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A mini-review on calcium hydroxyapatite composites for antibacterial applications: from inorganic to bioactive organic systems

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Bone regeneration of injured bones remains a significant clinical challenge due to persistent inflammation and microbial colonisation. Recent advances in biomaterials, such as calcium hydroxyapatite (CHA; $Ca_{10}(PO_4)_6(OH)_2$) composites have enabled the fabrication of functionally and biologically optimised materials. CHA has been used as a scaffold for bone tissue engineering, bone fillers, and bioactive coatings. However, clinical complications, including implant-associated infections, have raised concerns among researchers. Consequently, functionalisation of artificial bone composites is necessary to promote bone regeneration and repair. Notably, antibacterial activity plays a critical role in the treatment and prevention of infected bone defects. Therefore, offering antimicrobial properties to these materials is needed. Therefore, current research is focusing on the incorporation of CHA synthetic materials and compounds that possess antimicrobial properties to act as antibacterial agents. In this context, this article provides an extensive review of the recent advances in CHA composites with antibacterial properties for their potential use in several biomedical applications.

Keywords: calcium hydroxyapatite, composites, bioactivity, antibacterial

INTRODUCTION

Regenerative medicine struggles with critical challenges in bone regeneration and repair. Whether they are caused by bone diseases, fractures, or traumatic injuries, innovative solutions are needed to repair damaged bone tissue. The autologous bone graft is considered as the gold standard for the treatment of these issues [1]. However, this procedure has drawbacks, including restricted donor sites and morbidity, sever pain, increased operation time and potential for donor site infection [2–4]. Therefore, synthetic biomaterials are an ideal option for overcoming these limitations. Bone tissue engineering is considered a promising approach to address these demands through the development of novel strategies and efficient biomaterials for bone regeneration that could remodel the present criterion of tissue defect repair [5–7]. In the early 20th century, the innovation of antibiotics, vaccines, and sterilisation techniques directed a new era of medicine. Regenerative medicine appeared in the early of 1970s when scientists began to explore the feasibility of using biomaterials and cells to regenerate damaged tissue [8]. In the 1980s, the development of more sophisticated scaffolds that can support cell growth and boost tissue regeneration was enabled by improvements in biomaterials and tissue engineering techniques. This allows advances in bone tissue engineering that target the replacement, regeneration, or repair of damaged bone tissue [9].

Moreover, bacterial infections are the most significant complications associated with bone tissue regeneration and surgical implantation in orthopaedic and dentistry. Treatment of infected

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orthopaedic devices and dental implants can be painful, distressing, and the implant is often lost [10]. *Staphylococcus aureus* (*S. aureus*) is reported to be the most common bacterium responsible for infections of surgical sites in orthopaedic implants [11, 12]. 70% of infections related to orthopaedic implants are caused by *S. aureus*, while additional 8% are attributed to *Pseudomonas aeruginosa* (*P. aeruginosa*) [13]. An implant produced from a foreign synthetic biomaterial has a potential site for microbial attachment in the patient body. Decreasing the level of bacterial/implant adhesion is a significant factor, due to the development of implant-associated infections caused by the attachment of micro-organisms to the surface and the formation of a biofilm. If infection occurs, the process of tissue healing might be impaired, and if not treated, it could result in chronic infection, leading to bone necrosis and extending to adjacent soft tissues [14–17]. The essential strategies in clinical practice to impede or fight susceptible infections are mainly based on antibiotics, such as ciprofloxacin, tetracycline and gentamicin [18, 19]. Systemic delivery of antibiotics can be inefficient because of the low drug concentration and potential toxicity at the infected site [20]. Alternatively, grafts loaded with antibiotics have been employed to allow the controlled release of therapeutics and reduce possible side effects [21]. However, the main concern is the high risk of antibiotic resistance due to the overuse or misuse of antibiotics, which presents a hazard to global health. Such an issue requires the investigation and development of non-antibiotic materials with efficacy for bone regeneration as well as to be able to provide antibacterial properties to hinder growth of bacteria and decrease their adhesion.

Calcium hydroxyapatite (CHA; $Ca_{10}(PO_4)_6(OH)_2$) is a well-known biomaterial with outstanding properties, including biocompatibility, bioactivity and osteoconductivity. It is widely used in bone regeneration and replacement, and has numerous applications, including the repair of hard and soft tissues [22, 23]. CHA is a calcium phosphate mineral which is the main inorganic constituent of human bones and teeth. Bones contain inorganic matter of 70% that corresponds to CHA, 10% water and 20% of organic content, primarily collagen [24, 25]. Over the past few decades, CHA has attracted great attention as a bone substitute biomaterial for bone tissue repair due to it great biocompatibility and non-toxicity [26–28]. CHA is also sufficient for regeneration of soft tissues [29, 30].

CHA has a hexagonal structure with Ca^{2+} and PO_4^{3-} groups arranged on columns of OH^- groups, with the possibility of OH^- and PO_4^{3-} replacement by anionic groups, and Ca^{2+} by metal ions [31, 32]. Accordingly, CHA can be doped with various elements that enhance its properties, such as osteoconductivity (Cu) [33, 34], cell viability (Co) [35], and antibacterial activity (Ag) [36, 37]. Moreover, it can be incorporated with diverse materials, such as collagen, graphene, and carbon allotropes, to advance its mechanical properties for the cell scaffold design [38]. Several studies have reported that CHA can activate fibroblasts and increase endothelial cell vessels, thereby supporting wound healing [39, 40]. However, there is always a possibility of infection and biofilm formation on the surface of CHA implants [41, 42]. When biomaterials are implanted in the body, they are exposed to contamination by microorganisms, including bacteria and fungi which lead to implant-associated infections (osteomyelitis). The mechanisms of infection and contamination depend on the type of microorganism [43]. The antibacterial properties of CHA composites are crucial in terms of biocompatibility because infection-associated bacteria can result in critical complications in different biomedical applications, including dental implants, orthopaedic implants, and bone grafts. These infections can induce failure of implants and prolonged hospitalisation [44]. By incorporating designated materials as antibacterial agents into CHA, the possibility of infections is reduced. Composite materials provide advantages rather than a single component system, and the combination of properties can lower the risk of infections, hence, increase their potentials in orthopedic and dentistry applications [45]. Numerous studies have indicated that the synthesis of CHA with inorganic and organic materials can be employed in biomedicine field.

