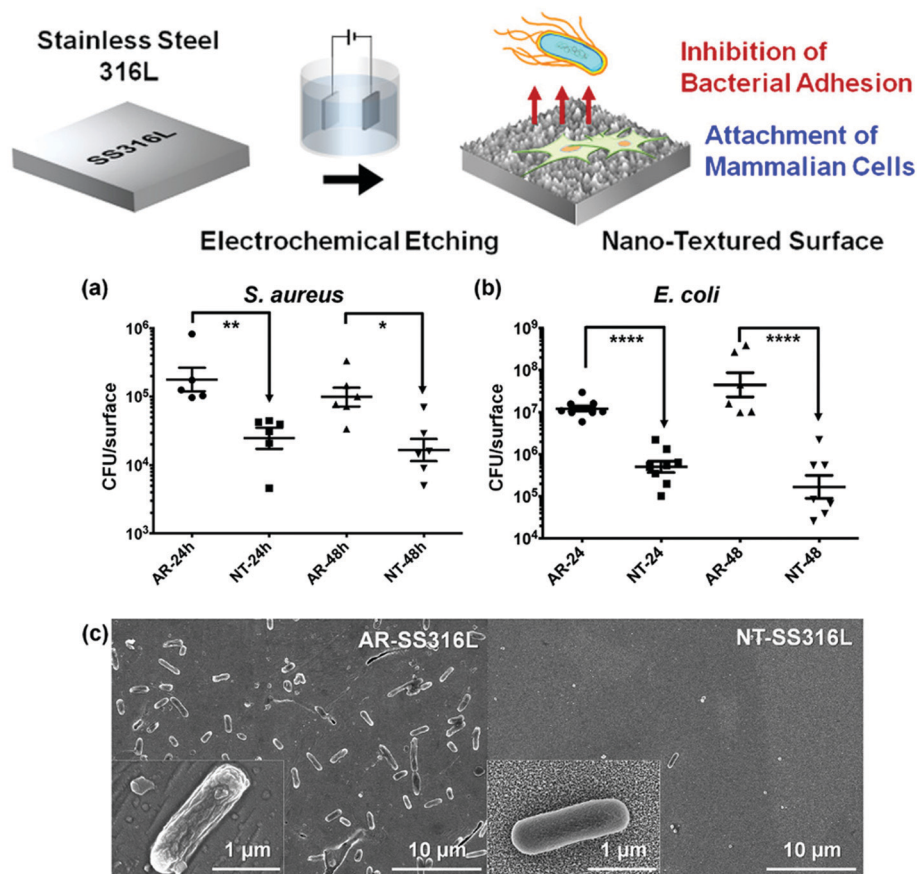


Fig. 6 Schematic representation of chemical etching process and its significance followed by bacterial adhesion on 316L SS surfaces. Number of adhered (a) *S. aureus* and (b) *E. coli* cells on as received (AR)- (●) and NT- (■) 316LSS surfaces for 24 and 48 h of incubation (data represent mean $\pm$ SEM (c), $N = 3$). Replicated with permission from ref. 47. Copyright 2014, American Chemical Society.

also significantly adhere to implant materials and cause infections.⁵²

To avoid bacterial infection in implant materials, vancomycin and gentamicin antibiotics were admixed with hydrogels and coated onto 3D printed implants using the selective laser melting method (Fig. 7a–d). Initially, two shapes of implants were fabricated and further treated with shot blasting to obtain perfection in the surface of the implant.⁵³ Planktonic bacterial growth inhibition was tested from SB (shot blasted) and NSB (non-shot blasted) implants containing antibiotics. The results stated that both SB and NSB implants eradicated planktonic bacterial growth within 24 h of incubation (Fig. 8a–f). Also, to avoid the usage of antibiotics for preventing bacterial colonization and subsequent infection or for treating established biofilms, surface tailoring or new material development has taken considerable attention in the past few decades.⁵⁴ The primary step of bacteria is to attach firmly onto a surface and develop biofilms, which will interfere with the surface-modified implant surfaces, thereby influencing infection risks. The prevention of biofilm formation is achieved by tailoring the implant material surface as a non-adhering state.

Miray bekbolet and Claudia araz studied the inactivation behaviour of *E. coli* bacteria containing 1 mg mL^{−1} irradiated TiO₂ particles under BLF fluorescent lamps and found that TiO₂ particles completely inhibited inactivated *E. coli* growth⁵⁵ in 60 min of exposure. Sunada *et al.* examined the antibacterial effect of *E. coli* by TiO₂ particles using Limulus tests. These tests analyzed the degradation rate of endotoxin from *E. coli* in which bactericidal activity was calculated. Their findings stated that TiO₂ particles exhibited higher antibacterial activity by degrading a large quantity of endotoxin from the bacterial cell wall.⁵⁶ Shiraishi *et al.* showed the photocatalytic effect of anatase TiO₂ particles by ultraviolet A (UV-A) irradiation effectively arrests *S. aureus* growth in 90 minutes of exposure time used for surgical site infection applications.

Further, the treatment of bacterially infected implants is a tedious process for hip and knee (load-bearing implants) implants. Hence, the addition of metallic materials containing antimicrobial activity into oxide based implants is an appropriate choice to enhance the antimicrobial property, mainly from implant-associated pathogenic bacteria.⁵⁷ Fig. 9 shows

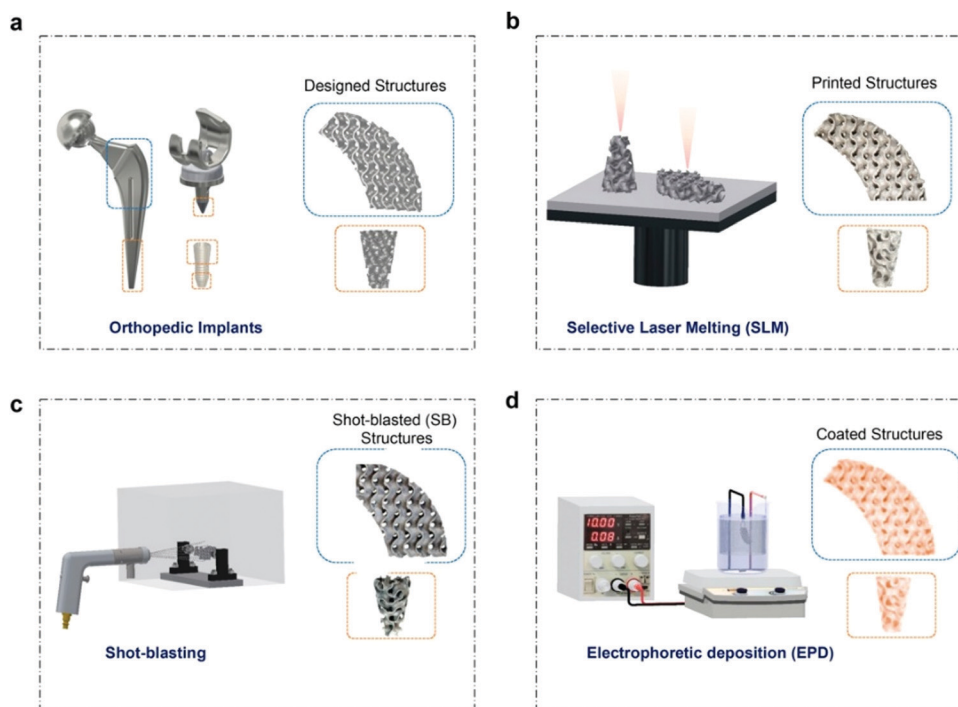


Fig. 7 Illustration of 3D printing and coating on stem and cone implants. (a) Designing implants to mimic real orthopedic implant structures. (b) Selective laser melting (SLM) method to fabricate the implants (c) Shot blasting technique to remove deficiencies from implant surfaces. (d) Antibiotic coated implants via electrophoretic deposition (EPD) technique. Reproduced with permission from ref. 53. Copyright 2018, American Chemical Society.

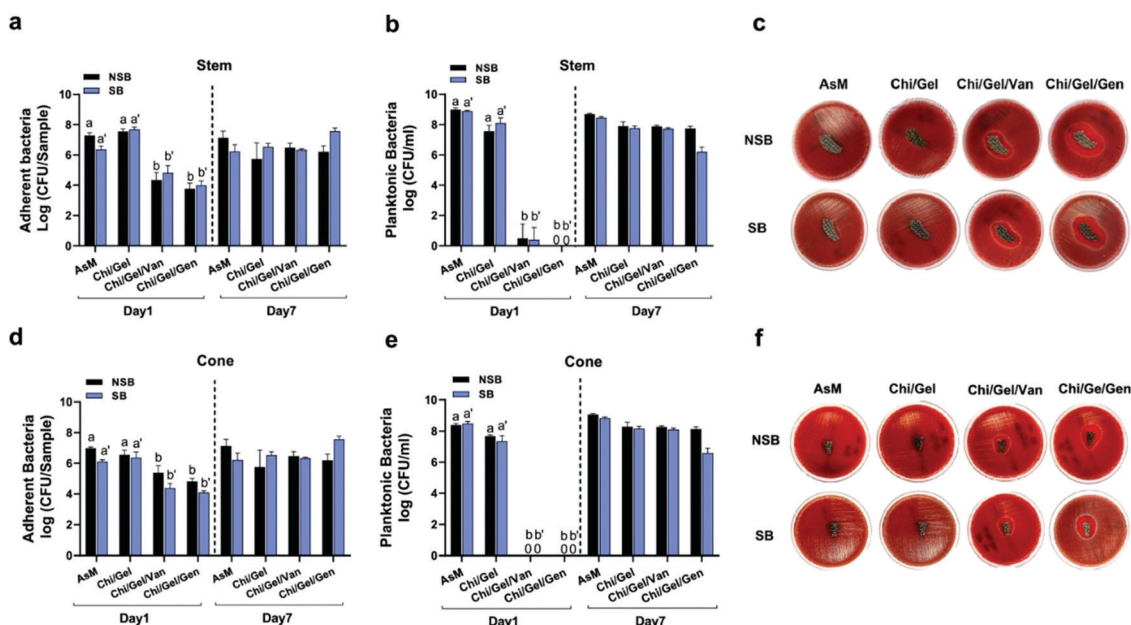


Fig. 8 Antibacterial efficacy of antibiotics coatings containing SB and NSB implants. (a and b) Quantification of CFU after 24 h incubation with antibiotics released from stem implants. (c) Inhibition of bacterial growth after 24 h on stem implants. (d and e) CFU quantification after 24 h incubation from antibiotic coated cone implant surfaces. (f) Bacterial growth inhibition after 24 h on cone implants. Data are represented as the mean $\pm$ SD ($P < 0.05$; a with b, a' with b', and no significant differences were observed between SB and NSB). Reprinted with permission from ref. 53. Copyright 2018, American Chemical Society.

the mechanism of antimicrobial activity.³⁷ Pradhaban *et al.*⁵⁸ deposited Ag-ZrO₂ composite coatings by pulsed laser deposition (PLD) and found increased anti-bacterial effect against *S. aureus*

and *E. coli* compared to ZrO₂ coating. Similarly, Heng *et al.*⁵⁹ studied antibacterial behavior against *A. actinomycetemcomitans* and *S. aureus* on ZrO₂ coating with different concentrations of

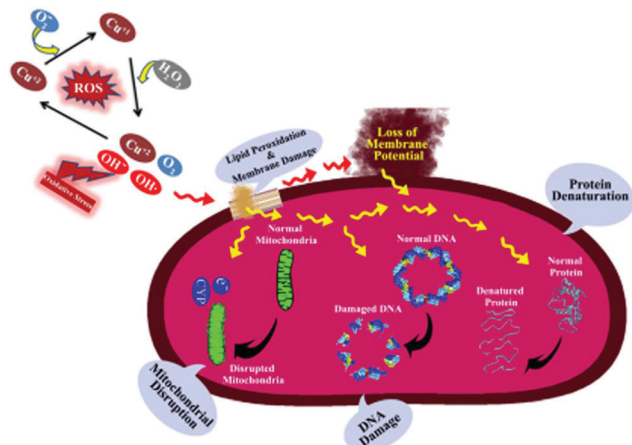


Fig. 9 Mechanism of antimicrobial activity. Reproduced with permission from ref. 37. Copyright 2012, Elsevier.

silver. The results showed that silver ions at 10.6% showed superior anti-bacterial activity and biocompatibility.

Premkumar *et al.*⁶⁰ coated various concentrations of zinc (Zn), which were incorporated into niobium oxide (Nb_2O_5) to make nanocomposite coatings using the sol-gel method. After deposition, they studied the antibacterial behavior against *E. coli* (Gram(–)ve) and *S. aureus* (Gram(+)ve) strains. Finally, they observed that increased antibacterial activity was obtained when increasing the concentrations of zinc. Hence, they revealed that zinc has antibacterial activity and is used for biomedical applications. Anthony *et al.*⁶¹ deposited TiZrN with different compositions of silver by a sputtering technique and studied their antibacterial activity against *Staphylococcus aureus* and *Staphylococcus epidermidis*. They stated that the bacterial respiration decreased with increasing silver concentration into TiZrN coating. Noda *et al.*⁶² developed next-generation Ag containing hydroxyapatite by thermal spray method. They analysed antibacterial activity in fetal bovine serum (FBS) solution and observed that the silver ion release enhanced the antibacterial activity to methicillin-resistant *S. aureus*. Further, sustainable Ag release was obtained after 24 h of incubation with 6500 PPb Ag release, and importantly, they found that the release of Ag is low in FBS solution. Ruan *et al.*⁶³ examined the antibacterial and osteogenic capability of HAp/Ag coating using vacuum plasma spraying. Morphology of HAp treated bacteria exhibited a healthy cell wall; whereas, a thin and sparse cell wall was observed in HAp/Ag coating. From the experiments, it divulged that silver-containing HAp significantly reduced initial bacterial adhesion as well as colonization.