This review aims to highlight developments in bone regeneration and the treatment of bone-related infections, showing recent research on hydroxyapatite and its composites with inorganic and organic materials and essential oils and their potential as antibacterial agents for use in biomedical applications.

INORGANIC CHA COMPOSITES

The effects of cation substitution on the antibacterial and other bioproperties of different phosphates, including CHA, have been summarised in a recent review article [46]. It was demonstrated that cationic substitutions emerged as a powerful tool for improving the chemical, physical and biological properties of potential biomaterials. The samples substituted with Li^+, Na^+ and K^+ ions showed excellent biocompatibility and osteointegration properties with additional antidepressant and better bone formation functions. Interestingly, CHA substituted with sodium demonstrated improved mechanical stability compared to pure hydroxyapatite (see Fig. 1) [47].

The introduction of magnesium and strontium into synthetic phosphate-based materials provided the development of novel materials for biomedical applications, including osteoregeneration with a good environment for osteoblasts [48, 49]. It is known that the biocompatibility, osteoconductivity and porous structure of coral make it a popular material for bone regeneration. In the study [50], CHA doped with osteoinductive elements (Sr, Mg and Sr-Mg) was synthesised via a hydrothermal reaction. The reaction equations for the conversion of coral to CHA and Sr/Mg-CHA are described in Eqs. 1 and 2, respectively,

$$10CaCO_3 + 6(NH_4)_2HPO_4 = Ca_{10}(PO_4)_6(OH)_2 + \\ + 10CO_2 + 12NH_3 + 8H_2O, \quad (1)$$

$$Ca_{10-x-y}(PO_4)_6(OH)_2 + xSr(NO_3)_2 + yMg(NO_3)_2 = \\ Ca_{10-x-y}Sr_xMg_y(PO_4)_6(OH)_2 + (x+y)Ca(NO_3)_2, \quad (2)$$

where x and y represent the moles of Sr and Mg doping, respectively.

Figure 2a shows the final Sr/Mg-CHA after washing and drying. SEM with EDX (Fig. 2b) illustrates the morphology and elemental distribution of the coral, Sr-CHA, Mg-CHA and Sr-Mg-CHA.

Transition-metal substituents, especially silver, manganese, copper and zinc, phosphate materials, are probably the most promising ones for future clinical applications to enhance different therapeutic multifunctional properties. These phosphate nanostructured biomaterials with a high biocompatibility and an increased antibacterial behaviour are the best candidates for applications in many biomedical fields, such as bone repair and tissue engineering, drug/gene delivery, magnetic targeting and hyperthermia treatment for cancer, bioimaging and theranostics. For example, CHA substituted with manganese and other phosphates were synthesised by a variety of preparation techniques and widely characterised [51–54]. Just a decade ago, based on the extraction assay for the cytotoxicity test, Mn-HA was announced to osteoblasts, and it was confirmed in later studies [55–57]. The original crystalline particles of Mn-HA were remodelled in the SBF solution, creating carbonated hydroxyapatite, and biological activity studies demonstrated that the presence of manganese in hydroxyapatite improved the biological activity of the biomaterial.

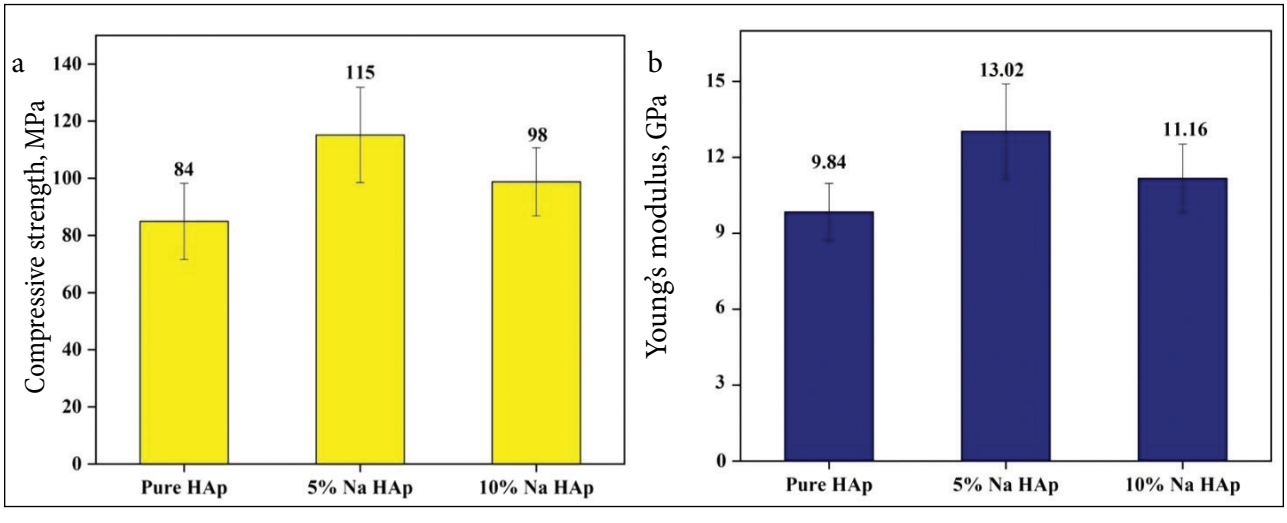

Fig. 1. Mechanical properties of pure CHA, 5% Na-CHA and 10% Na-CHA. (a) Compressive strength (MPa) and (b) Young's modulus (MPa) [47]