Subramanian⁶⁴ deposited thin film metallic glasses (TFMG) with the compositions of $\text{Ti}_{40}\text{Cu}_{36}\text{Pd}_{14}\text{Zr}_{10}$ by magnetron sputtering method onto medical grade 316L SS substrates. Since the TFMG coatings contain the Cu element, they studied the antibacterial effect of *E. coli* with different incubation time (0, 4, 8, and 12 h) periods. The results stated that the increased incubation time influenced the killing rate of bacterial survival, and the coating is used for potential implant applications.

In addition, two-dimensional graphene comprising of carbon atoms arranged in a hexagonal lattice has been used for versatile applications. In general, graphene exhibits excellent physical, chemical, and mechanical properties, which elevates wide applications. Graphene was deposited on modified aluminum plates via a chemical method. Priyadarshani and Sujoy prepared graphene oxide and reduced graphene oxide coating onto 3-aminopropyl triethoxysilane functionalized aluminum substrate (Fig. 10A–C). The antibacterial activity of GO and rGO coated Al substrates were studied against *E. coli* strain.⁶⁵

It was found that GO and rGO reduced *E. coli* growth by $80.39\% \pm 2.01\%$ and $96.6\% \pm 1.32\%$, respectively. Further, the bacterial killing rates of GO and rGO were $74.47 \pm 3.9\%$ and $93.21 \pm 2.86\%$, respectively. It was clearly stated that rGO had more bactericidal activity against *E. coli* than GO-coated Al substrates due to the dispersion rate in the medium (Fig. 11A–I).

Overall, most of the coatings depend on the encapsulation of various types of antibiotics and antifungal drugs to protect from implant infection by locally delivering the drugs. Many coatings have incorporated cyclodextrin (CD), having a hydrophilic exterior and a hydrophobic interior of cyclic oligosaccharides. This CD is frequently used in orthopedic surgery.⁶⁶ Particularly, the CD has been conjugated with antibiotics as a coating material onto metallic implant surfaces, minimizing the burst effect and preventing the drastic release of drug.⁶⁷ At the same time, these drugs can cause long-term toxicity to the microbes, which can lead to drug resistance microbes while the antibiotic is delivered at lower inhibitory concentration. In order to overcome the above problem, researchers have also been conducting the alternate approach to reducing drug resistance bacteria yet still attaining antimicrobial device coating. Recently, the technology has moved to focus on coatings with long-term intrinsic antimicrobial properties. Specifically, most of the research groups are concentrating on non-drug-eluting coatings by metal and polymer-based materials. The main advantages of these coatings include intrinsic antifungal and antibacterial properties without using any drug that provides much longer-lasting performance than drug-eluting coatings.⁶⁸

7. Biocorrosion behavior of surface modified materials

Biofilm formation by microbial invasion and subsequent extracellular substances that facilitate irreversible bacterial adhesion to the surface and inorganic precipitates in crystal form from the bulk aqueous phase elevates the corrosion products of the substrates. EPS constitutes a mixture of cell-derived proteins, polysaccharides, lipids, and nucleic acids.⁶⁹ After bacterial adhesion on any substratum, the metabolic activities produced a variety of by-products, e.g., exopolymers, enzymes, inorganic and organic acids, and volatile compounds such as hydrogen sulfide (H_2S) or ammonia (NH_3), which affects the corrosion process at cathodic and anodic surfaces, thereby altering the electrochemical process. In some bacterial invasions,

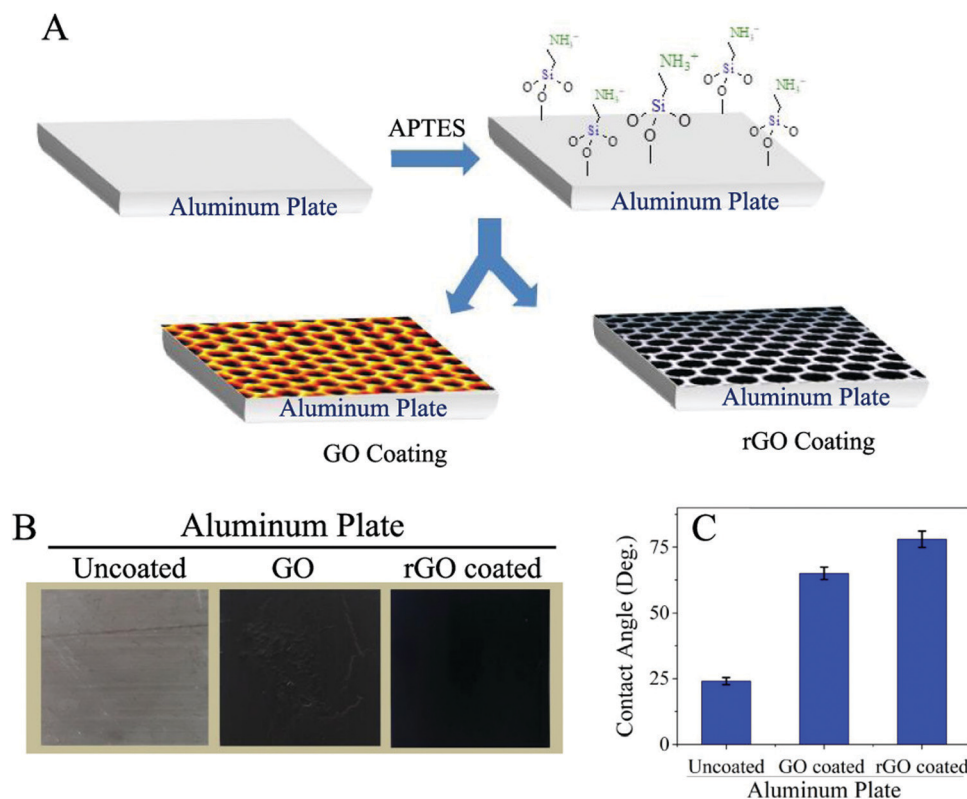


Fig. 10 Schematic representation of (A) GO and rGO coating on aluminum plate; color image (B); and (C) Wettability studies of uncoated, GO- and rGO-coated aluminum plate. Replicated with permission from ref. 65. Copyright 2019, American Chemical Society.

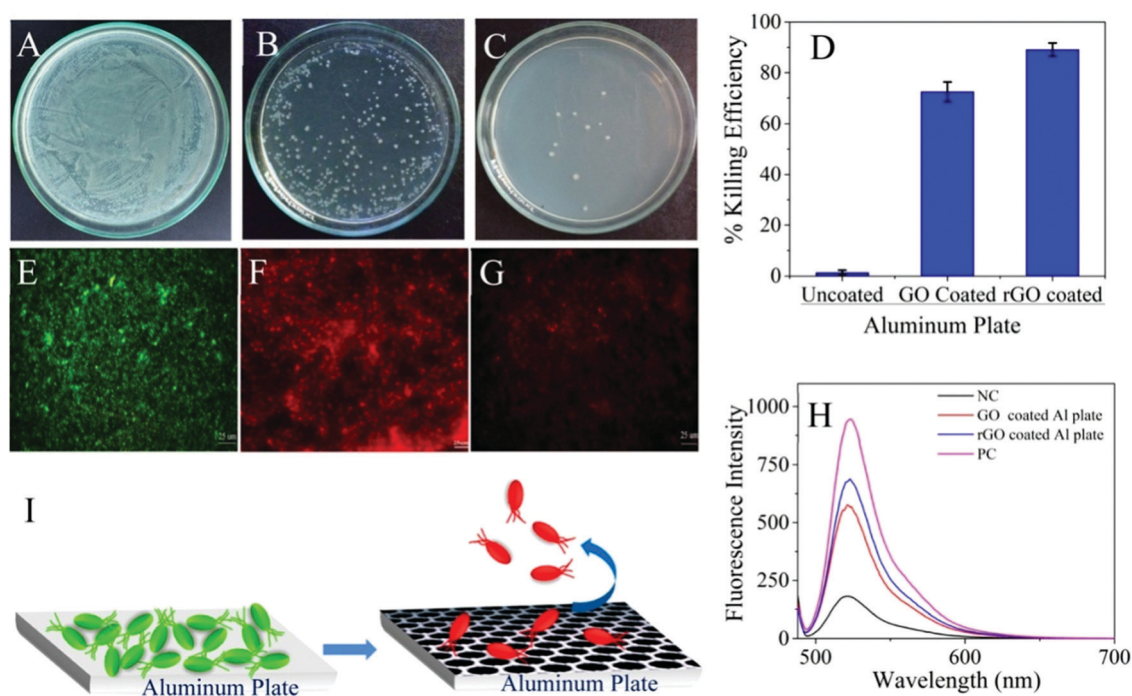


Fig. 11 Petri plate image of grown bacterial cells post-incubation with uncoated (A), GO- (B) and rGO-coated (C) aluminum plates. Antibacterial activity (D) and fluorescence images of uncoated (E), GO- (F), and rGO-coated aluminum plates (G) against *E. coli*. Determination of ROS production (H) by H_2 -DCFDA method. (I) Schematic view of antibacterial activity of uncoated and coated plates. Reprinted with permission from ref. 65. Copyright 2019, American Chemical Society.

the bacteria will produce hydrogen peroxide as a metabolic by-product, which accelerates the corrosion progress.

7.1. Ceramic coatings and their significance

Ceramics are classified based on macroscopic surface characteristics and chemical inertness. Five major ceramic materials fall in this category: alumina,⁷⁰ zirconia, glass ceramics, bio-active glass,⁷¹ and calcium-based ceramics.⁷² In general, most ceramic materials are used for various parts of the body. Among the various applications, some of the specific applications are listed as follows, (a) porous and chemically inert ceramics, in which creation of bone growth mechanical attachment occurs,⁷³ (b) the body cells are strongly attached to the surface of the chemically inert bioceramic on the roughened surface (c) after firm attachment of body cells to ceramic surfaces, the chemical bonding will be formed amidst the cell surface and materials (d) the resorbable ceramic materials eventually integrate with the host bone and will be replaced by the bone. The limitations of ceramic materials are their fracture toughness and low tensile strength and their usage in bulk form is limited to functions, where, only compressive loads are applied. The consequences of *ex vivo* push out tests have stated that the metal bond/ceramic would fail before the interaction of the tissue/ceramic bond and this examination is certified to the weak link in the body environment. Thus, there is a strong reason concerning bulk ceramic materials for metal/ceramic bonding and their reliability of interface over the service life of functional loading.

In modern-day industries, many surface modifying materials such as metals, metal alloys, ceramics, and polymers have been used for trauma and reconstructive surgery applications in the past few decades. Ceramics has considerable advantages among the numerous surface-tailored materials such as non-allergenic, chemical stability, resistance to corrosion, high mechanical strength, and enhanced biocompatibility.⁷⁴ Ceramic implants gained increased popularity among clinicians and patients owing to their pivotal good esthetics, wear resistance, and superior biocompatibility.⁷⁵ Yttria-stabilized zirconia (YSZ) used for dental implant applications has excellent toughness and mechanical strength.⁷⁶ ZrO₂ tends to change the phases from monoclinic to tetragonal and to cubic phase behaviour at elevated temperatures.⁷⁷ To stabilize the phase, yttria (Y₂O₃) was partially stabilized with zirconia as YSZ. In our previous studies,^{27,77} cubic phase of YSZ was coated on titanium samples and their biological responses were carried out. El-Ghany and Huseinsherief⁷⁸ thoroughly reviewed and declared the uses of *t*-YSZ in hip replacement and dental implant prosthesis. Hence, there is a controversy to examine better performance among monoclinic, *t*-YSZ, and cubic phase of ZrO₂ coatings. These materials not only fulfill the functional requirements but are also esthetically pleasing. In addition, transition metal nitrides like zirconium nitride (ZrN) and titanium nitride (TiN) have extensively been used in implantation, decorative and protective film applications for their aesthetic, gold colour appearance, and wear resistance coatings.⁷⁹

7.1.1. Electrochemical behavior of ceramic coatings. To elevate the corrosion protection property of implant materials, different types of surface modification techniques have been considered to improve the performance of stainless steel, titanium and its alloys for implant applications. PVD methods have received considerable attention among the various methods since it enhances defect-free coatings, high adhesion strength amidst coating and substrate interface, and high packing density. In general, ceramic materials such as ZrO₂, TiO₂, ZnO, CeO₂, *etc.*, were commonly deposited by PVD methods. In our earlier studies,⁸⁰ we studied the corrosion behaviour of H₂O₂ and lactic acid (LA) in hydrophilic ZrO₂ ceramic coated 316L SS substrate by electron beam evaporation (EBPVD) method. From the investigation, it observed that H₂O₂ and LA-containing artificial blood plasma showed excellent corrosion protection in ZrO₂ coating (Fig. 12a and b).

Since the ceramic materials exhibited a chemically inert nature, it showed higher corrosion-resistant nature than uncoated/bare substrates. Wang *et al.*⁸¹ deposited TiO₂ coating by a sputtering method and studied the corrosion behaviour in phosphate-buffered saline (PBS) solution. During the polarization studies, they observed that the TiO₂ coating exhibited higher corrosion resistance in nature. Similarly, Madaoui *et al.*⁸² studied the anti-corrosion behaviour of TiO₂ coating on 316L SS substrates by RF magnetron sputtering with a different bias voltage. After deposition, they studied the corrosion behaviour in a 3.5% NaCl solution and observed that TiO₂ exhibited better corrosion potential (E_{corr}) and less corrosion current density (I_{corr}) than uncoated 316L SS substrates. Jansen⁸³ investigated the application of magnetron sputtering to produce biocompatible ceramic coatings on implant applications.