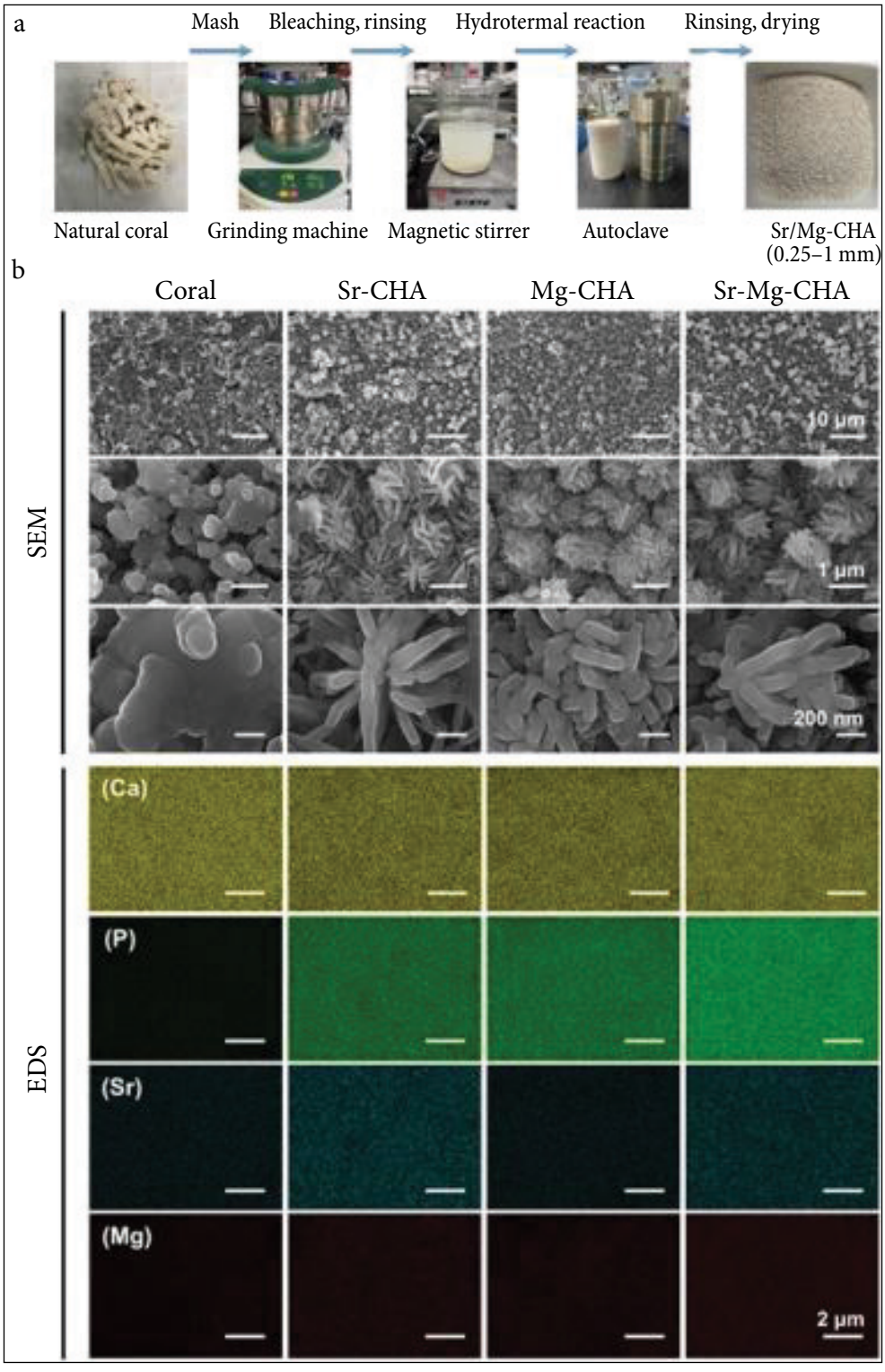

Fig. 2. Materials preparation, morphology and composition of the coral, Sr-CHA, Mg-CHA and Sr-Mg-CHA. (a) Preparation process. (b) SEM images and elemental mapping [50]

Different properties were investigated for CHA substituted with copper [58–60]. The biomedical properties of these Cu-substituted different phosphates have also been investigated [61–64]. Copper-substituted biphasic calcium phosphate ceramics have shown biocompatibility with bone marrow cells [61]. The good adherence of the Cu-doped biphasic calcium phosphate ceramic samples is highlighted in Fig. 3. Zinc-based degradable biomaterials have recently appeared due to their biocompatibility, biodegradability, and pro-regenerative properties [65–67]. CHA doped with Zn showed non-toxic

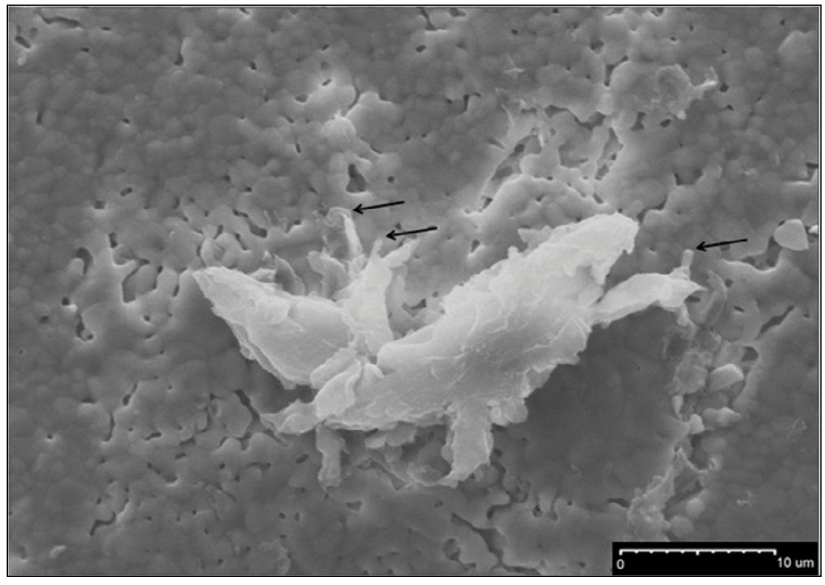

Fig. 3. Bone marrow adherent cell (black arrows) after 8 days of culture on a Cu-doped biphasic calcium phosphate ceramic disk [61]

characteristics with enhanced MG-63 cell proliferation activity. These results suggest that 1 mol% Zn-CHA scaffolds may have an enormous potential for bone repair and regeneration [68, 69]. These porous Zn-CHA scaffolds exhibit excellent antibacterial and bactericidal properties [69–71]. The findings of Ref. [72] demonstrate that co-doping CHA with Si and Zn synergistically enhances mechanical integrity, corrosion resistance and biocompatibility, making 5Zn/HA/4Si a strong candidate for next-generation implant coatings.

Additionally, mesoporous CHA co-doped with both zinc and silver exhibited a remarkably greater antibacterial activity against several Gram-negative and Gram-positive bacteria than undoped CHA. These nanocomposites are concluded to be a promising material also for water purification [73].

Cytotoxicity and antimicrobial effects have been observed in Ag-doped CHA prepared using different techniques [74, 75]. The effect of silver-doped CP nanoparticles on the viability of monocytes and T-cells is shown in Fig. 4. The authors concluded

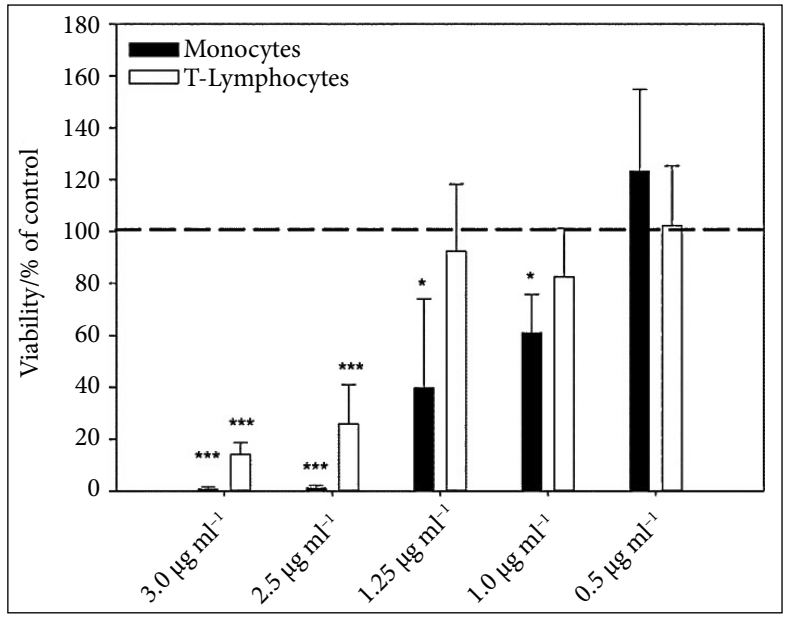

Fig. 4. Effect of silver-doped calcium phosphate nanoparticles on the viability of monocytes and T-lymphocytes cells [74]

that these types of biomaterials with great bactericidal effects potentially could be applied in tissue engineering or dentistry. Currently, the properties of Ag-CHA are being extensively investigated for biomedical applications [76–81]. It was shown that a minor amount of silver dopant cannot alter the microstructure, stability and crystallinity of the CHA structure and has a significant effect on new bone formation and bone remodelling processes.

Lanthanide-substituted compounds with very interesting biological properties have also been developed and investigated for biomedical applications [82–88]. These phosphate-based biomaterials, especially nanostructured ones, show a high biocompatibility and an enhanced antibacterial behaviour. Bioactive glasses that release calcium and silicate ions have been reported to boost the growth of fibroblasts, collagen production, and angiogenesis [89–92]. Moreover, they possess antibacterial properties on their own and have been investigated in combination with ceramic materials such as CHA.

Graphene and their derivative including graphene oxide (GO) and reduced GO (rGO) due to their exceptional physical and chemical properties have outstanding potential to be used in biomedicine, like cancer therapy, drug delivery, and tissue engineering scaffolds [93, 94]. The structures of graphene (G), graphene oxide (GO) and reduced graphene oxide (rGO) are presented in Fig. 5.

For instance, rGO provides a great biological activity, such as enhancing osteoblastic differentiation and antibacterial activity [95, 96]. A recent study integrated graphene and Zn-doped CHA and rGO to form a nanocomposite material. The antibacterial activity of the composites was significantly increased by Zn doping. Moreover, rGO effectively influenced the development of the antibacterial activity of nanoparticles [97]. Mesoporous silica nanoparticles also represent a versatile platform in biomedicine thanks to their unique structural properties and functional versatility [98].

Thus, numerous articles have concluded that the cationically substituted phosphates are irreplaceable candidates for applications in many biomedical fields, such as bone repair, tissue engineering, drug and gene delivery, magnetic targeting and hyperthermia treatment for cancer, bioimaging and theranostics. These studies have improved bone tissue engineering and regenerative medicine by enhancing our understanding of doped CHA and revealing new ways to overcome the problems associated with bone repair material.