In addition, hydrothermal treatment was used to synthesize the anatase phase of TiO₂ coating on titanium substrate to improve corrosion resistance and protect against bacterial invasion. Lorenzetti *et al.* developed TiO₂ anatase phase nanocrystal, which reduced the width between microasperities on the surface of Ti, reducing the green fluorescence protein expression of *E. coli* by about 50% compared to untreated Ti surface (Fig. 13a–d). Ti nanotubes with UV irradiated samples reduced bacterial adsorption significantly in the presence of pH 10 with tetramethylammonium hydroxide.⁸⁴

Gurappa⁸⁵ *et al.* developed a low-cost and efficient biomaterial using a surface engineering approach and delivered better corrosion resistance for 316L SS. Rajan *et al.*⁸⁶ deposited thin film metallic glasses (TFMG) with different compositions using a magnetron sputtering system. They conducted electrochemical corrosion experiments in simulated body fluid (SBF) solutions. They observed that Zr-based TFMG coating sustains corrosion-resistant nature with a lower penetration rate than bare crystalline titanium (Ti) substrate. Wang *et al.*⁸⁷ developed ceramic glass with hardystonite (HT) and sphene (SP) coatings manufactured using atmospheric plasma spraying techniques. They divulged that the coating has higher tensile strength and hardness.

Similarly, Subramanian⁶⁴ sputtered Ti₄₀Cu₃₆Pd₁₄Zr₁₀ TFMG using magnetron sputtering and studied the mechanical,

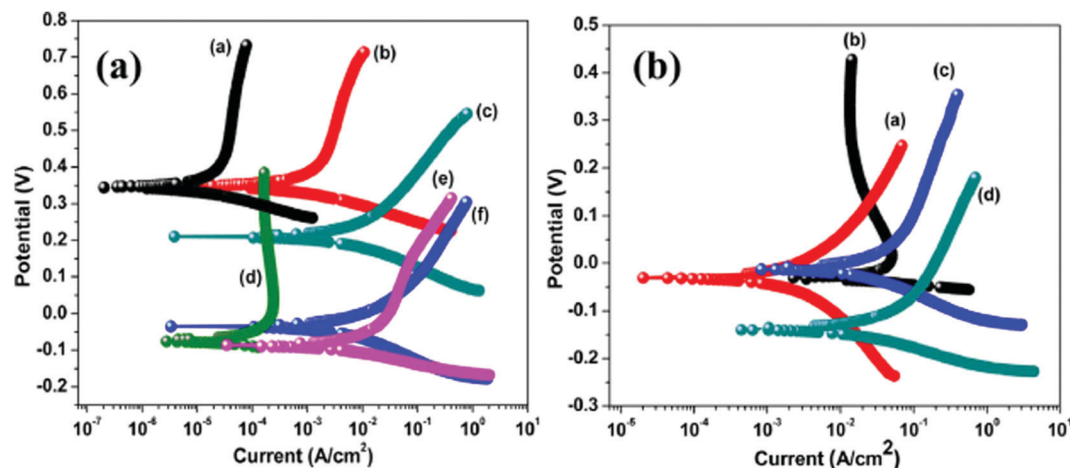


Fig. 12 Corrosion behaviour of various concentrations of (a) hydrogen peroxide and (b) lactic acid solution on ZrO_2 Coatings. Replicated with permission from ref. 80. Copyright 2018, Elsevier.

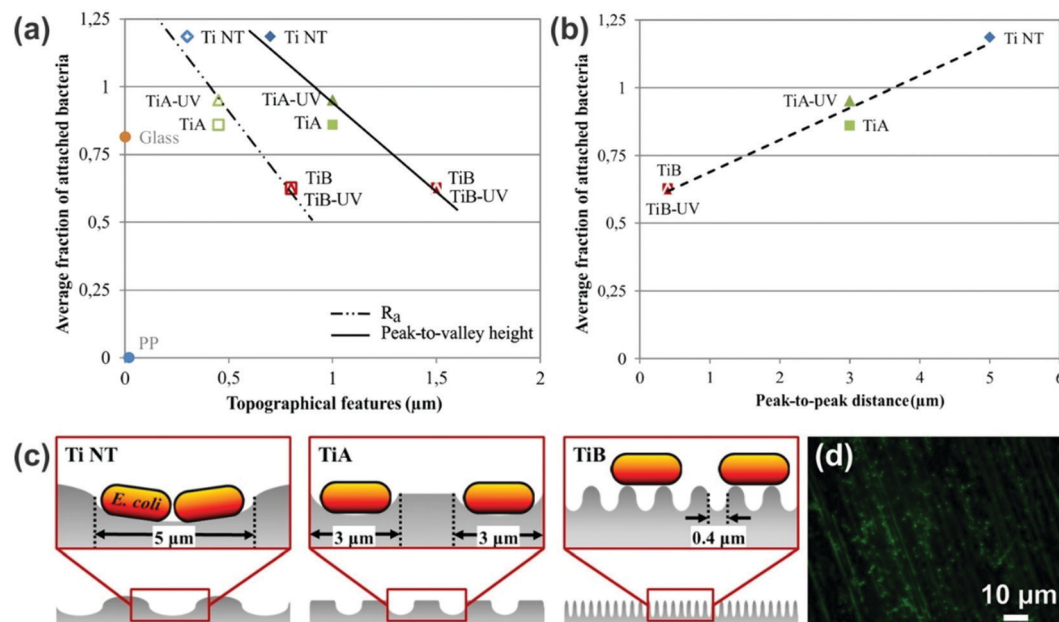


Fig. 13 Average fraction of adhered bacteria on Ti NT, TiA, TiA-UV, TiB, and TiB-UV samples versus (a) R_a roughness (open symbols) and peak-to-valley height (filled symbols) within the machined grooves (b) peak-to-peak distance. (c) Height vs. distance profiles for Ti NT, TiA, and TiB samples. (d) GFP-*E. coli* stained with Live/Dead kit on Ti NT. Replicated with permission from ref. 84. Copyright 2015, American Chemical Society.

biocompatibility, and corrosion behavior of the materials. They examined the coated and uncoated materials in SBF solution for electrochemical studies and found higher corrosion resistance in Ti-based TFMG coatings. Furthermore, bioceramics like HAP are also involved in protecting the corrosion of metallic substrates by surface coatings. Mohedano *et al.*⁸⁸ developed two types of ceramic coverings on the titanium surface of dental implant applications with a different Ca/P ratio. The bioactive coatings were deposited on Ti by plasma electrolyte oxidation (PEO). The morphology and composition of the samples were characterized before and after immersion in SBF at 37 °C for 4 weeks. Similarly, Brunello *et al.*⁸⁹ has

demonstrated ceramic coverings of bioactive glass silicate for orthopedic and dental applications. Besides, coatings developed onto Mg alloy samples were analyzed to play a specific role as protective barriers on Mg alloy and maintain mechanical integrity over a longer period.

Yugeswaran *et al.*⁹⁰ prepared YSZ reinforced HAP using gas tunnel type plasma spray method. Since HAP has inferior mechanical properties, different percentages of YSZ (10, 20 and 30 wt%) were admixed with HAP and deposited (Fig. 14a and b). The deposited HAP-YSZ composite coatings were analyzed to know the electrochemical behaviour in SBF solution. The corrosion analysis stated that the higher YSZ concentration

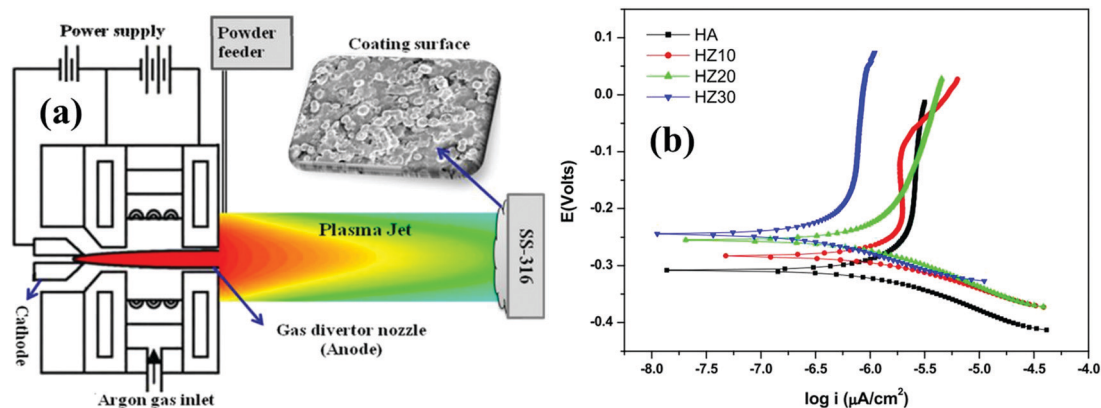


Fig. 14 (a) Schematic diagram of gas tunnel type plasma spray; (b) PDP curves of HA and YSZ reinforced HA coating in simulated body fluid solution. Reproduced with permission from ref. 90. Copyright 2012, Elsevier.

admixed HAP showed superior corrosion resistance than bare substrates. Zhang *et al.*⁹¹ introduced new zirconia/bioactive glass composites with high mechanical resistance and bio-activity to achieve the ideal dental implant.

The effect of gadolinium (Gd) and zinc (Zn) in Mg alloying elements were analyzed by Bian *et al.*⁹² They observed that different concentrations of Gd in Mg-alloy could improve the corrosion-resistant property than pure Mg samples in biological solution. In particular, 2.0% of Gd containing Mg alloy showed better performance than pure Mg (Fig. 15a–d).

In the oral environment, several microbial flora is seen that adhere to the implant surfaces. The bacteria undergo different attachment stages during the bacterial cell and implant interaction process, thereby forming a biofilm that leads to implant infection. Some antimicrobial agents such as mouthwashes, mouth rinses, and other prophylactic agents are used to prevent microbial-oriented diseases from reducing bacterial infection. In this view, Gobi Saravanan *et al.*⁹³ conducted a study on the corrosion behavior of ZrO₂ coating onto 316L SS samples in acidulated artificial saliva with and without the addition of

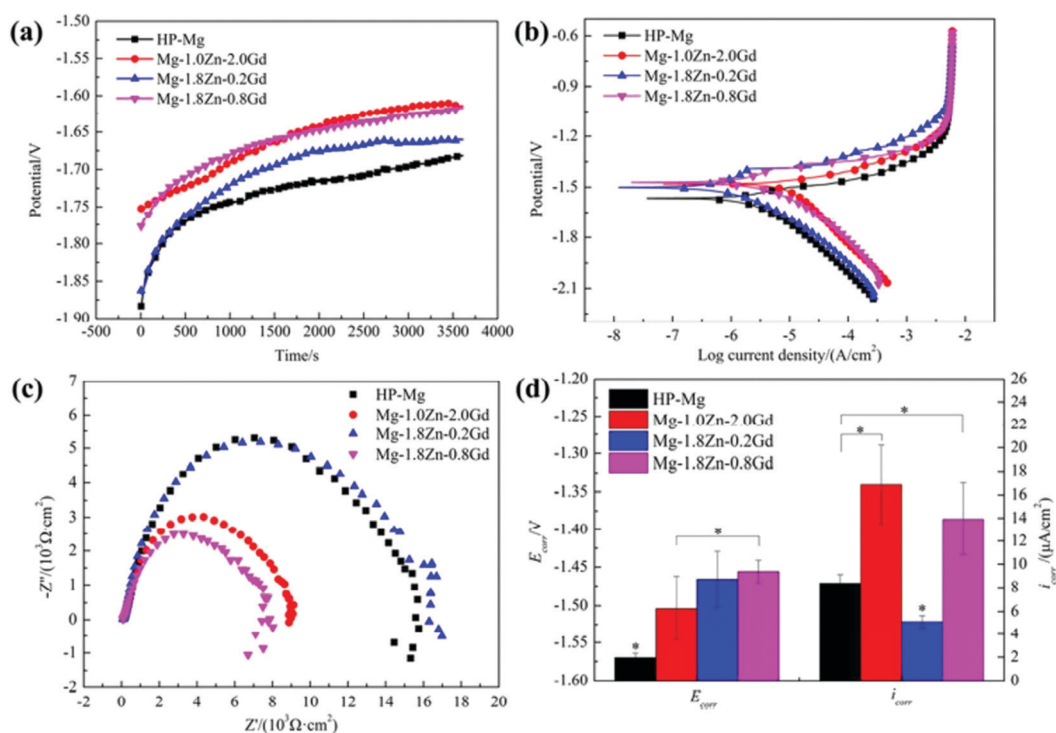


Fig. 15 Corrosion behavior of the Mg-based alloys in Hank's solution: (a) OCP curves, (b) potentiodynamic polarization (PDP) curves, (c) Nyquist plots, and (d) histogram of electrochemical data. E_{corr} means corrosion potential and i_{corr} represents corrosion current density. Reprinted with permission from ref. 92. Copyright 2016, American Chemical Society.

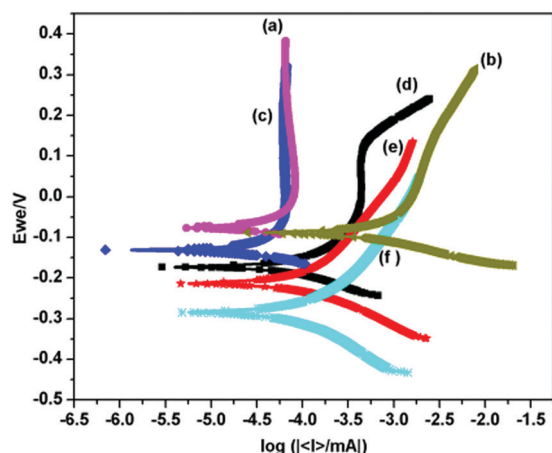


Fig. 16 PDP curves of ZrO_2 coating and uncoated 316L SS substrate. (a) acidic AS alone + ZrO_2 coating (b) acidic AS alone + uncoated 316L SS substrate (c) acidic AS + 0.2% NaF + ZrO_2 coating (d) acidic AS + 2% NaF + ZrO_2 coating (e) acidic AS + 0.2% NaF + uncoated 316L SS substrate (f) acidulated AS + 2% NaF + uncoated 316L SS substrate. Replicated with permission from ref. 93. Copyright 2018, Elsevier.

sodium fluoride (NaF) solutions. The results stated that ZrO_2 deposited 316L SS exhibited higher corrosion protection nature than bare substrates due to the chemical inertness and oxide nature on ZrO_2 coating (Fig. 16) surface.

All-encompassing, the survey of surface modification conveys the importance of various ceramic coatings and their properties in the biological environment. In particular, the stable and chemically neutral along with the biocompatible nature of ceramic coatings are expected to reduce immunogenic reactions in local tissues. Further, the coatings significantly reduce the progression of corrosion by hydrogen peroxide, lactic acid, proteins, and enzymes present in the human blood plasma.³⁷ In addition, these ceramic coatings protect the earlier adhesion of human pathogenic bacteria like *Pseudomonas aeruginosa*, *Porphyromonas gingivalis*, and calcium precipitating oral bacteria due to the surface smoothness of the coatings.⁹⁴ The nanostructured grains with nanolayer thickness of ceramic coatings are significantly used for antimicrobial and bone regeneration applications.⁹⁵ However, the nanolayer coatings could not withstand aggressive ions present in the body fluid, which causes pitting corrosion due to the microporous nature of the nanolayer coatings. In order to make thicker ceramic coatings, thermal spray and plasma spray coatings are generally approached, which make the surface rougher. Though the high surface roughness elevates the bone cell interaction,⁹⁶ there is also a possibility of pathogenic bacteria adhesion and subsequent biofilm formation. Besides, the higher thickness of the bioceramic coating exhibit superior corrosion protection; at the same time, it undergoes severe adhesion problem as well as it loses nanostructured properties as the higher thickness ceramic coating act as a bulk material.

7.2. Hydroxyapatite (HAp) as bioceramics

Calcium phosphate (Ca_3PO_4), generally known as ceramics, is widely used in implant materials, since it comprises a high

percentage of similarity with mineral compositions of human bone. Moreover, calcium phosphate ($\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2$) in the form of HAp is comprehensively used in a physiological condition in the human body due to its superior biological response. In general, bone consists of non-collagenous proteins, HAp, collagen, and water. HAp is $\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2$ with a Ca/P ratio of 1.67, which has a high resemblance with hard tissues such as teeth and bone.

Hence, HAp is used as a primary implant material owing to its exceptional osteoconductivity, biocompatibility, and good bioactivity.⁹⁷ Lacefield⁹⁸ studied bioactive ceramic coatings that are osteoconductive with porous calcium phosphate to improve bone growth. Roy *et al.*⁹⁹ deposited HAp using RF magnetron sputtering on Cp-Ti substrates and evaluated their mechanical and biocompatibility nature. The deposited HAp coating and observed superior biocompatibility in *in vitro* as well as *in vivo* conditions.

Cheng *et al.*¹⁰⁰ carried out hydrothermal treatments to form hydroxyapatite (HA) at the nanoscale on micro-arc oxidation coatings (MAO) to investigate hierarchical structures of HAp. These structures were evaluated for cell activity using preosteoblast cell lines (MC3T3-E1 cells). Wan *et al.*¹⁰¹ synthesized HAp coatings under various conditions such as different targets, argon (Ar) partial pressure, and discharge power. After the sputtering process, the films were treated with the hydrothermal method and achieved homogeneous, smooth and dense morphology of HAp coating. Dinu *et al.*¹⁰² deposited HAp coating on various Mg substrates using RF-magnetron sputtering technique and evaluated the tribological behaviour of the coating in the presence of physiological saline. They observed the lower wear rate on coated films than uncoated substrates. Furko *et al.*¹⁰³ developed a bioactive ceramic (CPC) coating made from calcium phosphate for the application of implants. Sankar *et al.*¹⁰⁴ studied the electrochemical behaviour of HAp coating developed by PLD and electrophoretic methods. They studied the corrosion behaviour of HAp coatings using Hank's Balanced Salt Solution (HBSS) with a pH of 7.4. The corrosion results reveal that electrophoretically coated HAp coating showed superior corrosion protection than HAp coating deposited by the PLD method.

Similarly, Yugeswaran *et al.*¹⁰⁵ prepared HAp-titania nanostructured composite coatings by a gas tunnel type plasma type spray technique. The authors studied electrochemical behaviour in SBF solutions to determine the corrosion behaviour of nanocomposites and HAp coatings. The results revealed that HAp- TiO_2 nanocomposites coatings exhibited higher corrosion protection due to high compact coating than HAp coating alone.

7.2.1. Metal doped HAp. Numerous implant materials have been used for internal fixation devices in recent years, and total joint arthroplasties are showing increased demand worldwide. Due to various reasons, the demand for orthopedic implants showing high biocompatibility and corrosion-resistant properties. However, the common issues associated with patients lead to revisional surgeries that cause aseptic loosening, infection, wear, periprosthetic fracture, and growth failure. In particular, the microbial invasion followed by infection is an important

crisis that forms biofilms onto implant materials surface that produce secondary metabolites, paving the way for the microbes to escape from antimicrobial agents. In this regard, numerous researchers extensively studied the behaviour of bioceramics consisting of metallic nanoparticles having antibacterial activity against implant-associated infection-causing bacteria for dental and orthopaedic implant applications. Nathan *et al.* studied the effect of silver in HAP coating against *S. epidermidis* and *P. aeruginosa* pathogens and observed good antibacterial activity in the presence of silver-containing HAP.¹⁰⁶ Chen *et al.* deposited Ag-doped HAP by co-sputtering using the magnetron sputtering method and investigated its bactericidal property against Cowan I strain and RP 12 strains of *S. aureus*. The deposited coatings exhibited hydrophilic surfaces and showed good antibacterial performance against *S. epidermidis* and *S. aureus*.¹⁰⁷ Huang *et al.*¹⁰⁸ demonstrated that the growing integration layer (GIL) method of the reactive integration layer could produce Sr-doped hydroxyapatite (Sr-HA) deposition on α -Ti alloy sample surfaces at ambient temperature. The results of potentiodynamic polarization (PDP) and EIS tests revealed good corrosion potential. The GIL process requires no vacuum or other complicated equipment, and it consumes little power. GIL technology could be used in biomedical science and biological engineering in larger scientific and technical areas. In addition, they observed that the HAP coating would be delaminated while adding silver.

Multiple ion co-doping into HAP has been attempted to tailor structural stability and improve biocompatibility. Sr and F⁻ doped hydroxyapatite was synthesized by Wang and his

co-workers in 2019.¹⁰⁹ The investigation stated that the doping of Sr improved the lattice of HA, which showed better structural stability and promoted osteogenic cell differentiation. Similarly, F⁻ ions doping into HA significantly arrested the growth of *S. aureus*. Similarly, ZnO doped HAP containing polypyrrole (PPy) films by *in situ* oxidative polymerization method improved antibacterial and osteointegration properties. The multifunctional composite coatings by PPy encapsulation drastically reduced the release of Ca²⁺ and Zn²⁺ ions and improved antibacterial properties against *E. coli* and *S. aureus* as well as mesenchymal stem cell attachment and proliferation. Fig. 17 shows the antibacterial property and cell attachment, wherein the formation of PPy macromolecular chain followed by HA with Ca²⁺ and OH⁻ formation acted as an antibacterial agent and promoted the growth of VEC.¹¹⁰

Similarly, other microbicidal agents such as copper (Cu) and zinc (Zn) have been used for incorporation in HAP for biomedical applications. Zn-loaded amorphous calcium phosphate nanorods were prepared by chemical synthesis method and performed the antibacterial activity against *Aggregatibacter actinomycetemcomitans*, *Fusobacterium nucleatum*, and *Streptococcus mutans* of oral cavity pathogens.¹¹¹ Since HAP exhibits lower mechanical strength, ZrO₂ nanoparticles are added to the HAP particles to improve the mechanical strength.¹¹² Similarly, copper substituted HAP nanoparticles also expressed excellent antibacterial activity through lysis of bacteria against *E. coli*.¹¹³ In addition, sodium fluoride was also added to the HAP-ZrO₂ composite materials to improve the antibacterial performance.

Altogether, HAP is an unavoidable material, especially bone ceramics, due to its chemical and structural similarities with

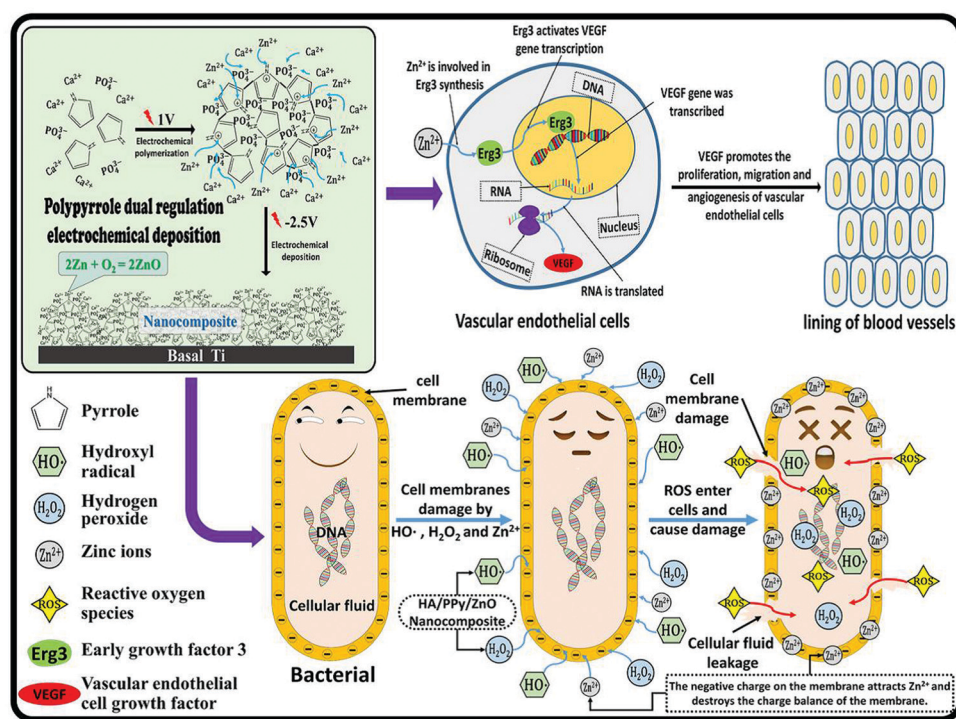


Fig. 17 Synthesis of HAP/ZnO/PPy coating, showing antibacterial test and the mode of action of growth of vascular endothelial cells and angiogenesis. Reproduced with permission from ref. 110. Copyright 2020, Elsevier.

natural bone. The proper structure, phase, composition, and morphology of the HAp coating significantly promote the growth of osteoblast cells and their adhesion, proliferation, and differentiation for better healing rates. Fig. 18 shows the calcein staining used to specify intracellular esterase activity in live cells.¹¹⁴ From Fig. 18a–c, it is revealed that HAp and m-HAp coated samples exhibited a large quantity of elongated and polygonal proliferated cells than uncoated Ti6Al4V alloy samples.

Particularly, Ag, Cu, Zn, and Mg admixed HAp improves broad spectrum of antimicrobial activity as well as low toxic effect with mammalian cells.^{115–118} For instance, strontium doped HAp promoted the formation of bone and reduced bone resorption.¹¹⁹ Similarly, Mg-doped HAp exhibited better osteoblast cell adhesion strength than pure HAp.¹²⁰

Although HAp mimics natural bone and promotes osteoconductivity properties, it is highly susceptible to brittleness due to its higher stiffness. During *in vitro* analysis, the metal-doped HAp coating failed to release the metal ions in a sustainable manner due to its less compactness. The drastic release of metal ions accumulated in the surrounding body cells and tissues subsequently creates an immunogenic response. To obtain more compactness of the coating, researchers have been developing metal-doped HAp coating in the presence of polymers such as collagen, alginate, agarose, and chitosan.¹²¹ However, the polymeric material encapsulates the metal-doped HAp, which hinders its performance towards effective

bone regeneration and other properties due to its very less pore size.¹²²

7.2.2. Electrochemical behaviour of HAp and its nano-composite coatings. Dunne *et al.* deposited crystalline HAp onto biomedical grade Mg-alloy by blast coating technique at ambient temperature. The deposited coatings exhibited better adhesion strength in the range of 48 MPa. The crystalline HAp coating exhibited lower corrosion current density rather than Mg alloy in simulated body fluid solution. Similarly, Meng *et al.* carried out comparative studies on HAp deposition by electrodeposition as well as pulsed electrodeposition to evaluate the improved properties. They found that pulse electrodeposition showed better performance in biological behavior and corrosion resistance properties than electrodeposited HAp due to its unfavorable effects.¹²³

Similarly, HAp coating was developed by plasma electrolytic oxidation to study their structural, coating density, and corrosion behavior.¹²⁴ The study stated that direct current mode and unipolar pulse (10 Hz) enhanced HAp coating and further improved the corrosion resistance of titanium-modified HAp coatings. Similarly, Sankar *et al.*¹⁰⁴ studied the comparative analysis of HAp coating prepared by electrodeposition and pulsed laser deposition (PLD). Slower degradation was achieved in HAp coating prepared by the PLD technique. Similarly, HAp coating by the PLD method significantly improved corrosion resistance property by 96.97% and then electrodeposited HAp coating by 51.5%. From the observation, they concluded that

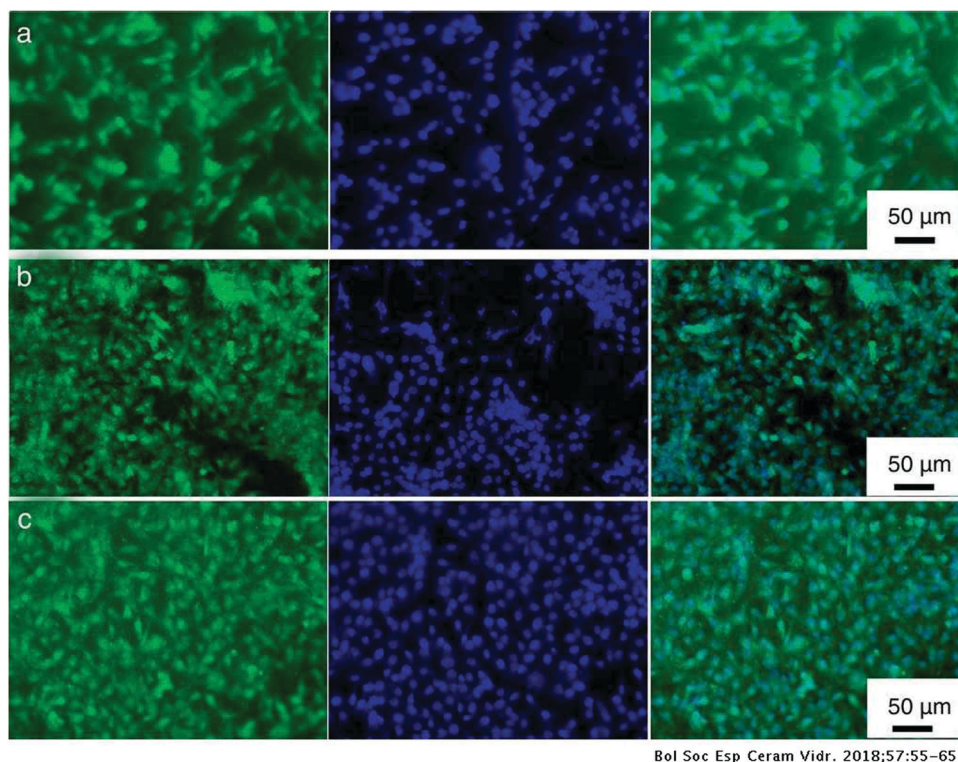


Fig. 18 Fluorescence images of calcein-AM (green emission), nucleus (with DAPI, blue emission) and merged Mg-63 cells cultured fluorescence for 2 days in the presence of DMEM medium containing (a) titanium alloy (b) HAp, and (c) mHAp coatings. Reprinted with permission from ref. 114. Copyright 2018, Elsevier.

the PLD effectively improved the corrosion resistance performance due to dense and porous free coatings.