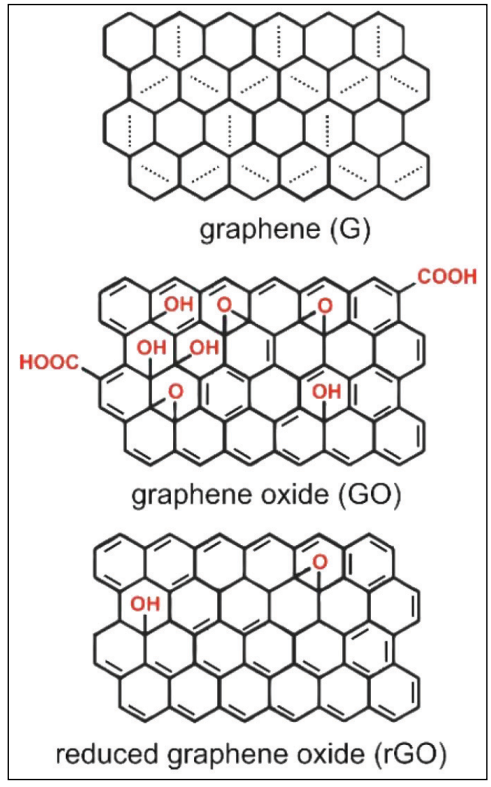

Fig. 5. Structures of graphene (G), graphene oxide (GO) and reduced graphene oxide (rGO) [94]

ORGANIC CHA COMPOSITES

The essential structural protein of the extracellular matrix is collagen, and it provides the strength and flexibility to connective tissues. Its significance in wound healing is due to its fibrillar structure, which helps fibroblast cells attach, move and proliferate [76]. Therefore, biocomposites of CHA-collagen have attracted research interest in recent years. A recent study presented composites of CHA/collagen with variation in a component, and these composites exhibited a good antimicrobial activity against several bacterial and fungal strains, indicating their potential in medical applications [99]. Recently, composite materials fabricated by combining apatite crystals with polymers from natural or synthetic sources have captured a great attention because of their resemblance with the natural extracellular matrix [100–102]. Particularly, CHA/collagen-based composites have been extensively investigated by researchers [103]. Scaffolds of CHA with a grid-like microstructure were prepared using a FFP printer, as illustrated in Fig. 6a. As shown in Fig. 6b, four groups

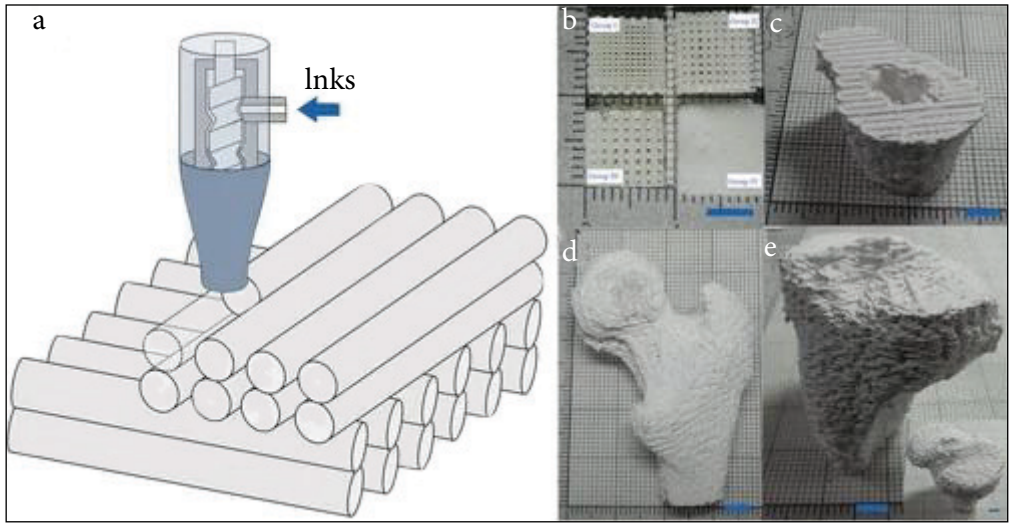

Fig. 6. (a) Schematic of the robocasting fabrication process. (b) Gross view of the surface morphology of the experimental collagen/hydroxyapatite (CHA) composite scaffolds. The printed scaffolds had a grid-like microstructure with pore widths of 400 μm and rod widths of 300 μm (group I), 600 μm (group II), or 900 μm (group III). Group IV was nonprinted scaffolds. Gross views of the structure of example printed complicated scaffolds: bone with marrow cavity (c), femoral head (d) and tibial plateau (e). Scale bar: 5 mm [103]

of CHA scaffolds were produced using robocasting printing. High-resolution SEM images showed that both printed and nonprinted scaffolds had a relatively smooth surface and a platelike crystal internal microstructure, similar to cancellous bone.

However, the high cost of collagen molecules minimises their use in the biomedical applications.

Another famous type of biocomposites is chitosan-based composite, which is widely used in wound healing and tissue engineering applications [104, 105]. Chitosan displays biocompatibility and antibacterial activity. Therefore, it is considered a potential candidate in dentistry [106, 107]. Chitosan and hydroxyapatite 3D scaffolds/composites were prepared with a sustainable process, with a dissolution-precipitation mechanism [108]. Different reaction times were considered. The morphology of the scaffolds was studied and a high level of porosity was observed (Fig. 7). CHA/chitosan composites presented antibacterial properties, especially towards Gram-positive bacteria.

According to the World Health Organization's classification of essential medicines, bone infections such as osteomyelitis are most often treated using the antibiotic gentamicin, because of its low toxicity and wide range of Gram-positive and Gram-negative bacteria [109]. In a later study, CHA containing chitosan was loaded with gentamicin. The synthesised composites showed potential antibacterial activity against *S. aureus*, *E. coli*, *P. aeruginosa* and *K. pneumoniae*, which suggests their effect for the treatment of bone infection-causing bacteria [110].