It is well known that HAp coatings are used as artificial bones, which are robust, chemically inert, bioactive, and can survive extreme stress and abnormal pH conditions. These coatings enhance better interaction amidst the coating and host system to induce a rate of healing, which is confirmed by bone morphogenetic proteins (BMP) and other gene expression studies. Further, better mineralization and hemocompatibility were observed. In addition, corrosion resistant nature was obtained and could withstand the body fluids. However, the HAp coatings exhibit low fracture toughness and low tensile strength, restricting their heavy load applications. Further, coating thickness, the release of debris, and the degradation behavior of ceramic coatings restrict its wide applications. Hence, the development of composite coatings like ceramic-polymer or ceramic-ceramic coatings for metallic implants elevates better mechanical properties.

Composites are the combination of two or more materials or phases to obtain both the metal characteristics in single metal alloys or composites to benefit from the prominent features of each constituent. It is a predominantly requisite that each component of the metals that are compounded should be biocompatible and should not degrade between the interfaces of the constituents.¹²⁵ The fabrication of composites in the desired shape is also very difficult, and hence, they are yet to meet technical development for these applications.¹²⁶ Composite materials have been used in clinical practice for various implant applications. In dental implant applications, polymethyl methacrylate (PMMA) polymer has been used to replace dental fillings for the past few decades. However, dental amalgam composite materials are still used as dental fillers due to their superior mechanical and compressive properties. The monomer to polymerization affects the mechanical stability and biocompatible behaviour of the implant materials. Microcavities, dimensional stability, polymerization shrinkage, and wear resistance of the materials play an important role in curing conditions during the polymerization process. A low degree of conversion of the polymerization process leads to the cytotoxic effect on the biological systems.

In dental implant applications, composite materials such as silicon carbide (SiC), carbon fiber, or carbon-reinforced fiber have been mainly used for endosseous implants due to their superior advantages over metals and alloys. The composites PTFE, carbon, and alumina are used in maxillofacial surgery and exhibit significant inflammatory responses.¹²⁷ Nanocomposite-based scaffolds are mainly used for bone graft applications. Even though hydroxyapatite (HAp) is used in various implant applications, the mechanical property of HAp limits its wide range of applications and exhibits poor antimicrobial and anti-cancer activity performances. To enhance the mechanical property of HAp, Htun *et al.* studied the strength and toughness improvement by producing calcium oxide and zirconia (ZrO₂) reinforced HAp sintered with the small addition of CaF to improve the sinterability and phase stability of the composites.¹²⁸ The investigation suggested that reinforcing ZrO₂ into

the HAp drastically improved the strength from 35.70 MPa to 52.88 MPa.

Razavi *et al.* prepared magnesium-fluorapatite composites using the compression method and studied their corrosion behavior in the ringers electrolyte solution. From the results, they observed that magnesium-fluorapatite composites exhibited better corrosion resistance rather than Mg alone.¹²⁹ Fares *et al.*¹³⁰ investigated the ability to cover titanium implants with SiC and determined whether the coating could remain intact following the simulated placement of the implant. Similarly, Khalajabadi *et al.* studied the corrosion and mechanical behaviour for cold sintered Mg/HAp/MgO composite materials. Different wt% of Mg and HAp powders were ball milled, sintered, and annealed at a high temperature. Mechanical and corrosion behavior were examined for the sintered specimens. The corrosion experiments were performed with the addition of different wt% of MgO into Mg and HAp particles. Finally, they revealed that corrosion resistance was observed with the addition of MgO particles.¹³¹

Huang *et al.* deposited hydroxyapatite/magnesium phosphate/zinc phosphate (HMZ) coating by electrodeposition for the first time. They carried out the electrochemical and degradation tests along with cytocompatibility and hemolysis studies. They found that due to dense structure and less porosity, the HMZ coating exhibited improved corrosion resistance properties rather than magnesium phosphate coating/hydroxyapatite and zinc phosphate coating/hydroxyapatite coatings.¹³² Cheng *et al.*¹³³ investigated the tribocorrosion behavior of ceramic coatings such as conventional monolithic micron alumina (IDA), YSZ composite coating (IDAZ), and layer-by-layer nanostructured titania and alumina/YSZ (IDZAT) onto Ti-6Al-4V alloys prepared by an atmospheric plasma spraying technique (Fig. 19a and b).

The tribocorrosion test indicated that the ceramic coatings had not undergone corrosion or wear-induced corrosion during the tribocorrosion process. Finally, the ceramic covering could provide better protection in a tribocorrosion environment. Kwok *et al.* studied corrosion behavior of carbon nanotube reinforced HAp deposition on Ti-6Al-4V alloy using the electrophoretic method. During the deposition, three different sizes of HAp were performed (spherical, needle, and flake shape) with CNT. The deposited HAp-CNT composite films achieved better adhesion strength, crack-free film, and higher corrosion-resistant properties than electrodeposited HAp films.¹³⁴ Lacefield's¹³⁵ research into the biocompatibility nature of dental implant materials is discussed with the mechanical features of the materials. Protective oxide coatings characterize a metal implant, but the release of ions is still more common with the materials and is a function of composition, passivation state, and corrosion potential. This type of dental alloys (titanium alloys), which contains niobium, and zirconium along with high-strength ceramics like zirconia, may offer some specific advantages (lower modulus of elasticity) over conventional materials. Shojaei and Afshar obtained a flake-like structure with a regular flower shape structure and studied the influence of ZrO₂ into HAp coating in bonding strength, coating, and

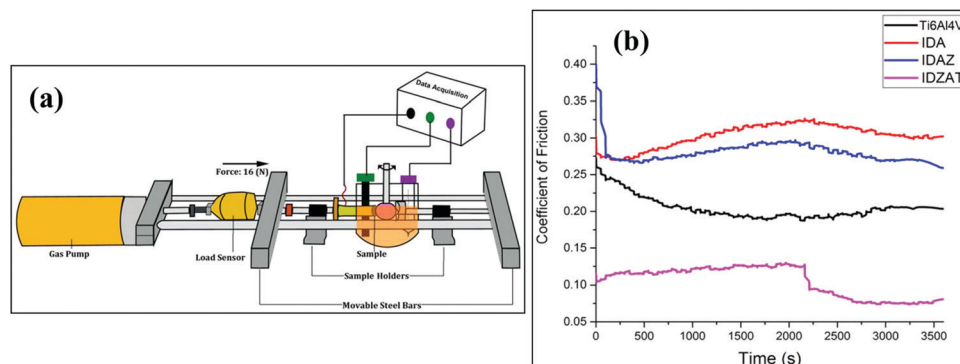


Fig. 19 (a) Hip simulator tribocorrosion set up. (b) Friction coefficient graph of zirconia allotrope coatings. Reproduced with permission from ref. 133. Copyright 2019, American Chemical Society.

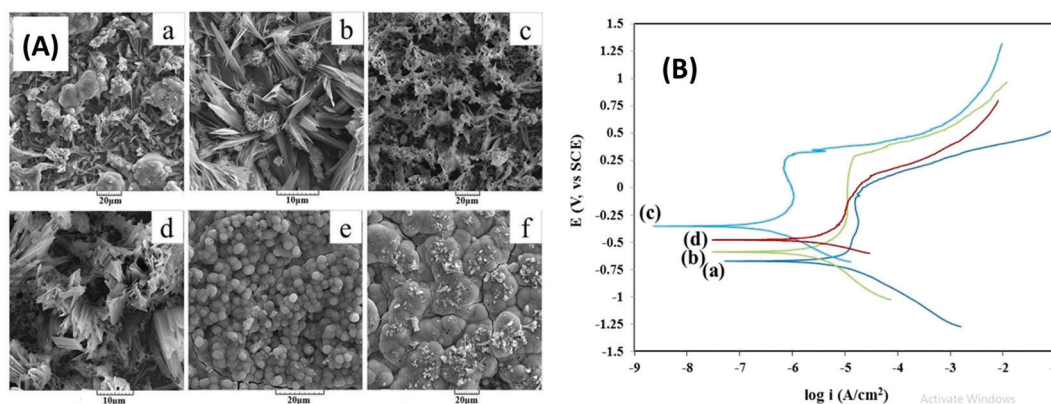


Fig. 20 (A) SEM images of (a-b) HAp, (c-d) HAp-5Z, (e) HAp-10Z, (f) HAp-15Z coatings after immersion in SBF for 30 days; (B) PDP curves of (a) HAp, (b) HAp-5Z, (c) HAp-10Z, (d) HAp-15Z at 37 °C. Copied from the permission of ref. 136. Copyright 2015, Elsevier.

corrosion behavior (Fig. 20A and B). They examined that higher concentration of ZrO_2 increases adhesion strength than HAp coating alone. Further, higher concentration of ZrO_2 containing HAp coating significantly decreased corrosion rate and stated that HAp- ZrO_2 coating can be used as a good material for implant applications.¹³⁶

Coquillat *et al.*¹³⁷ studied a combined coating strategy to control implant degradation and cellular regulation processes were evaluated, including plasma electrolytic oxidation (PEO). The findings suggest that modified poly(ϵ -caprolactone) (PCL), PCL-PEO-coated Mg hierarchical structures as biodegradable implants with bioactive properties could become better aspirants for applications in bone reconstruction plates or cardiovascular stent design. Chakraborty *et al.* deposited different ratios of CaP with multi-walled CNT using electrophoretic deposition method and achieved a highly compatible young's modulus value of 6–10 GPa, which is similar to natural bone. Further, they investigated the biological and corrosion behavior of HAp-MWCNT composite coatings and observed that the composite coatings exhibited better biological as well as corrosion-resistant properties.¹³⁸ Similarly, alumina (Al_2O_3) coating has been used as a prominent material for biomedical applications. Wang *et al.* deposited Al_2O_3 coating onto NiTi alloy materials to enhance the corrosion property of the material. In addition,

a thin HAp layer was coated by polydopamine (PDA) as an inducer onto Al_2O_3 to improve the bioactive properties. The studies revealed that the coating improved osteogenic cell differentiation. Further, electrochemical properties divulged that the nickel element release was decreased for HAp- Al_2O_3 coating ($0.6 \mu\text{g mL}^{-1}$) than Al_2O_3 coating alone ($1.9 \mu\text{g mL}^{-1}$) after the samples were soaked in SBF solution for about 56 days.¹³⁹ Similarly, the same research group deposited HAp- Al_2O_3 composite coatings using cathodic plasma electrolytic deposition (CPED) technique with two different phases of Al_2O_3 (α and γ phases) and HAp composite coatings exhibited higher corrosion resistance behavior than HAp coating alone. The results of electrochemical corrosion revealed that CPED-HT coating expressed a significant drop ($0.7 \mu\text{g mL}^{-1}$) in corrosion current rather than uncoated NiTi alloy ($18.0 \mu\text{g mL}^{-1}$).

Many studies have proved the usage of metallic implant materials such as stainless steel, titanium, Ti alloys, and Ni-Cr alloys could cause health issues due to the release of metal ions (Al, V, Ni, Cr) from metallic surface to surrounding tissues due to continuous interactions with aggressive body fluids (Na^+ , Cl^-). To protect the metal ion release and improve the osteo-integration property, surface modifications by hydroxyapatite make a preferred candidate to improve implant functionality. To improve the corrosion behaviour of HAp, several metal

oxides (TiO_2 , ZnO , ZrO_2 , Al_2O_3) and carbon based materials have been effectively applied as potential bioimplants.^{140–143} Numerous methods of coating techniques such as plasma spray coating, electrodeposition, PVD coatings, sol-gel coating and, dip coatings have existed.

In the body environment, pure HAP coating undergoes high dissolution, which diminishes the performance and durability, and leads to failure of the implant.¹⁴⁴ Several metal and metal oxide reinforcements into HAP have been considered for better performance of ceramic coatings.¹⁴⁵ Though HAP coating exhibited better bioactivity nature, it failed to prove its corrosion-resistant capability.⁹⁰ The corrosion resistance nature of bioceramic coating predominantly depends on the quality of deposition by means of adhesion strength, film compactness, thickness of the coating, *etc.* The HAP and its composite coating produced by sol-gel, electrodeposition, and dip-coating method exhibit poor adhesion strength with non-uniformity of the coating through which aggressive ions could easily interact with surface metal ions and corrosion progression occurs.

Conversely, HAP coating deposited by PVD and plasma spray could withstand long term due to improved adhesion strength. In spite of having some advantages while preparing HAP coating by PVD method, it exhibits a very low deposition rate, with amorphous HAP and high porous structure susceptible to corrosion.¹⁴⁶ Similarly, the thermal spray method undergoes a lack of uniformity, with poor adhesion HAP coating onto substrate material and crack formation limiting its corrosion-resistant nature.¹⁴⁷

8. Amorphous alloy coatings

Bioactive glass (BG) is considered significantly due to its excellent corrosion resistance, biocompatibility, and antibacterial properties. In general, BG is prepared using sol-gel and co-precipitation methods. However, it has been evolved with limited applications due to its brittleness and low fracture toughness behaviour. Hence, there is a need to add a bioactive material to BG to improve its properties. In this regard, Khanmohammadi *et al.* prepared BG reinforced with 50 wt% and 75 wt% of whisker HAP by an electrophoretic deposition method. The prepared coatings exhibited better adhesion strength and antibacterial activity. In particular, freeze-dried BG powder releases more antibacterial agents than calcinated BG powder due to its density and exhibited higher antimicrobial properties.¹⁴⁸ Wen *et al.* used one-step micro-arc oxidation to develop HAP/graphene oxide nanocomposite coatings on Mg alloy substrates. HAP-GO nanocomposite coatings enhanced the higher resistance behavior due to sealing of partial pores and decreased the diameter of pores in Mg alloy substrates.¹⁴⁹

Similarly, the different dosages of graphene in Mg alloy with copper (Cu) and aluminium (Al) were prepared using spark plasma sintering (SPS). Antibacterial property of Mg–1Al–Cu/*x*Gr alloy was tested with *S. aureus* and *E. coli* bacterial strains. The performance of anti-bacterial activity drastically increased with the addition of Gr into the Mg–1Al–Cu matrix. Mg–1Al–Cu/0.18Gr

affected 3 and 5 fold of *S. aureus* and *E. coli* bacterial growth, respectively, compared to non-Gr Mg–1Al–Cu samples. At the same time, Mg–1Al–Cu/0.5Gr showed 3 and 1.1 fold inhibition growth for *S. aureus* and *E. coli*, respectively. Fig. 21a–f reveals copper (Cu) leaching in two different concentrations, indicating that both Gr and Cu played a significant role in bacterial inhibition. Further, SEM images showed that Mg–1Al–Cu/0.18Gr induced significant morphological changes on both *S. aureus* and *E. coli* compared to Mg–1Al–Cu/0.18Gr samples.¹⁵⁰

Various studies conclude that the BG are predominant materials for tissue and bone repair as well as reconstruction as the BG induces effective bonding to both soft and hard tissue cells for self-repair and regeneration. Silicate-based BG is the important category of glasses exhibiting superior bioactive nature employed in clinical applications. Borate and phosphate-based BG showed a high healing rate by promoting epithelial tissue growth factor.¹⁵¹ BG coatings exhibit some major advantages such as high integration rate, high strength to the bone than bare metallic implants, and faster bone adhesion. Hence, BG coating (a) avoids degradation and corrosion issues raised post-implantation; (b) protects implant surrounded tissues from adverse effect and degradation; (c) enhances anchoring of bio-active fixation to the bone stimulating osseointegration.¹⁵² BG coatings permit prostheses to adapt to a cavity of the bone to protect fibrous tissue formation amidst the bone and implant; thereby, irritation, inflammation, and tissue damage can be prevented.¹⁵³ Unfortunately, owing to its poor mechanical properties, including low bending strength, brittle nature, and fracture toughness of the BG coating, restricts its wide applications in biomedical industries.

9. Metal nitride coatings and their electrochemical analysis

Nitride-based coatings have been deposited to improve the surface properties and bio performance of metallic implant materials. Nitride coatings have been developed in several forms, such as laser nitriding, and plasma nitriding, to improve the mechanical and corrosion resistance and protect bacterial adhesion property of implant materials. In particular, high-temperature gas nitriding shows great potential for biomedical applications due to its coatings onto complex-shaped structures, which are particularly used to implant prostheses. Lin *et al.* studied bacterial adhesion and corrosion behaviour against TiN coating deposited by multi-arc-ion plating technique onto Ti alloy surface. The study concluded that TiN coating reduced the corrosion potential by three-fold (-0.0682 V) than bare TC4 substrates (0.302 V) due to its excellent chemical stability in the corrosion medium.¹⁵⁴ Zhao *et al.* coated TiN by plasma-sprayed technique, performed post-annealing at 800°C for 6 h and then carried out corrosion analysis. The results concluded that the heat-treated samples exhibited more than 20 times corrosion resistance performance than deposited TiN coated samples due to blockage of cracks and pores at high-temperature treatment.¹⁵⁵ Similarly, TiN was deposited by magnetron sputtering onto

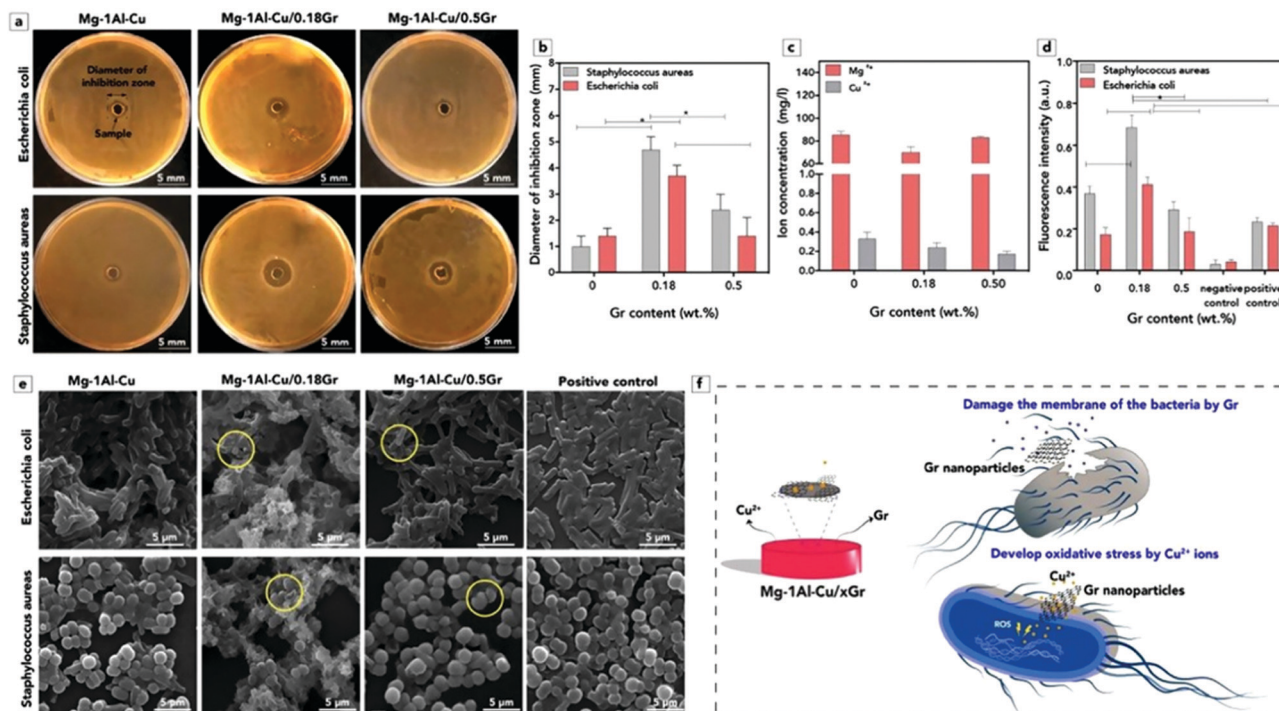


Fig. 21 *In vitro* antibacterial activity of Mg-1Al-Cu/xGr ($x = 0, 0.18$, and 0.5 wt%) samples against *E. coli* and *S. aureus* bacteria after 24 h of incubation. (a) Inhibition zone observed by stereoscopic images. (b) Comparative analysis of zone inhibition ($*P > 0.05$), (c) ion release studies of Mg-1Al-Cu/xGr nanocomposites. (d) Relative fluorescence intensity showing reactive oxygen species (ROS) generation ($*P > 0.05$). (e) SEM images of bacteria morphology. (f) Schematic diagram of the mechanism of action by Gr and Cu nanoparticles. Reproduced with permission from ref. 150. Copyright 2020, American Chemical Society.

Ti-Ta-Zr alloy prepared by arc melting methods. The deposited TiN coating underwent corrosion analysis in 0.9% NaCl solution. The results concluded that TiN nanotube coated Ti-Ta-Zr alloy significantly decreased the corrosion rate than uncoated samples.¹⁵⁶ Singh and his co-workers used laser surface processing (LSP) to achieve nitriding onto Ti6Al4V alloy to improve hardness, microstructural changes and electrochemical processes in physiological solutions.

Laser surface processed nitriding samples reduced 1/3 of corrosion current compared to untreated samples. Further, they stated that laser nitriding samples evolved a positive shift towards the noble direction and reduced the pitting corrosion in alkaline (pH = 4.0) and acid electrolyte (pH = 9.0) media compared to non-nitride samples.¹⁵⁷ Similarly, Man *et al.* prepared laser surface nitrided NiTi shape memory alloys and studied their corrosion resistance performance in Hanks solution. The study concluded that the surface nitrided NiTi samples showed excellent corrosion protection efficiency due to their chemical inertness even after the immersion period of 15 days.¹⁵⁸ Huang *et al.* developed TiN and ion-nitride coating onto titanium for dental implant applications to evaluate the best performance amidst the cathodic arc plasma and nitriding process. They carried out electrochemical corrosion studies in artificial saliva solution for dental implant application. The improved polarization resistance was observed in the order of TiN deposited Ti ($8.1 \text{ M}\Omega \text{ cm}^2$) > ion nitride Ti ($3.7 \text{ M}\Omega \text{ cm}^2$) > untreated Ti ($1.2 \text{ M}\Omega \text{ cm}^2$).¹⁵⁹ TiON and ZrON coated and bare

316L SS samples were analysed for their electrochemical behavior in artificial blood plasma (ABP) in the presence and absence of hydrogen peroxide (1% and 10%) solutions (Fig. 22a–c). The results divulged that TiON and ZrON coatings exhibited higher corrosion resistance in H_2O_2 solution than bare 316L SS substrate material. Since the hydrogen peroxide solution exhibits a higher oxidation effect, a higher corrosion potential was observed in H_2O_2 solution.⁹⁴

Other nitride materials such as zirconium nitride (ZrN), vanadium nitride (VN), and TiN/VN multilayer coatings are also used for orthopedic, cardiovascular, and dental implant applications. Roman *et al.* deposited ZrN coating at different substrate temperatures by direct current reactive magnetron sputtering onto NiTi shape memory alloy substrate. By depositing ZrN coating, they improved the hardness behavior with increasing temperature due to high crystallinity. In corrosion analysis, open circuit potential (OCP) of TiN coated NiTi alloy exhibited higher potential at high temperatures (500°C). For potentiodynamic polarization (PDP) measurement, the high passive region with low corrosion current density was observed in TiN deposited at 500°C due to spontaneous oxide formation than uncoated NiTi alloy.¹⁶⁰ Some other transition metal nitrides, especially titanium, vanadium, and zirconium, have received considerable interest from researchers due to their corrosion protection, wear resistance, improved hardness, and superior biocompatibility nature.¹⁶¹ Vanadium nitride coating deposited by Caicedo *et al.* exhibited higher hardness from 11 GPa to 20 GPa when the bias voltage was

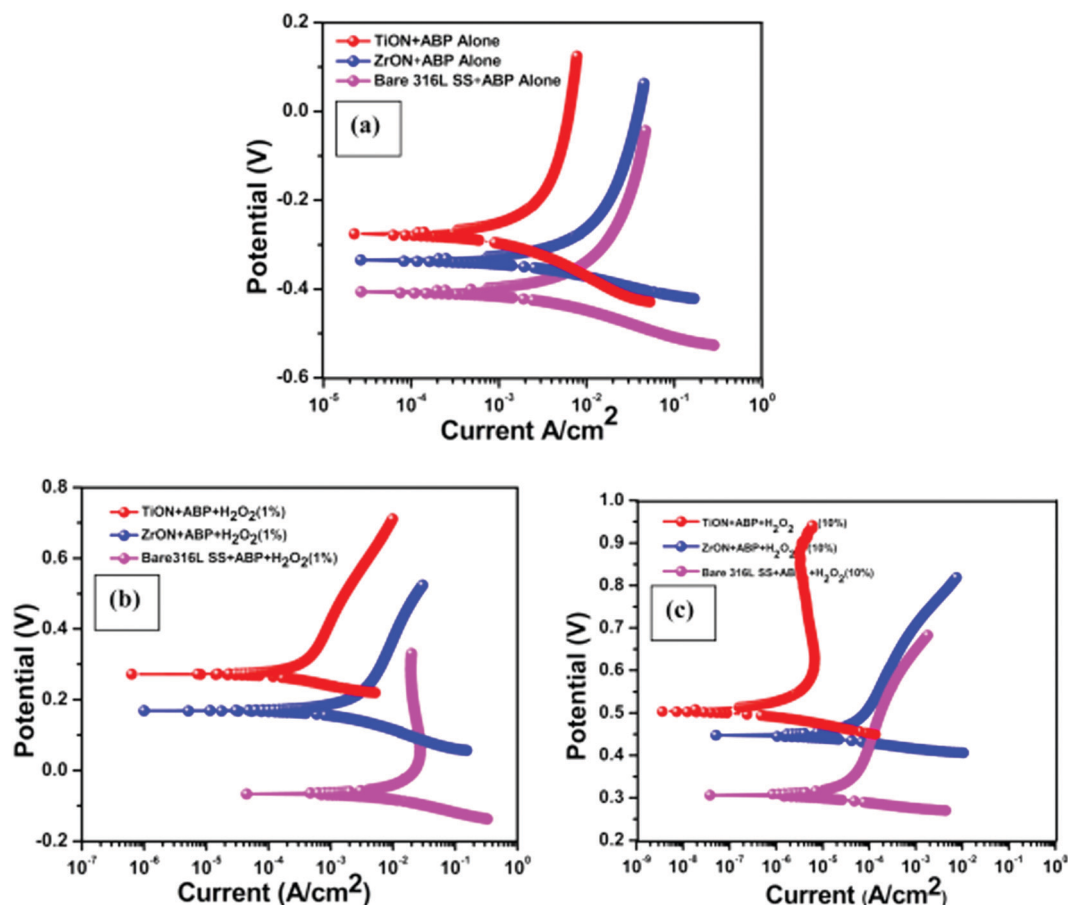


Fig. 22 Potentiodynamic polarization (PDP) studies of TiON and ZrON coatings onto 316L SS substrates in artificial blood plasma (ABP) solution with and without the addition of H_2O_2 solution. Reprinted with permission from ref. 94. Copyright 2018, IOP Publishing.