At present, composite materials formed by biopolymers and inorganic materials have enhanced biological performance. Thus, they can replace autologous grafts treatments and, besides, the biopolymer or the matrix of inorganic or both can be used as drug systems with a controlled supply to avoid infections and pain [111]. Alginate (ALG) is a candidate biopolymer that can fulfil these objectives due to its biocompatibility, biodegradability and low toxicity. It is non-immunogenic effects and negatively charged groups, namely, carboxylates, where biogenic hydroxyapatite could be deposited in nu-

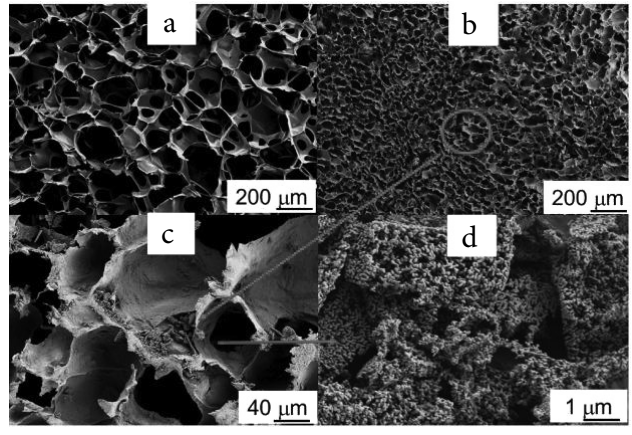

Fig. 7. SEM images of (a) chitosan sample, (b) chitosan/CHA composite sample, (c, d) chitosan/CHA composite sample with higher magnification [108]

cleation sites [112]. Although alginate is a popular biocompatible material, its low mechanical strength makes it inadequate to keep a well-defined form for suitable bioactive material–tissue interactions, which result from swelling [113]. To improve the biological properties of ALG toward a broad-spectrum bacterium, combining it with other polymers such as gelatin has been universally researched [114]. In this study, CHA-containing alginate–gelatin films were prepared by the solution casting method by blending alginate (A) and gelatin (G) solutions, followed by crosslinking with calcium chloride (see Fig. 8).

Gelatin is one of the most intriguing protein-based biopolymers, which is made by gradually melting Type I collagen. In comparison to collagen, gelatin is less expensive and less complicated to synthesise. In addition, CHA/gelatin composites are more efficient than CHA/collagen in generating osteoblast reactions [115, 116]. Moreover, silk fibroin (SF) is a natural protein that is satisfactory as orthopaedic medical materials with osteogenic ability. Studies have shown that SF has a similar architecture to type II collagen, which further deposits calcium and contributes to the generation of CHA nucleation sites [117]. In this context, Mobika et al. [118] developed composites of CHA/silk fibroin/gelatin with different gelatin ratios, and the composites proposed in this work exhibited a great antimicrobial activity against Gram-positive and Gram-negative bacteria. Figure 9 presents the antibacterial activity of the CHASG composites with four different concentrations (50, 75, 100 and 125 μL) against Gram-positive (*S. aureus*) and Gram-negative (*P. aeruginosa*) bacterial strains.

Currently, several plants are economically valuable, with an estimated 700,000 species of tropical plants demonstrating medicinal properties and acting as antibacterial, antifungal, anticarcinogenic and antiviral agents [119–121]. Essential oils (EOs) are natural bioactive compounds derived from plants that have garnered over wide attention as antimicrobial agents in biomedical applications due to their safety and effective antimicrobial performance [122, 123]. Rosemary essential oil is one of the natural products with robust antibacterial and antioxidant properties. It is also known for its antimicrobial, anti-inflammatory, antitumorigenic and neuroprotective effects. Furthermore, it has therapeutic benefits on mood, memory, pain and sleep [124, 125]. Also, aromatic herbs such as peppermint, lavender, basil, oregano and thyme have been widely used in the pharmaceutical applications and the food industry because of their absolute effects on health [126, 127]. Badea et al. [128] reported research on hydroxyapatite coated with peppermint essential oil (CHA-P) (see the Table).

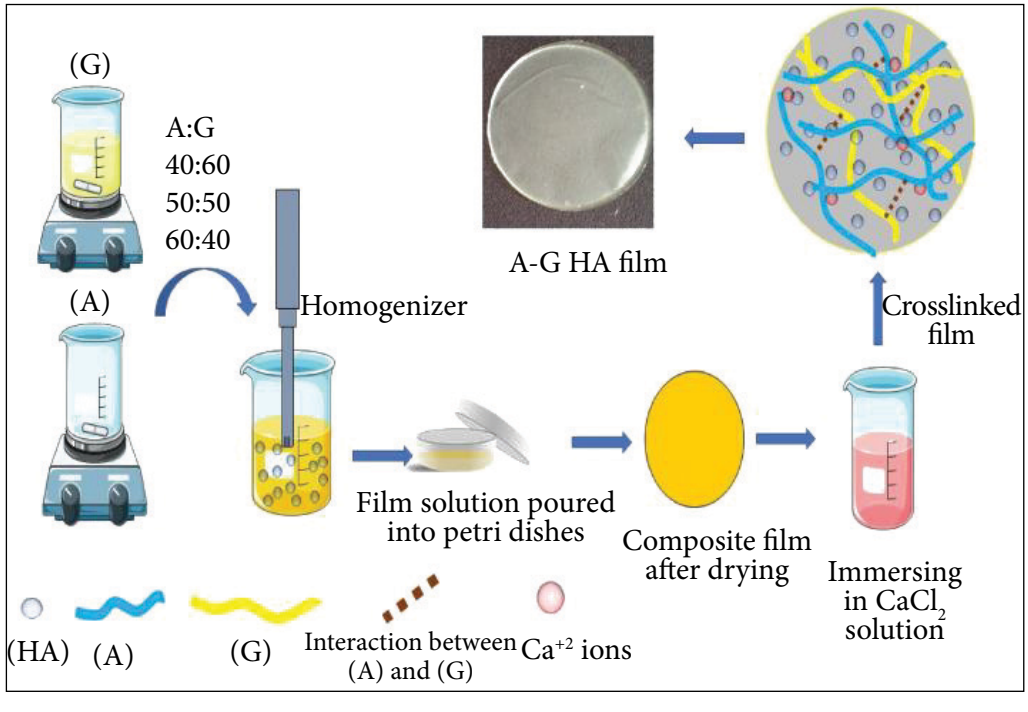

Fig. 8. Schematic illustration showing the preparation process of A-G-CHA composite film [114]