increased. Also, improved corrosion potential was observed with higher bias voltage due to its improved crystallinity in films.¹⁶²

Subramanian *et al.*¹⁶³ deposited single and multi-layered TiN/VN coating by magnetron sputtering technique. In the study, multi-layer films exhibited low friction coefficient than single-layer films. To evaluate corrosion studies, Fusayama simulated body fluid was used, and multilayer TiN/VN coatings exhibited more corrosion resistance than single-layer coatings. Another study pointed out that multilayer CrN/TiN coating using magnetron sputtering with different bias voltage exhibited higher mechanical strength and lower surface roughness (16.2 nm). In addition, there is no sign of corrosion in multi-layered coatings in the presence of perchloric acid as an electrolyte medium.¹⁶⁴ Subramanian *et al.*¹⁶⁵ conducted a study about the corrosion behaviour of TiN, TiON, and TiAlN coatings developed by reactive sputtering technique, and they analyzed the corrosion resistance behaviour for TiAlN followed by TiON and TiN coatings. In our previous study, we deposited TiN/TiAlN multilayer coatings by sputtering deposition, conducted the corrosion study in the presence of 3.5% NaCl solution, and observed the superior corrosion resistance property of multi-layered coatings.¹⁶⁶ We have also deposited TiZrN using the reactive magnetron sputtering method and determined bacterial invasion, hemocompatibility, and electrochemical corrosion.

The study concluded that TiZrN coating showed excellent corrosion-resistant nature than bare 316L SS substrates.¹⁶⁷

Moreover, oxynitride coatings have become attractive materials due to their mechanical behavior,^{168,169} corrosion resistance, and chemical stability in physiological saline. Since oxides and nitrides of titanium (TiN_xO_y) and zirconium (ZrN_xO_y) exhibit combined¹⁷⁰ properties, they have been used in various applications, including electrically switchable windows,¹⁷¹ transparent window electrodes,¹⁷² memory devices, *etc.* Also, ternary nitride coatings (TiAlN, TiCrN, and TiZrN) have enhanced corrosion resistance, hardness, oxidation resistance, and enhanced compatibility owing to their alloying effects. Similarly, Subramanian *et al.*¹⁶⁵ studied the importance of surface modification by nitrides, oxynitrides, and ternary nitrides, including TiN, TiON, and TiAlN, onto medical grade 316L SS substrates and analyzed their electrochemical behaviour using simulated body fluid solution (SBF). The results stated that the ternary nitride coating TiAlN exhibited superior corrosion protection than TiN, TiON, and titanium metallic substrates.

The all-inclusive nitride-based coating is mainly used to enhance the material properties by encouraging hemocompatibility with negligible hemolytic nature, wear and abrasion resistance properties. Importantly, TiN coatings are increasingly used as ventricular-assisted devices for cardiac patients

with heart-related disease.¹⁷³ In neurology, the researchers have been developing TiN coated electrodes implants as chronic implant devices for spinal cord injury treatment.¹⁷⁴ Other nitride-based TiON, ZrON, and TiZrN coatings reduced the metal ion leaching (Ni, Cr, Fe) for dental and orthopedic applications by corrosion resistance property.^{5,94,167} However, from our investigation, it is revealed that nanolayer thickness (<500 nm) of nanostructured nitride coatings could not exhibit superior corrosion resistance than higher thickness nitride coatings (>2 μm). Though nitride coatings exhibit a very smooth surface with hydrophilic nature, there is a possibility of bacterial invasion post-implantation due to its negligible antimicrobial properties. In addition, the nitride-based coatings failed to express bone morphogenetic proteins (BMP's) compared to pure ceramics such as metal oxide and hydroxyapatite ceramic coatings due to their superior surface hardness.

10. Bio-inspired coatings as effective bone repair

The construction of surface-modified biomaterials is a powerful approach to modify its surface by nano functionalization and biomimicry. Specifically, the topography of the material surface at micro or nanoscale environment is involved in electrochemical reaction in physiological body environment to acquire specific surfaces/interfaces interactions, post-implantation.¹⁷⁵ As we know very well, hydroxyapatite coating is an important approach for effective bone repair treatment. In addition, researchers have investigated graphene oxide-based PDA films containing BMP-2 and antibiotics for inducing antimicrobial property and bone regeneration capability.

Xie and his co-workers prepared a nanostructured GO/chitosan scaffold for effective osteoconductivity. The prepared GO/chitosan multilayer hybrid nanofilm, biomimetically mineralized by supersaturated octa calcium phosphate, formed a porous hierarchical structure, promoted cell adhesion, and proliferation.¹⁷⁶ In addition, biopolymer-like gelatin has been used to induce cartilage regeneration to repair osteochondral defects.¹⁷⁷ Han *et al.* prepared GO nanosheet coated Ti scaffold along with drug-loaded gelatin microsphere as bone regeneration application. The scaffold exhibited dual properties (antimicrobial and osseointegration properties), and it was stated that the scaffold was a suitable candidate for drug delivery and enhanced cellular adhesion.¹⁷⁸

To further improve the healing rate and biocompatibility nature of HAp, several polymers and metallic nanoparticles have been incorporated as metal-doped hydroxyapatite or polymer-HAp nanocomposite coatings. Xie *et al.*¹⁷⁹ developed BMP and silver-containing hydroxyapatite coating by an electrochemical deposition method. They electrostatically immobilized BMP amidst heparin and chitosan and successfully demonstrated the release of silver and BMP in a sustainable way, which was confirmed by the *in vivo* model (Fig. 23a–d). From histological analysis, new bone tissue formation was observed from the implant surface to host cells with no silver toxicity on BMP/CS/HAp–Ti implant, which indicated the

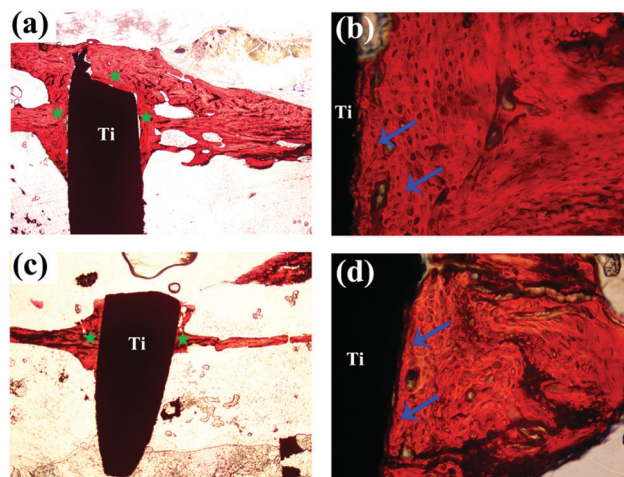


Fig. 23 Histological view of Ti coated implants with Van Gieson's picric acid–fuchsin staining, at 12 weeks of post-implantation. (a) BMP/CS/Ag/HAp–Ti, (b) enlarged image of (a), (c) BMP/Ag/HAp–Ti and (d) enlarged image of (c). Replicated with permission from ref. 179. Copyright 2014, American Chemical Society.

superior osteogenic nature (Fig. 23b). Conversely, the less osteogenic response was obtained in BMP/HAp–Ti implant (Fig. 23c). In addition, 10% of BMP was released on the first day, whereas 56% of BMP was released on the 25th day from the coating surface and subsequently improved the bone regeneration process.¹⁷⁹ Similarly, Kim *et al.* functionalized BMP using a chemical cross-linking reaction and achieved 69% release efficiency in one day.¹⁸⁰ Macdonald *et al.* emphasized the drug-eluting coating for inducing growth factors for bone regeneration.¹⁸¹ They functionalized BMP in layer-by-layer polyelectrolyte (multilayer) film by self-assembly method and observed 10 μg of BMP release for the first 2 weeks and less than 1% of BMP was examined in the first 3 h.

Polydopamine (PDA) contains amino and catechol groups that mimic the structural resemblance of mussel adhesive proteins and exhibit multiple reaction sites for growth factor immobilization. Xie *et al.* formed BMP-loaded polydopamine–HAp films by pulse electrochemical driven layer-by-layer assembly technique for effective bone regeneration using the *in vivo* model (Fig. 24a–d). They observed more sustainable release efficacy of BMP-2 protein in HA–PDA film (60%) rather than PDA films alone (96%) at 25 days of incubation for effective bone regeneration.¹⁸² Multilayer BMP–(HA–PDA) films were inserted into Sprague–Dawley (SD) rats for osteoconductivity evaluation. After incubation, the histological view represented that BC (bone to sample contact) and BA (bone area ratio) of (HA–PDA) 10–Ti are higher than pure Ti and PDA films and it indicated that HA incorporated films effectively improved osteoconductivity. Conversely, no new bone formation was observed onto PDA–HA and pure Ti bars scaffolds after 12 weeks of implantation.

Conductive polymers have also received considerable attention to protect tissues and cells from ROS scavenging. Polypyrrole–polydopamine–hydroxyapatite (PPy–PDA–HA) nanoparticle film was prepared through the layer-by-layer pulse electrodeposition

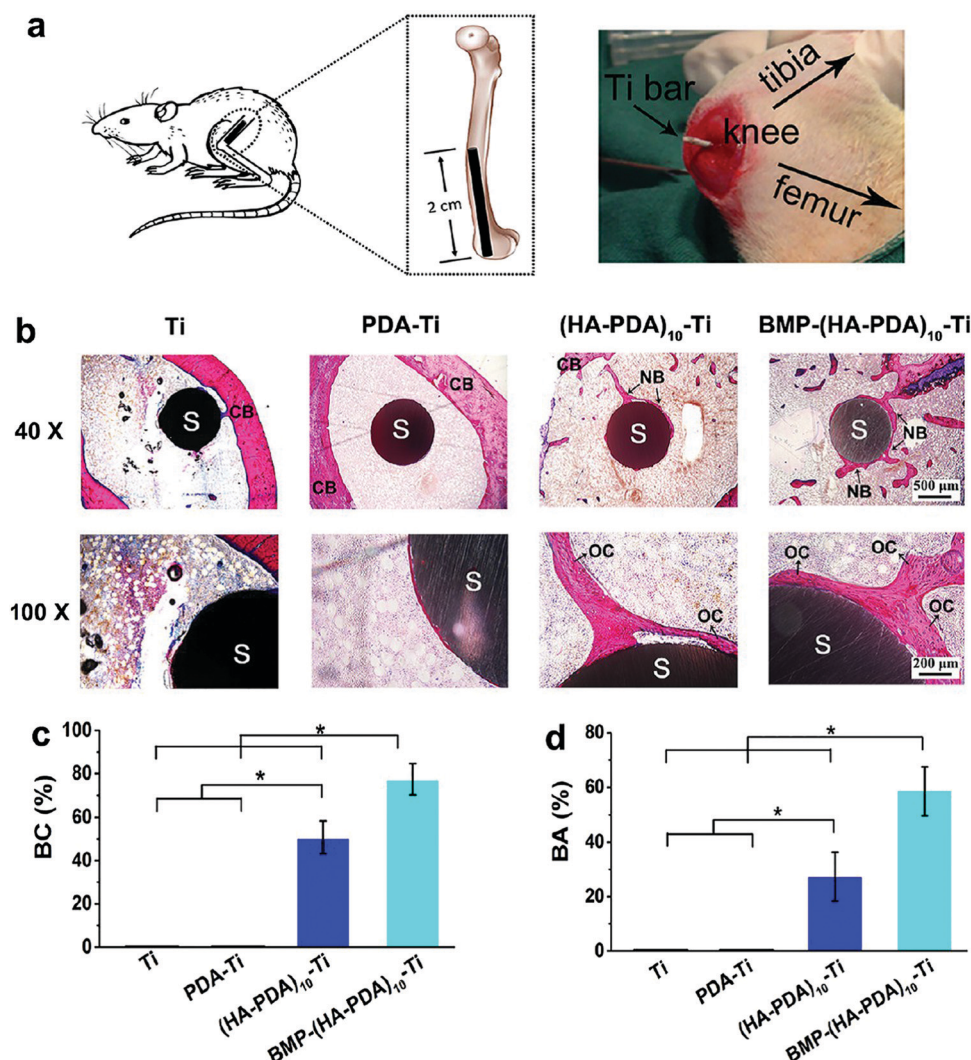


Fig. 24 (a) Schematic representation of the implant insertion site. (b) Histological view of implants stained by basic fuchsin and methylene blue after 12 weeks of implantation. (c) Bone to implant contact (d) bone area ratio analysis by histomorphometry. S – sample; NB – new bone; CB – cortical bone; OC – osteocytes. Reproduced with permission from ref. 182. Copyright 2016, American Chemical Society.

method.¹⁸³ The sustainable release of Ca^{2+} ions from PPy-PDA-HA film was obtained to the localized site and allowed more Ca^{2+} ions into the cells, and simultaneously, an electric field was applied to PPy, which enhanced the osteogenic protein expression pattern. The biocompatibility of prepared films was analyzed by bone marrow-derived stem cells to determine the electroactivity nature of PPy, cell affinity ability PDA, and osteoconductivity behavior of HA (Fig. 25a-h). Enhanced BMSCs cells observed in non-ES PDA films indicated its better cell anchorage capability. While applying different voltages (300, 600, 900 mV) of ES to PDA and PPy-PDA films, increased cell spreading and proliferation with osteogenic gene expression were observed on PPy-PDA compared to PDA film alone electro-active nature of PPy. In addition, enhanced cell proliferation and differentiation were obtained in PPy-PDA-HA films with 300 mV ES; cell proliferation was inhibited at 900 mV ES due to cellular damage. Shi *et al.* fabricated 5% PPy with 95% poly(L-lactic) acid (PLLA) to promote cytokine electrical

stimulation secretion. The findings stated that electrically stimulated PPy/PLLA polymeric blends significantly enhanced cytokine secretion for several days even after applying electrical stimulation (ES) than non-ES control.¹⁸⁴ PDA decorated bovine serum albumin containing HAP nanoparticle films were synthesized through the oxidative polymerization method by Wang and co-workers.¹⁸⁵ After implantation, no new bone growth was observed on the pristine Ti surface. New bone was observed on nano-HA-containing films. The encapsulated BMP-2 protein into BSA nanoparticles could promote better proliferation and adhesion of bone marrow stromal cells. Similarly, the same group has prepared mussel-inspired poly-dopamine nanoparticles containing HAP nanorod film by an oxidative self-polymerization process with surface-immobilized BMP-2 proteins. The *in vivo* studies clearly exhibited that the BMP-2 protein enhanced the formation of new bone tissues compared to control PDA-HAP films.¹⁸⁶ Although BMP-loaded PDA showed effective osteointegration, PDA-loaded BMP-2

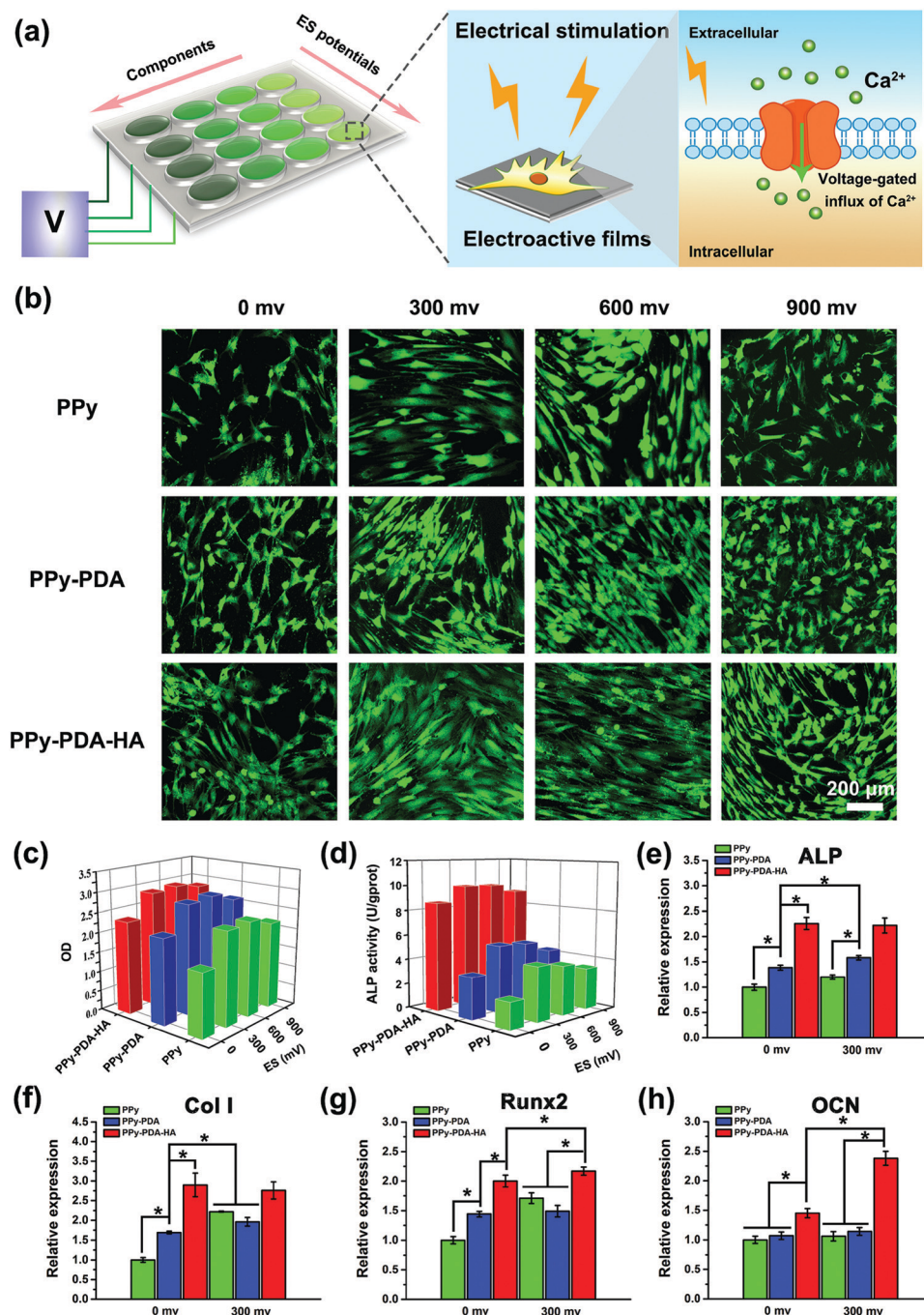


Fig. 25 Stimulation of BMSCs on various surfaces with different components and ES. (a) Schematic diagram showing ES and conductive polymers activate Ca^{2+} channel in the cell membrane by EC, thereby extracellular Ca^{2+} can easily enter into the cell and stimulate Ca^{2+} transduction pathway. (b) Confocal microscope images; (c) proliferation and (d) differentiation on different films with various EC potentials. (e–h) Gene expression of BMSCs presence and absence of ES. Reprinted with permission from ref. 183. Copyright 2019, Wiley.

might undergo burst release in a short period of time, and these proteins exhibit fragile nature that causes a short half-life period.

In order to protect the BMP-2 effectively, a protective carrier needs to be formed. Recently, a metal–organic framework has attracted tremendous advantages as nanocarriers due to its large surface area, high porosity, and ease of tenability of organic ligands.^{187,188} Sun and co-workers reviewed the

importance of metal–organic frameworks (MOF) for effective structural stability and biofunctionality.¹⁸⁷ They described that the MOFs could be effectively encapsulated with biological entities such as enzymes, DNA, microorganisms, and virus due to their ultrahigh loading capacity. They strongly suggested that biological entity preservation by MOF might bring technical innovation for biomedical and industrial engineering applications. Jiang *et al.*¹⁸⁹ designed gelatin-based 3D printed

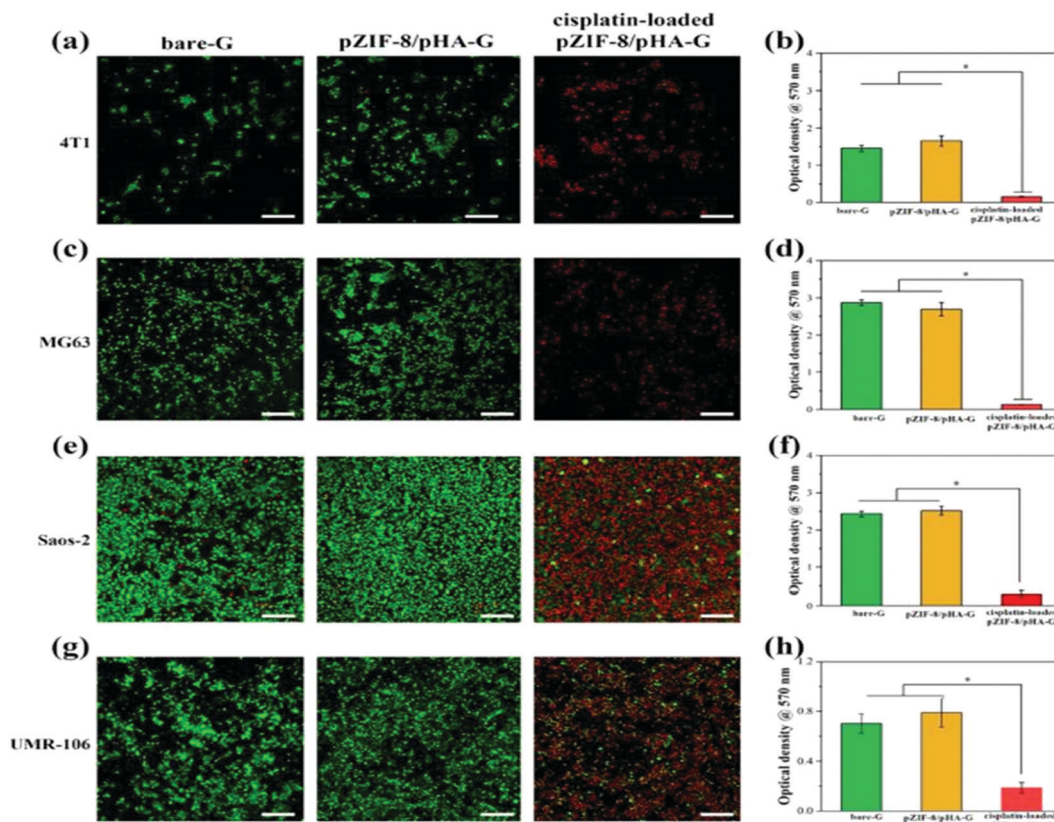


Fig. 26 *In vitro* antitumor efficacy study of scaffold material against different types of cancer cells by live/dead cell analysis. (a) 4T1 (c) MG-63 cells (e) Saos-2 cells (g) UMR-106 cells. (b, d, f and h) – MTT assay after 3 days of tumor cell culture treated with a prepared scaffold. Copied from the permission of ref. 189. Copyright 2021, Elsevier.

implants by PDA hybridized imidazole zeolitic framework with decorated HAP particles for anti-tumor therapy treatment. *In vitro* live/dead cell analysis and MTT assay of various types of cancer cells against prepared scaffold determined that cisplatin-pZIF-8/pHA-G scaffold effectively killed all types of cancer cells (red fluorescence) by inducing tumor cell apoptosis (Fig. 26a–h) than other scaffolds. In addition, BMP-2-loaded pZIF-8/pHA-G could produce new bone formation after 12 weeks of implantation by mice model. Hence, HAP based nanocomposite coatings/scaffolds are used for effective bone repair by the sustainable release of bone morphogenetic protein. In addition, electric stimulation on scaffold material could accelerate the bone healing process.

11. Summary and future perspectives

Surface tailoring of implant materials is a promising technique to enhance the durability of the implant material. In surface modification, various coatings techniques, namely, sol-gel method, PVD, CVD, spin coating, electrochemical deposition, pulsed electrodeposition, *etc.*, are conventionally employed. Metal nitrides, oxides, ternary and multicomponent coatings prepared by magnetron sputtering show excellent wear resistance and corrosion resistance with biocompatible properties.

Ceramic coatings such as HAP, ZrO₂, YSZ, and MgSZ prepared by plasma spray and EBPVD method exhibit better corrosion protection, mechanical strength, and biocompatible properties. Moreover, coatings of ZrO₂ and its allotropes (m-ZrO₂, t-ZrO₂, c-ZrO₂) exhibit better corrosion resistance properties in biological fluid containing H₂O₂, LA, and BSA proteins.

Antibiotic-loaded polymeric coatings show sustainable release of drugs that drastically arrest the growth of pathogenic bacteria. Further, photocatalytic coatings using TiO₂ and ZnO effectively kill surface adhered bacteria. Metal doped HAP and its nanocomposite coatings act as good candidates in antimicrobial, corrosion resistance, mechanical strength, anticancer activity, and biocompatible perspectives than HAP coating alone. In addition to these, bioactive glass coatings have evolved with superior wear resistance and improved biocompatible nature. Polymer-based drug-eluting and growth promoter encapsulated polymers coatings/hybrid scaffolds significantly enhance antimicrobial and rate of wound healing properties. Hence, from the overall review, it is concluded that surface tailoring is a boon to metallic implants combining multiple properties on the surface through surface coatings for better durability.

The huge demand for improved bone-bonding, implant's osseointegration, antibacterial performance, corrosion resistance, and wear resistance with biocompatible character imposes an

urgent need for surface tailoring of metallic implants with high hardness, better substrate adhesion, resistance to crack formation, low friction coefficient, absence of toxic reaction with surrounding cells and tissues, and good cell and protein adsorption. In this view, it is mentioned that bioactive coatings are actively involved in enhancing biological fixation amidst metal implants and bone despite the poor tribological and mechanical properties of some ceramics, *i.e.*, hydroxyapatite, tricalcium phosphate, and Al_2O_3 . On the other hand, the ceramic nanocomposite coatings such as hydroxyapatite-metal oxide nanocomposite coatings, zirconia allotrope coatings, magnesia stabilized zirconia (MgSZ), and zinc oxide stabilized zirconia (ZnSZ) coatings have been employed to enhance tribological, mechanical, antibacterial, biocompatible, and bioactivity properties, which are important considerations for clinical applications of implants. In order to fulfill these requirements, ceramic coatings with a unique combination of properties need to be produced. Also, the additive manufacturing process helps in manufacturing patient-specific complex 3D ceramic structures with different shapes, sizes, and designs that can be very helpful for orthopedic and dental implants. Hence, the bioceramic coatings could be a better choice, and this field is still in progress, aiming to develop ideal implants by various manufacturing processes to find enhanced performance and promote the expansion of these bioceramic coatings on a global level.

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

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