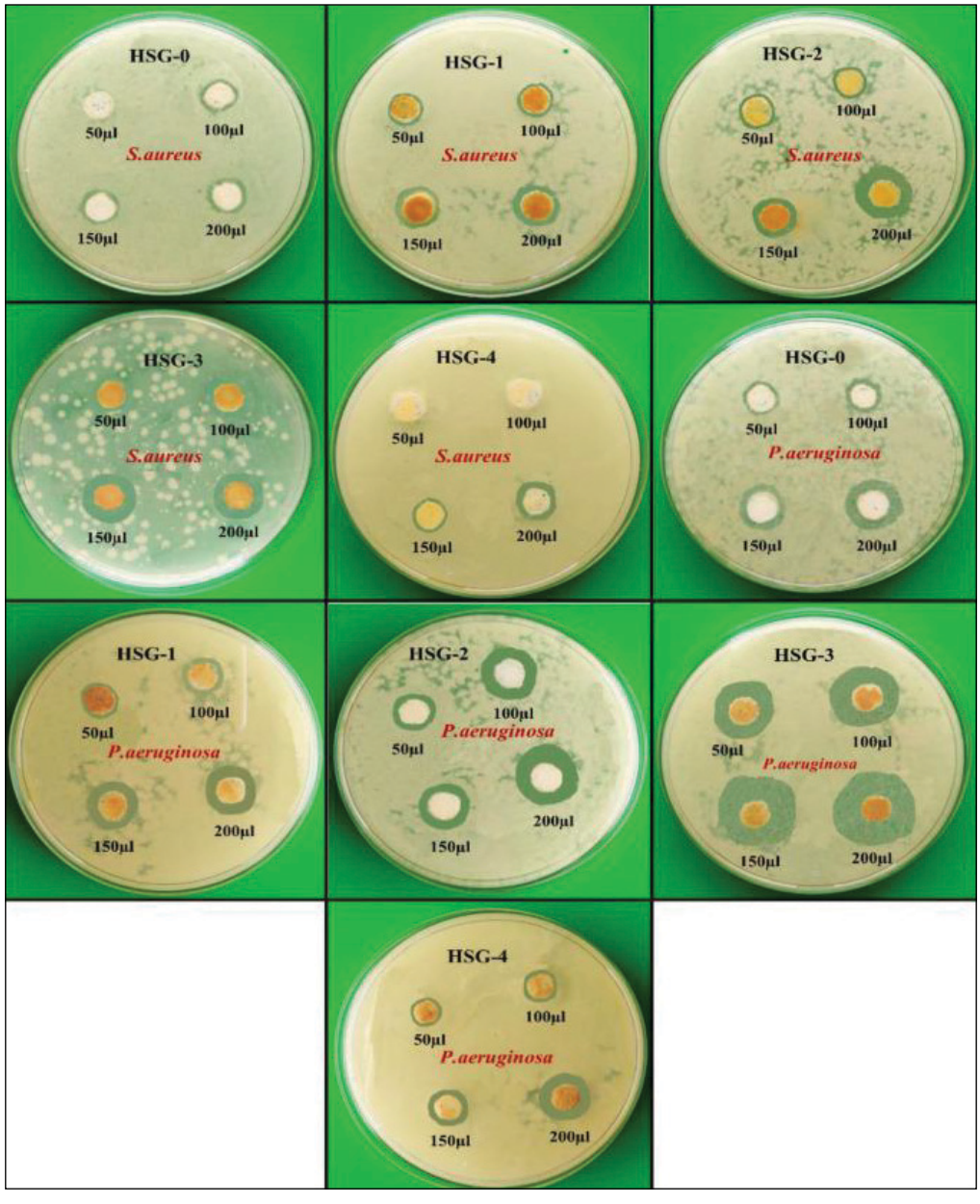

Fig. 9. Antibacterial activity of various CHASG composites on *S. aureus* and *P. aeruginosa* bacterial strain [118]

Table. **The diameters of inhibition growth zones (mm) [128]**

Microbial strains	P-EO	CHA-P	HAp	DMSO
Escherichia coli ATCC 25922	22 ± 0.2	8 ± 0.2	0 ± 0.1	0 ± 0.1
Escherichia coli C5	20 ± 0.3	7 ± 0.3	0 ± 0.1	0 ± 0.1
Pseudomonas aeruginosa ATCC 27853	10 ± 0.5	7 ± 0.5	0 ± 0.1	0 ± 0.1
Pseudomonas aeruginosa ATCC 9027	11 ± 0.3	6 ± 0.2	0 ± 0.1	0 ± 0.1
Staphylococcus aureus ATCC 25923	12 ± 0.3	10 ± 0.5	0 ± 0.1	0 ± 0.1
Staphylococcus aureus ATCC 6538	8 ± 0.2	7 ± 0.6	0 ± 0.1	0 ± 0.1
Methicillin-resistant *Staphylococcus aureus* (MRSA) 388	10 ± 0.5	0 ± 0.1	0 ± 0.1	0 ± 0.1
Enterococcus faecium DSM 13590	0 ± 0.1	0 ± 0.1	0 ± 0.1	0 ± 0.1
Candida parapsilosis ATCC 22019	0 ± 0.1	0 ± 0.1	0 ± 0.1	0 ± 0.1

The minimum inhibition concentration (MIC) and minimum bactericidal concentration (MBC) measurements determined that the antimicrobial activity of CHA-P was significantly higher than that of CHA.

In other studies, lavender and basil essential oils with hydroxyapatite were synthesised [129]. These studies indicated that lavender essential oil had a better adsorption on the surface of hydroxyapatite nanoparticles and a superior antibacterial activity against *S. aureus*, *E. coli*, and methicillin-resistant *Staphylococcus aureus* (MRSA) bacterial strains than those covered with basil essential oil. Additionally, cinnamon essential oil, which is derived from aromatic crust of the cinnamon tree, has a long history of use in medicine, especially in the treatment of skin wounds and aliments. Its strong antibacterial and anti-inflammatory properties are associated with its ingredients, including linalool, eugenol and cinnamaldehyde [130, 131]. A recent study investigated the development of a bioactive material for wound dressings by combining collagen, hydroxyapatite and essential oils from cinnamon and basil. The study concluded that incorporating a combination of cinnamon and basil greatly improved the antimicrobial efficacy compared to samples with basil essential oil [132].

Moreover, eugenol (EUG) and its isomer isoeugenol (ISOEUG) are widely known for their antimicrobial and anesthetic properties. Bioactive compounds such as EUG and ISOEUG, with antibacterial activity, could act as substitutes for antibiotics against several microbial pathogens, and hence decrease microorganisms' resistance to antibiotics. Incorporating eugenol into biomaterials, such as hydroxyapatite, could be an interesting approach for biomedical applications. In our recent study, composites of hydroxyapatite with EUG or ISOEUG were developed, and both composites exhibited antibacterial effects against Gram-positive and Gram-negative bacteria [133]. A schematic illustration of CHA/ISOEUG interactions and their possible mechanisms of antimicrobial activity are depicted in Fig. 10.

CONCLUSIONS

Composites of hydroxyapatite are a highly promising category of biomaterials for advanced bone regeneration. This combination integrates the biocompatibility and bioactivity of hydroxyapatite. When functionalised with antimicrobial agents, including metallic ions, polymers, or essential oils, these composites can trap infection colonisation and promote tissue regeneration. It is worth mentioning that for each application, there are specific challenges to be faced in the development of antibacterial composite. For example, for wound healing, the material should demonstrate antioxidant, blood clotting, and healing properties, in addition to antibacterial properties. For materials used in tissue engineering, bioactivity should be balanced with their mechanical properties. Overall, re-

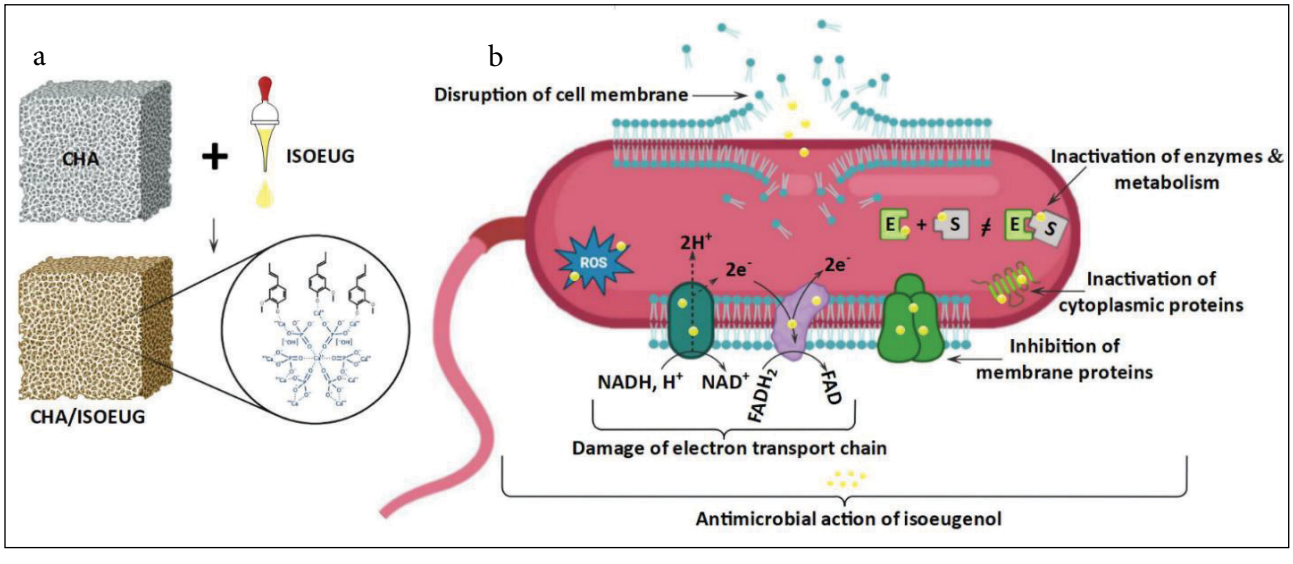

Fig. 10. Schematic illustration of CHA/ISOEUG interactions (a) and their possible mechanism of antimicrobial activity (b) [133]

searchers have been developing new antibacterial composites to achieve optimum antibacterial activity.

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TRUMPA APŽVALGA APIE KALCIO HIDROKSIAPATITO KOMPOZITUS ANTIBAKTERINIAM NAUDOJIMUI: NUO NEORGANINIŲ IKI BIOAKTYVIŲ ORGANINIŲ SISTEMŲ

S a n t r a u k a

Kalcio hidroksiapatito (CHA; $Ca_{10}(PO_4)_6(OH)_2$) ir jo kompozitų naujausi sintezės pasiekimai leido sukurti funkciškai ir biologiškai optimizuotas biomedžiagas. CHA buvo naudojama kaip pagrindas kaulinio audinio inžinerijai, kaulų užpildams ir bioaktyvioms dangoms. Tačiau klinikinėje praktikoje išlieka komplikacijų, įskaitant su implantais susijusias infekcijas, problema. Todėl, siekiant užtikrinti kaulų regeneraciją ir audinių atstatymą, būtinas dirbtinių kaulų kompozitų funkcionalizavimas. Pažymėtina, kad antibakterinis aktyvumas vaidina labai svarbų vaidmenį gydant ir užkertant kelią infekuotiems kaulų defektams. Todėl reikia suteikti šioms medžiagoms antimikrobinių savybių. Dabartiniai tyrimai ir yra sutelkti į CHA sintetinių medžiagų ir junginių, turinčių antimikrobinių savybių, kūrimą, kad jie veiktų kaip antibakteriniai agentai. Atsižvelgiant į tai, šiame straipsnyje pateikiama išsami naujausių CHA kompozitų, turinčių antibakterinių savybių, pažangos apžvalga, siekiant juos potencialiai panaudoti įvairiose biomedicinos srityse.